MEDICAL SCIENCE
PULSE
Opole Medical School

Scientific Quarterly
January–March 2020,
Vol. 14, No. 1
e-ISSN 2544-1620

Publisher:
Opole Medical School
(PMWSZ w Opolu)

Sources of funding:
statutory activity
of the PMWSZ in Opole

Tasks: "Purchase of digital object identifiers for electronic documents; Purchase of software to manage editorial and publishing works; Purchase of anti-plagiarism programme; Linguistic correction of scientific articles in the journal; Improvement of substantive level of reviews; Dissemination of information about the journal" are financed by the Ministry of Science and Higher Education de minimis programme within the framework of "Support for scientific journals" project – contract number 147/WCN/2019/1.

EDITORIAL OFFICE:
ul. Katowicka 68,
45-060 Opole
tel. (+48) 77 442 35 46
fax (+48) 77 442 35 25
e-mail: mspjournal@wsm.opole.pl

Contact:
Deputy Editor –
Bożena Ratajczak-Olszewska
tel. (+48) 77 442 35 46
e-mail:
ratajczakb@wsm.opole.pl

The editors reserve the right to shorten and edit texts submitted.

The issue is closed: 31.03.2020

The publisher does not offer subscriptions.
The journal appears in the original electronic version on the website:
www.medicalsciencepulse.com

Editorial, graphics, composition:
Studio IMPRESO Przemysław Biliczak
45-360 Opole, ul. Plebiscytowa 82
e-mail: wydawnictwo@impreso.studio
tel. (+48) 77 550 70 50

TABLE OF CONTENTS

Prof. Donata Kurpas MD, PhD
Editor-in-Chief

Andrei Shpakou MD, PhD
Deputy Editor

Bożena Ratajczak-Olszewska MSc
Deputy Editor

Ladies and Gentlemen, Faculty, Graduates and Students of Universities, Readers and Enthusiasts of *Medical Science Pulse*!

We are pleased to announce the publication of the first issue, in 2020, of the scientific quarterly *Medical Science Pulse*. We invite our readers to cooperate with the editorial team as section editors or reviewers, submit your manuscripts and publish your text in an accessible environment.

We invite students, graduates, scientists and employees of medical universities and schools as well as other scientific and research institutions: to build your academic achievements, increase potential citations of your research, participate in the important process of popularizing science, and to publish theses in the form of a scientific article.

Medical Science Pulse offers: international reach, Open Access to ensure wide reach to readers, short time to publication, high editorial and reviewing standards, high language quality provided by native English speakers, publishing free of any charges.

The constantly improving quality of research articles, increasing internationalisation and the dynamic growth of the journal allows it to meet the professional assessment criteria assessed by health scientists and medical experts. Last year Medical Science Pulse was positively evaluated by experts in a competition by the Minister of Science and Higher Education under the "Support for scientific journals" de minimis programme and awarded 20 points.

Tasks: "Purchase of digital object identifiers for electronic documents; Purchase of software to manage editorial and publishing works; Purchase of anti-plagiarism programme; Linguistic correction of scientific articles in the journal; Improvement of substantive level of reviews; Dissemination of information about the journal" are financed by the Ministry of Science and Higher Education de minimis programme within the framework of "Support for scientific journals" project – contract number 147/WCN/2019/1.

For the last seven years, the first issue of each calendar year has accompanied the *International Conferences Medical Science Pulse* in Opole Medical School. Originally planned for the 7 and 8 May 2020, the 7th Conference entitled *Promoting research visibility: management of Open Access data* has been rescheduled due to the COVID-19 pandemic and will now take place in May 2021 at the earliest. Invited speakers from the USA, Greece, United Kingdom, Russia, Lithuania, Belarus, Ukraine, Bulgaria and many Polish academic facilities are unanimously following quarantine measures in their home countries. The current events show the importance of academic research, methodology, sharing of knowledge and introducing reproducible results into practice.

The current COVID-19 pandemic has rapidly impacted every area of our lives and, in particular, is creating an unprecedented challenge to our health and care systems worldwide. Governments across the globe are taking numerous measures to respond to the urgent care needs of those impacted by SARS-CoV-2 virus, while at the same time trying to reduce the long-term impact on vulnerable people as much as possible. The editorial board of Medical Science Pulse recognizes the extraordinary pressures that this crisis has imposed on health and care decision-makers, but particularly on system managers and frontline staff. Our thoughts are with you all.

The science-oriented sections of the quarterly presents works on: pulmonary tuberculosis in childhood,

hypergonadotropic ovarian insufficiency in women of late reproductive age, organizational forms and methods of early diagnosis of hereditary tumors, somatic symptoms and level of anxiety and depression in self-referral patients at the emergency department, awareness of nursing staff having direct contact at professional work with antineoplastic agents, physiotherapeutic management of a patient after craniocerebral trauma in the intensive care unit, the changes in proportion and body composition of a woman practicing group fitness training, extracorporeal shock wave therapy (ESWT) in chronic low back pain: a systematic review of randomized clinical trials and an interesting opinion paper on how to write a good abstract for a biomedical paper. We hope that this section of the publication will meet the expectations of people, particularly of young researchers, who are increasingly willing to submit their manuscripts to our Quarterly.

Submit your paper:
– https://medicalsciencepulse.com/resources/html/cms/DEPOSITSMANUSCRIPT

Join our editorial team:
– http://wsm.opole.pl/3550/5690/dolacz-do-zespolu-redakcyjnego.html

e-ISSN 2544-1620

Medical Science Pulse 2020 (14) 1

Original papers

Published online: 30 Mar 2020

DOI: 10.5604/01.3001.0014.1037

PULMONARY TUBERCULOSIS IN CHILDHOOD: CLINICAL FEATURES, TREATMENT SIDE EFFECTS AND FACTORS ASSOCIATED WITH RADIOLOGIC IMPROVEMENT

Sehra Birgül Batmaz[A–C,E,F]
• ORCID: 0000-0003-1913-5346

Tokat State Hospital, Pediatric Allergy and Clinical Immunology Clinic, Tokat, Turkey

A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: Tuberculosis (TB) is a common public health problem and early diagnosis and treatment is important.

Aim of the study: The aim was to evaluate complaints and radiological features, drug side effects, changes in radiological findings after treatment, and to evaluate the factors affecting this change in patients with pulmonary TB.

Material and methods: One hundred patients with pulmonary TB were evaluated, and the following data recorded: age, gender, contact with TB patient, complaints, physical examination, tuberculin skin test, acid resistant bacillus, polymerase chain reaction and culture results, posteroanterior/lateral chest radiographs and thorax computed tomography findings at presentation and after treatment, treatment duration, and side effects. Treatment adherence and follow-up data were evaluated, and radiological findings before and after treatment were compared. In predicting radiological improvement, the effects of age, sex, duration of complaints, living in in rural/urban areas, treatment duration, treatment adherence, follow-up, and presence of cavitation were examined.

Results: Mean age was 6.0 ± 4.2 years. 66 of the patients had contact history with TB patients. The most common complaint was cough, whilst infiltration and/or mediastinal lymphadenopathy were the most common findings in radiological examination at presentation. 84 patients were scheduled a treatment program for 6 months. Improvement in radiological findings were significantly better in patients who adhered to medication and follow-up protocols. Age, sex, complaint duration, living in rural/urban areas, treatment duration and presence of cavitation were not significantly associated with radiological improvement.

Conclusions: Pulmonary TB should be considered in patients presenting with cough, even if their physical examination and chest radiographs are normal. Adherence to anti-tuberculosis treatment and follow-up were the most important factors in radiological improvement.

KEYWORDS: child, prognosis, pulmonary, radiological, tuberculosis

Background

Tuberculosis (TB) is an important health problem in developed and developing countries [1]. With a burden of disease that accounts for more than 10 million new cases per year, the annual decline in the global TB incidence rate is currently 1.5% [1]; between 2000 and 2017, the global number of TB deaths fell by 42% [2]. TB can affect anyone, but specific population groups, e.g. people living with HIV infection, health workers, and others in settings with a high risk of transmission of *Mycobacterium tuberculosis*, have a higher risk of acquiring TB infection and progressing to disease once infected. More than a million incident cases were estimated among children (aged <15 years) [3].

Over the past decade there has been a decrease of 5% in the incidence of TB in Turkey; in 2005, the total number of registered TB cases was 20,535 and the incidence rate was 29.4 per 100.000 population, which decreased to 14.6 per 100,000 population in 2017 [4].

The presence of TB in children is closely related to the prevalence of TB in adults. Therefore, it is of great importance to determine the index cases with childhood pulmonary TB source [2].

The diagnosis of childhood TB generally depends on clinically appropriate symptoms, contact history, positive tuberculin skin test (TST)/interferon-γ release assay (IGRA) result and the presence of radiological findings. Specifically, for children over 5 years old, IGRA is preferred over TST. Since the count of TB bacilli is low in primary lung TB in children, the contribution of microbiological methods for the diagnosis is limited. Microbiological methods used for diagnosis include direct smear, molecular techniques, and TB bacterial cultures [5].

Posteroanterior and lateral chest radiographs, which are the first imaging modalities in the diagnosis of pulmonary TB, have been reported to be normal in 25-40% of cases. Thorax computed tomography (CT) can be useful in patients with normal posteroanterior and lateral chest X-rays [3].

The goals of children's follow-up during TB medication are, in order of importance, to ensure compliance with treatment, monitoring of drug side effects, and evaluation of clinical, radiological and microbiological response [4].

Aim of the study

Our aim was to evaluate the complaints and radiological features, drug side effects, changes in radiological findings after treatment, and to evaluate the factors affecting this change in patients with pulmonary TB.

Material and methods

Study design

We retrospectively evaluated 100 patients who were diagnosed with childhood pulmonary TB at the Pediatric Infectious Diseases Clinic of the Health Sciences University Ankara Sami Ulus Maternity, Child Health and Diseases Training and Research Hospital. We evaluated data recorded both during treatment, and 2 months post treatment, in order to determine the level of remission and potential drug side effects. No exclusion criteria were utilized.

Data sources

The diagnosis of pulmonary TB was confirmed by the history, clinical, radiological and/or microbiological findings. Recorded measures included: patients' age, gender, place of residence, whether there was contact with adult patients with TB, symptoms at admission, duration of complaints between the time of the first complaints and the time of admission to our department, respiratory system examination findings, tuberculin skin test (TCT) results, acid-resistant bacillus (ARB) in fasting gastric juice and/or sputum, polymerase chain reaction (PCR) (TB AMPLICOR 1994; Roche Diagnostic Systems, Inc., Branchburg, N.J.), and Löwenstein-Jensen (LJ) (Salubris, İstanbul) culture results, posteroanterior and right side chest X-ray and thorax CT findings at presentation and following treatment, index case detected by the family scan, treatment regimen, side effects, and the time of the occurrence of side effects during treatment. Patients presenting from the city center were recorded as urban areas, all others were recorded as rural.

The hemogram, serum transaminase, and uric acid levels were recorded both during and 2 months after treatment in order to determine drug side effects, with specific reference made to the timing of any incidents. Posteroanterior and lateral chest X-ray and/or thoracic CT results were recorded 2 months after the treatment was stopped. Initial radiological examinations were compared with those taken 2 months after treatment ceased, with patients being divided into 2 groups according to their remission as either complete or persistent/partial remitters.

Bioethics committee approval

The study was approved by the Ankara Sami Ulus Maternity, Child Health and Diseases Training and Research Hospital local ethics committee (24.05.2009/240).

Statistical methods

Statistical analysis was performed using SPSS for Windows 22.0 (Statistical Package of Social Sciences Inc., Chicago IL). For normally distributing data, mean and standard deviation, for non-normally distributed data median values were reported. For categorical variables, chi-square test was used for group comparisons. To identify the parameters predicting the normalization of radiological findings after treatment, logistic regression analysis was used and $p < 0.05$ was considered as significant.

Results

Participants

Files of all patients with childhood pulmonary TB during the study period (n=100) were retrospectively evaluated.

The mean age of the patients was 6.0 ± 4.2 years (2 months-16 years); 20 (20%) were 0-2 years old, 27 (27%) were 2-5 years old, 35 (34%) were 5-10 years old, and 19 (19%) were 10-16 years old. Sixty-eight of the patients were male (68%). Of the patients, 24 (24%) were from rural areas, and 76 (76%) from urban areas.

Main results

Symptoms were observed in 78 (78%) patients, 22 (22%) were asymptomatic. The most common complaint was cough (66%); this complaint was present for more than 2 weeks in 58 (87.8%) of these patients. The distribution of the patients according to their complaints is shown in Figure 1. Asymptomatic patients were as follows: 12 (54.5%) had contact history with a TB patient, 8 (36.4%) had TST positivity, and 2 (9.1%) had pathological chest radiological findings.

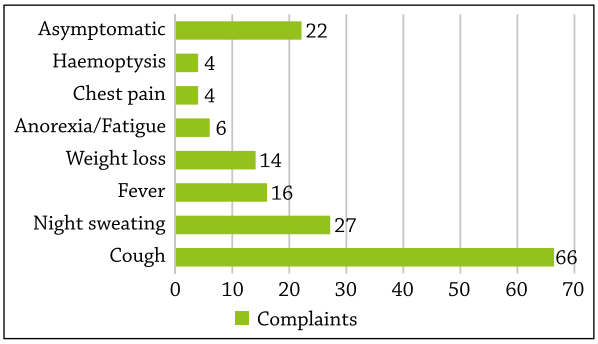

Figure 1. Patient complaints at presentation.

There was a history of contact with an adult with TB in 66 (66%) patients. Of these, 39 (59%) had contact with an adult living in the same house, and 27 (40.9%) had contact with an adult outside their home. Contact with mother and/or father occurred in 23 patients (23%), 15 patients (15%) with uncle/aunt, 23 patients (23%) with grandparents, 2 patients (2%) with schoolmates, 1 patient (1%) with brother, 1 patient with cousin (1%), and 1 patient with neighbor (1%).

Normal respiratory system examination findings were observed in 92 (92%) patients; 3 patients (3%) had rales, three (3%) had rhonchus, 1 (1%) had elongation of expirium, and 1 (1%) had decreased breath sounds.

TCT was found to be negative in 39 (39%) patients, and positive in 61 (61%) patients.

ARB in fasting gastric juice or sputum was negative in 91 (91%) patients and positive in 9 (9%) patients. Two of the 52 patients (3.8%) were found to have positive tuberculosis PCR results in fasting gastric juice or sputum. Four of the 44 patients (9.1%), whose fasting gastric juice or sputum culture results were available, had culture positivity. According to these microbiological data, 10 (10%) of the patients in our study were "definite TB cases".

The distribution of the posteroanterior, lateral chest radiographs and thorax CT findings of the patients were shown in Tab. 1.

The respiratory system examination and posteroanterior and lateral chest radiograph results were normal in 21 patients, and 5 of these patients were asymptomatic.

Eighty-four (84%) patients were planned to be treated for 6 months, 15 (15%) patients for 9 months, and 1 (1%) patient for 12 months. Seventy-eight of these patients (78%) completed the planned treatment regimen. The treatment of three patients (3%) was still ongoing at the time of writing. As 19 (19%) patients were lost to follow-up, the treatment completion data of these patients was not available.

Planned initial treatment regimens were as follows: 94 patients (94%) had INH (isoniazid) + RIF (Rifampicin) + PZA (pyrazinamide) / MZA (morphozinamide), 3 patients (3%) INH + RIF + PZA / MZA + ETB (ethambutol), 1 patient (1%) INH + RIF + MZA + prednisolone, 1 patient INH + RIF + MZA + SM (streptomycin) + prednisolone, and 1 patient and INH + RIF + PZA + SM. The daily The daily dosage was 10 mg/kg for INH, 15 mg/kg for RIF, 20 mg/kg for PZA/MZA, 25 mg/kg for ETB, 20 mg/kg for SM, and 1 mg/kg for prednisolone.

Drug side effects were reported in 23 (26.1%) of the 88 patients who came to control at least once during the treatment. Time of the occurrence of these side effects was as follows: in 14 patients at the 1st-2nd week of treatment, in 5 patients at the 4th week of the treatment, in 1 patient at the 12th week of the treatment, in 1 patient at the 32nd week of treatment, in 1 patients at the 1st and the 4th week of the treatment, and in 1 patient at the 1st week and 10th week of the treatment. Nine of the patients (39.1%) had elevated levels of transaminases, 12 (52.2%) had elevated uric acid levels, 1 (4.3%) had neutropenia, and 1 (4.3%) had gastrointestinal side effects. The treatment of 13 patients was discontinued due to adverse effects and resumed a week later after the control of biochemistry values, or the discontinuation of the treatment was extended.

Table 1. The distribution of radiological findings at presentation.

Radiologic findings	Posteroanterior chest x-ray		Lateral chest x-ray		Thorax CT	
	n	%	n	%	n	%
Infiltration	48	57.1	38	51.3	32	37.2
Mediastinal lymphadenopathy	7	8.3	7	9.4	28	32.6
Cavitation	2	2.4	-	-	2	2.3
Infiltration + Mediastinal lymphadenopathy	1	1.2	-	-	17	19.8
Pleural effusion	-	-	-	-	2	2.3
Cavitation + Mediastinal lymphadenopathy	-	-	-	-	1	1.2
Cavitation + Pleural effusion	1	1.2	-	-	-	-
Infiltration + Mediastinal lymphadenopathy + Cavitation	-	-	-	-	1	1.2
Normal	25	29.8	29	39.18	3	3.48
TOTAL	84	100	74	100	86	100

When 81 patients were evaluated at the end of the treatment period, in terms of regular follow-ups and medication adherence, 69 (85.1%) patients came to regular controls and were adherent to their medications, and 12 (14.8%) patients did not attend regular follow-ups or were not adherent to their medications.

Posteroanterior/lateral chest X-ray and/or thorax CT results of 80 patients were available after 2 months of treatment. The radiological findings of the patients whose chest X-rays and/or thorax CT results were available at the end of the treatment are shown in Tab. 2.

Table 2. The radiologic findings of the patients after treatment.

Radiologic findings	Complete remitters		Persisters/partial remitters	
	n	%	n	%
Positive findings in posteroanterior chest x-ray or thorax CT	55	67.9	26	32.1

Complete radiological improvement was found to be significantly higher in patients who were adherent with their treatment and who attended regular follow-ups compared to those who did not attend regular follow-up controls and who were non-adherent to treatment (p <0.001) (Tab. 3).

Table 3. The distribution of the radiological findings according to treatment adherence and attendance to regular follow-ups.

	Complete remitters	Persisters/ partial remitters	p
Treatment adherent and attending regular follow ups	53 (76.8%)	16 (23.2%)	<0.001
Non adherent and/or not attending regular follow-ups.	2 (16.7%)	10 (83.3%)	

Age, gender, rural/urban presentation, duration of complaints, duration of treatment, non-compliance to treatment/absence of regular controls, and the effect of cavitation on radiology were evaluated by multivariate logistic regression analysis. Age (p = 0.167), gender (p = 0.641), duration of complaints (p = 0.642), rural/urban presentation (p = 0.378), duration of treatment (p = 0.123) and presence of cavitation in radiology at presentation (p = 0.499) were not found to be significant in predicting radiological prognosis. Non-adherence to treatment or regular follow-up was associated with a poor prognosis (B = 4.221, p = 0.001).

Discussion

Prevention, early diagnosis and appropriate treatment of TB are important for public health [5]. Cough is one of the most common symptoms, and a child with cough lasting more than 3 weeks should be investigated for pulmonary TB [3,6]. In our study, most of the patients were symptomatic. The most common presenting symptoms were cough lasting more than 2 weeks, followed by night sweats, fever, weight loss. Although it was rare in children, hemoptysis was detected in 4 patients. Physical examination findings of pulmonary TB in childhood vary with age. As the airway diameter is small in infants, wheezy breathing, tachypnea and respiratory sounds may be associated with the growth of paratracheal or hilar lymphadenopathy [6]. In our study, abnormal respiratory system findings were detected in only 8 patients, which were rales, rhonchus, elongation of expirium, and decreased respiratory sounds.

Although physical examination and direct X-rays may be normal in patients presenting with the typical complaints, thorax tomography examination and microbiological examinations should be performed and pulmonary TB diagnosis should be excluded [7,8]. In our study, the physical examination and direct radiographs of 16 patients who presented with various complaints were found to be normal.

Since many childhood TB cases are diagnosed clinically rather than by the isolation of the bacteria, the detection of index cases is important in terms of obtaining microbiological data. Further, drug resistance of the index case is important in the treatment of pediatric patients. If the index case is drug resistant, the pediatric case needs to be treated considering this resistance. In addition, the benefit of detection of the index case is important in the control of TB in preventing the occurrence of new cases by providing treatment and isolation [9–11].

Five TB positive patients in our study were asymptomatic, and had both normal respiratory system examinations and normal chest radiographs; they were included as a result of history of contact with the index case or due to their TCT positivity. It is of great importance to educate the community about the role of contact with the index case in the progression of the disease by identifying the asymptomatic cases and starting treatment. Although two-thirds of our cases had a history of contact with an adult TB patient, the index case was identified in only half of this group. The reason for this may be due to the screening of only the family members in the tuberculosis dispensary. In our study, almost half of the index cases were out-of-home contacts. This result showed us the importance of questioning the contacts outside the home, especially at school.

In our study, TST was found to be positive in only 61% of the cases. The negative value of TST in 39% of our patients who were diagnosed with TB may be considered as false negative results; this may be due to tuberculosis disease itself causing anergy. Cytokines formed during TB infection may cause cell apoptosis and anergy, thereby leading to a non-responsiveness to the skin test. It is also believed that cytokines of the innate immunity may be responsible for this non-responsiveness [12–14].

In adults, the diagnosis of TB is proven bacteriologically, whereas in children, the disease has paucy-bacillary character, which means low bacterial load, and in childhood it is difficult to diagnose TB bacteriologi-

cally due to the low number of M. tuberculosis colonies as a result of the absence of cavity formation [8,15–17]. In our study, the diagnosis of tuberculosis was confirmed microbiologically only in 10 (10%) patients. The low rate of microbiological diagnosis was consistent with the rates reported in the literature [11,18].

In children, in pulmonary TB, pulmonary or segmental infiltration, intrathoracic lymphadenopathy with infiltration, and intrathoracic lymphadenopathy are the most common radiological findings. In our study, the most common radiological findings were infiltration and mediastinal lymphadenopathy consistent with the literature [12]. Cavitation in children is rare in radiological findings; it is seen in 5-16% of patients [13]. Similar to the literature, only 4 of the patients in our study had cavitation.

Male sex, advanced age, previous history of TB, drug resistant TB, cavity and presence of fibrotic lesions have been identified as poor prognostic factors in terms of radiological improvement after TB treatment [14]. In our study, radiological improvement was detected at the end of the treatment or 2 months after, and the factors determining the prognosis in radiological recovery were examined by regression analysis. It was found that lack of drug compliance or irregular follow-ups predicted incomplete radiological improvement after treatment. Patients who did not have radiological improvement or were partially recovered were less likely to be treatment adherent or to attend regular follow-up. This has demonstrated once again the effect of treatment compliance and regular follow-up on prognosis, in line with the literature [19]. Since the number of patients who had cavity in their radiology at presentation was low, this may explain why the presence of cavity at presentation did not affect radiological prognosis.

In our study, approximately one quarter of patients had transient transaminasemia, transient hyperuricemia, neutropenia or gastrointestinal side effects such as nausea and vomiting. Similar to our study, the most common side effects in patients receiving pulmonary TB treatment were reported as transaminase elevation and hyperuricemia Drugs responsible for these side effects are INH and RIF [8,20,21].

Neutropenia was seen in the second week of treatment in a patient receiving INH, RIF and PZA treatment, and improved when RIF therapy was discontinued after 2 weeks. Neutropenia is a very rare side effect of antiTB drugs and has been reported rarely in the literature [17]. We also investigated the time of occurrence of side effects; although the side effects of antituberculosis drugs in the literature most frequently occurred after 2-3 weeks [22], it was shown that treatment side effects may even occur in the 12th and 32nd weeks of treatment, and the importance of regular follow-up of the patients after the first weeks has been demonstrated.

Some limitations of the study are as follows: since the study was designed retrospectively, more up to date diagnostic methods like interferon-gamma release assay were not available in the patients' files. Some of the data were based on patients' self-reports, therefore there may be issues with reliability. This study was conducted in only one tertiary medical facility, which may limit the generalization of the results.

Conclusions

In our study the most common complaints were cough, night sweating and fever, and the most frequently encountered radiological finding was infiltration. The patients mostly had elevated transaminase and uric acid levels as side effects. Although chronic respiratory symptoms, fever, weight loss, fatigue, physical examination and plain radiographs are normal, detailed history and diagnostic tests should be considered for pulmonary TB. Patients undergoing drug therapy should be closely monitored for side effects and for treatment adherence. In this way, the morbidity caused by the side effects may be prevented, and complete radiological improvement will be ensured by regular drug use.

Acknowledgements

This article is based on the author's pediatrics dissertation. The author would like to thank Associate Professor Gönül Tanır, MD for her guidance during the preparation and writing of the dissertation.

References

1. World Health Organization. Global tuberculosis report. Geneva: World Health Organization [online] 2017 [cit. 27.11.2017]. Available from URL: http://apps.who.int/iris/bitstream/10665/259366/1/9789241565516.
2. Seddon JA, Shingadia D. Epidemiology and disease burden of tuberculosis in children: a global perspective. Infect Drug Resist 2014; 7: 153–165.
3. World Health Organization. WHO guidelines on tuberculosis infection prevention and control, 2019 update. Geneva: World Health Organization; 2019.
4. Kara F, ed. Tüberküloz tanı ve tedavi rehberi. 2. Baskı. Ankara: T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü; 2019. (In Turkish).
5. Nahid P, Dorman SE, Alipanah N, Barry PM, Brozek JL, Cattamanchi A, et al. Official American thoracic society/centers for disease control and prevention/infectious diseases society of America clinical practice guidelines: treatment of drug-susceptible tuberculosis. Clinical Infectious Diseases 2016; 63(7): e147–e195.
6. Toma P, Lancella L, Menchini L, Lombardi R, Secinaro A, Villani A. Radiological patterns of childhood thoracic tuberculosis in a developed country: a single institution's experience on 217/255 cases. Radiol Med 2017; 122(1): 22–34.
7. Tanır G. Tüberkülozlu çocuk hastanın antitüberküloz tedaviye uyumu ve tedavi sırasında izlemi. In: Özçelik U, Kocabaş E, Ersu R, Gürkan F, ed. Çocukluk Çağında Tüberküloz. Istanbul: Toraks Kitapları; 2017: 91–98. (In Turkish).

8. Chheng P, Nsereko M, Malone LL, Okware B, Zalwango S, Joloba M, et al. Tuberculosis case finding in first-degree relative contacts not living with index tuberculosis cases in Kampala, Uganda. Clin Epidemiol 2015; 7: 411–419.

9. O'Garra A, Redford PS, McNab FW, Bloom CI, Wilkinson RJ, Berry MP. The immune response in tuberculosis. AnnuRev Immunol 2013; 31: 475–527.

10. Gürkan F, Karabel M. Akciger tüberkülozunda klinik özellikler. In: Özçelik U, Kocabaş E, Ersu R, Gürkan F, ed. Çocukluk Çağında Tüberküloz. Istanbul: Toraks Kitapları; 2017: 13–16. (In Turkish).

11. Al Marri MR. The tuberculin skin test in confirmed pulmonary tuberculosis in the state of Qatar: where we stand? Qatar Med J 2013; 2012(2): 16–19.

12. Carvalho ACC, Cardoso CAA, Martire TM, Migliori GB, Sant'Anna CC. Epidemiological aspects, clinical manifestations, and prevention of pediatric tuberculosis from the perspective of the End TB Strategy. J Bras Pneumol 2018; 44(2): 134–144.

13. Lindenau JD, Salzano FM, Hurtado AM, Hill KR, Hutz MH. The role of variants from the innate immune system genes in tuberculosis and skin test response in a Native American population. Human Immunology 2016; 77(10): 981–984.

14. Shingadia D, Novelli V. Diagnosis and treatment of tuberculosis in children. Lancet Infect Dis 2003; 3(10): 624–632.

15. Aye S, Majumdar SS, Oo MM, Tripathy JP, Satyanarayana S, Kyaw NTT, et al. Evaluation of a tuberculosis active case finding project in peri-urban areas, Myanmar: 2014–2016. Int J Infect Dis 2018; 70: 93–100.

16. Saunders MJ, Wingfield T, Tovar MA, Baldwin MR, Datta S, Zevallos K, et al. A score to predict and stratify risk of tuberculosis in adult contacts of tuberculosis index cases: a prospective derivation and external validation cohort study.Lancet Infect Dis 2017; 17(11): 1190–1199.

17. Ogbudebe CL, Adepoju V, Ekerete-Udofia C, Abu E, Egesemba G, Chukwueme N, et al. Childhood tuberculosis in Nigeria: disease presentation and treatment outcomes. Health Serv Insights 2018; 11: 1–7.

18. Sakhno LV, Tikhonova MA, Tyrinova TV, Leplina OY, Shevela EY, Nikonov SD, et al. Cytotoxic activity of dendritic cells as a possible mechanism of negative regulation of T lymphocytes in pulmonary tuberculosis. Clin Dev Immunol 2012; 2012: 628635.

19. Cruz AT, Starke JR. Clinical manifestations of TB in children. Paediatr Respir Rev 2007; 8(2): 107–117.

20. Thomas TA. Tuberculosis in Children. Pediatr Clin N Am 2017; 64(4): 893–909.

21. Ning-ning T, Yi-fan L, Yun-xia L, Jin-yue L, Wan-mei S, Yao L, et al. Epidemiological characteristics of pulmonary tuberculosis among children in Shandong, China, 2005–2017. BMC Infect Dis 2019; 19: 408.

22. Ziemele B, Ranka R, Ozere I. Pediatric and adolescent tuberculosis in Latvia, 2011–2014: case detection, diagnosis and treatment. Int J Tuberc Lung Dis 2017; 21(6): 637–645.

Word count: 3114 • Tables: 3 • Figures: 1 • References: 22

Sources of funding:
The research was funded by the author.

Conflicts of interests:
The author reports that there were no conflicts of interest.

Cite this article as:
Batmaz SB.
Pulmonary tuberculosis in childhood: clinical features, treatment side effects and factors associated with radiologic improvement.
MSP 2020; 14, 1: 4–9. Published online: 30 Mar 2020.

Correspondence address:
Sehra Birgül Batmaz, MD
Pediatric Allergy and Clinical Immunology Clinic,
Tokat State Hospital, 60100, Tokat, Turkey
Phone: +90 356 2145400
E-mail: drsehra@yahoo.com

Received: 8.07.2019
Reviewed: 29.03.2020
Accepted: 29.03.2020

e-ISSN 2544-1620

Medical Science Pulse 2020 (14) 1

Original papers

Published online: 30 Mar 2020

DOI: 10.5604/01.3001.0013.9720

HYPERGONADOTROPIC OVARIAN INSUFFICIENCY IN WOMEN OF LATE REPRODUCTIVE AGE

Natalia V. Khvoryk[1 A–G]
• ORCID: 0000-0002-2901-7389

Hamed Asaad Aljazaa[2 E–F]
• ORCID: 0000-0002-5350-7003

[1] Department of Obstetrics and Gynecology, Grodno State Medical University, Grodno, Belarus

[2] Grodno State Medical University, Grodno, Belarus

A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: At present, the increasing frequency of hypergonadotropic ovarian insufficiency in women of late reproductive periods is associated with various problems, which requires the development of new criteria and an integrated approach to solving these problems.

Aim of the study: To investigate the causes, clinical manifestations and diagnostic criteria of hypergonadotropic ovarian insufficiency in women of late reproductive age.

Material and methods: We examined 42 patients with clinical and laboratory criteria for hypergonadotropic ovarian failure. The causes and clinical manifestations of hypergonadotropism, as related to ovarian failure, in women of late reproductive age were revealed through this analysis.

Results: Women aged 36–42 years that have had previous surgery on pelvic organs often undergo changes typical of hypergonadotropism. Certain clinical indicators such as lability of follicle-stimulating hormone (FSH) levels and other direct and indirect signs of decreased ovarian reserves allow practitioners to prescribe appropriate therapy on time. Timely diagnosis and an individualized approach can help prevent symptoms of hypoestrogenia and related complications. The results of this study show that early detection of a luteal out-of-phase (LOOP) event, along with a more detailed history was diagnosed in 16 (38.1%) of cases. Early detection allows more timely changes in diagnosis, may noted signs that can reflect both the normal state and pathology.

Conclusions: Levels of Anti-Müllerian hormone, basal levels of FSH in two successive cycles, early detection of an LOOP-event and the use of ultrasound are significant factors that can help in the assessment of ovarian reserves.

KEYWORDS: reproductive age, ovarian reserve, damaging factors, surgical interventions

Background

Significant reductions in the ovarian reserves of women of older reproductive age is an urgent problem that has been on the rise in recent decades. Increases in average life expectancy and the tendency to postpone the birth of offspring to a late reproductive period are factors that may contribute to current medical and social reproductive issues that women face today. Age is a significant determinant of the well-being of reproductive function. At the age of 27–28, the first signs of decreases in reproductive function appear. At this stage, basal levels of gonadotropins begin to rise. By 45 years, reproductive capacity approaches zero, and by 55 hormonal function starts to die out. The rate of aging of the reproductive system is determined by the interaction of genetic factors and the diverse influences of the environment [1,2].

Cessation of ovarian function in women under 40 is an indication of premature ovarian failure (POF) or hypergonadotropic ovarian insufficiency. The main clinical and laboratory symptoms of cessation of ovarian function are amenorrhea, an increased concentration of gonadotropic hormones in the blood and hypoestrogenism and its consequences [1–4]. Interestingly, in the case of viral infections, especially frequently recurrent variants, cellular immunity is activated. This includes the production of antigens of the major histocompatibility complex (MHC) class II, which is increased not only in cells of the immune system, but also in cells of the ovarian epithelium, which leads to the production of anti-ovarian antibodies that are associated with POF and other autoimmune disorders [1,4,5]. The consequences of surgical interventions on pelvic organs may

stimulate the development of problems associated with decreased reproductive and hormonal potentials. It is well known that surgical aggression may be one of the reasons for the development of POF [1,6,7]. Women with infectious processes in the reproductive system including paramyxovirus (mumps), human immunodeficiency virus (HIV) or pelvic inflammatory disease represent a risk group for the development of premature ovarian failure [1,5,8].

According to the recommendations of the American Society for Reproductive Medicine (2008), 3 reproductive periods are distinguished before menopause, which are characterized by an increased level of FSH and a reduced ovarian reserve. These stages include the so-called 'late reproductive period', perimenopause, which is divided into early and late stages. Clinically, menstrual transition is associated with hypoestrogenia in which woman may complain of dryness in the vagina, decreased libido, weight gain, deterioration in the condition of hair and nails, irritability, night sweats and increased blood pressure. Traditionally, the classification of the stages and criteria for the functioning of the reproductive system (Stages of reproductive aging workshop – STRAW) is based on the menstrual transition period which begins with changes in the duration of the menstrual cycle and a monotonous increase in FSH levels [9].

In the updated STRAW + 10 system (2011), the functional phase is stage -3b, which is characterized by a regular menstrual cycle and a normal level of FSH in the early follicular phase, and the -3a stage is associated with shortening of the menstrual cycle and elevated levels of FSH [8]. The refined criteria determine the entry into the early menstrual transition period, which is characterized by menstrual cycles that are variable in length with a difference of 7 or more days, followed by the preservation of this difference at least once during 10 cycles. At the same time, additional criteria include elevated levels of FSH, volatile, low Anti-Müllerian (AMH) hormone levels, and low numbers of antral follicles [1,9,10].

Aim of the study

This study was conducted with the aim to investigate the causes, clinical manifestations and diagnostic criteria of hypergonadotropic ovarian insufficiency in women of late reproductive age.

Material and methods

Study design, setting and duration, study population

We examined 42 patients with clinical and laboratory criteria for hypergonadotropic ovarian failure. Ages ranged from 36 to 42 years, averaging 37.3±2.2 years. A control group for comparison consisted of 18 women who were comparable in age and underwent preventive examinations.

Inclusion criteria

The criteria for selecting patients in the study were: menstrual irregularities and clinical indications of estrogen deficiency, FSH levels in serum of more than 25 mIU/L at least in a single definition (FSH study was conducted twice according to the criteria of the European Society of Human Reproduction and Embryology, 2015) and episodic or stable amenorrhea among women under 42 years old.

Exclusion criteria

Excluded from the study were patients with a diagnosis of polycystic ovary syndrome, hyperprolactinemia or amenorrhea of central origin. The diagnosis of ovarian failure was based on anamnestic, clinical and laboratory data and instrumental examination methods.

Methodology

The functional state of the hypothalamic-pituitary-ovarian system was determined and based on hormonal status, including levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, estradiol and Anti-Müllerian (AMH) hormone. The levels were determined by using enzyme immunoassays with measurements of plasma concentrations of the aforementioned hormones. A transvaginal ultrasound was performed to evaluate the volume of the ovary, the number of follicles and the pathology of the uterus.

Ethical considerations

The study was conducted after ethical approvals were obtained from the Grodno State Medical University – ethical Committee (no.: 23/2018).

Statistical analysis

Statistical analysis was performed using the software set Microsoft Excel and Statistica 6.0. To describe the obtained results of the studied phenomena, we calculated the frequency indices of the studied phenomena (p) with a statistical error (Sp), arithmetic mean (M) and arithmetic mean error (m).

Characteristics of the study group

Almost all examined patients had a higher education, (39 women, or 92.9% of all cases), or secondary special education (3 women, or 7.1% of all cases). In the group, 7 women (16.7%) had smoking habits. During treatment, patients' main complaints were menstrual irregularities, which occurred in 31 patients, or 73.8% of all cases. Oligomenorrhea occurred in 32 cases (76.2%), shortening of the menstrual cycle was noted in 37 cases (88.1%), while amenorrhea was diagnosed in 5 cases (11.9%). Subjective symptoms of ovarian function depletion in the form of hot flashes, decreased libido, headaches, fatigue, sleep disturbances and vaginal dryness were reported by 32 women (76.2%).

Results

The average age of the onset of menarche was 13.4±0.5 years. The onset of sexual activity of the patient was on average 19.1±1.4 years. In most cases, i.e. in 39 cases (i.e. 92.9% of all cases), a regular menstrual cycle lasting 28.9±2.5 days was observed after menarche. Analysis of reproductive function indicators showed that the majority of women, 40 (95.2% of all cases), had undergone childbirth, however, in 2 patients (4.8%) reproductive plans were not implemented. Of the women who had children, 36 (85.7%) had 2 births, 3 (7.1%) had three births and 1 (2.4%) woman had only one child. Abortions were observed in 12 (28.6%) women. Eight (19%) women had a history of unsuccessful in vitro fertilization (IVF) attempts. Of extragenital diseases, thyroid pathology was most often encountered, with autoimmune thyroiditis occurring in 5 women (11.9%). Other pathologies included childhood and acute respiratory infections, diseases of the cardiovascular system (9 women, or 21.4% of total cases), urinary tract infections (4, or 9.5%), gastrointestinal tract problems (5, or 11.9%), and endocrine-metabolic disorders (3, or 7.1%). Of particular relevance was the analysis of gynecological pathology. It was found that more than half of the patients (29, or 69.0% of total cases) underwent different types of treatments for different pathologies. The different gynecological pathologies found in the group of women studied is presented in Tab. 1.

Table 1. Gynecological pathology of the examined women.

Gynecological pathology	Number of patients	
	absolute	%
Benign Cervical Disease	11	26.2
Cervical Dysplasia	1	2.4
Endometrial polyps	8	19.0
Uterine fibroids	6	14.3
Cysts and ovarian cyst (including endometriosis)	14	33.3
Ovarian apoplexy	12	28.6
Inflammation of the uterine appendages	14	33.3
Infertility	18	42.9
Ovarian Endometriosis	7	16.7
Adenomyosis	4	9.5
External genital endometriosis	4	9.5
Ectopic pregnancy	6	14.3
Atonic uterine bleeding after labor	1	2.4

As can be seen in Tab. 1, the most common gynecological pathology was infertility, both primary and secondary, which was found in 42.9% of all cases. To help treat this pathology, the women underwent diagnostic and/or therapeutic laparoscopy. Most of these patients (10, or 55.5% of all cases) were diagnosed with ovarian endometriosis and/or external genital endometriosis. Appropriate treatment was provided for these conditions. Next in frequency of occurrence were ovarian cysts and cystoma, as well as chronic inflammatory diseases of the uterus (6, or 33.3%). Surgery for ovarian cysts was carried out on an emergency basis due to rupture and bleeding in the abdominal cavity. Cystomas were removed as planned by laparoscopic access. Most often (in half of the cases) these were endometrioid cysts. A hormonal study conducted in the early follicular phase showed that fluctuations in FSH levels ranged from 9 to 38 mIU/L. The average normal value is 28.6±7.4 mIU/L. During a menstrual cycle, the study was conducted twice in succession and the hormone fluctuations during repeated determination ranged from 25 to 49 mIU/L. In cases when women had amenorrhea, a hormonal study was performed once and the levels of FSH corresponded to a hypergonadotropic state. Fluctuations in hormone levels ranged from 52 to 105.5 mIU/L. Comparing the FSH indicator with the levels in patients of the control group (8.6±1.8 mIU/L), we obtained significant differences ($p<0.001$). In women who had a clinical LOOP (luteal out-of-phase) event, we noted signs that can reflect both normalcy and pathology.

LOOP-event assessment in the studied objects

A LOOP event represents an atypical sharp increase in estradiol in the second phase of the menstrual cycle followed by a sharp decrease, which leads to a menstrual cycle of less than 21 days if ovulation occurs, with the subsequent cycle being abnormally long (more than 36 days) in cases where an LOOP event does not end with ovulation [11]. Therefore, clinically the LOOP-event with a more detailed history was diagnosed in 16 patients (38.1% of all cases).

In cases where the menstrual cycle lasted 21 days or less, the level of FSH did not exceed 12 mIU/L. However, in the subsequent anovulatory cycle, the duration of which was more than 36 days, the level of FSH in most women corresponded to hypergonadotropic values reaching 52 mIU/L. LH levels in the early follicular phase for women of the main group corresponded to 18.8±8.1 mIU/L, whereas in the control group the values were 5.1±1.9 mIU/L ($p<0.001$). We did not notice any significant differences in the LH/FSH ratio between the main group (0.62±0.2) and the control group (0.58±0.5), which indicates interdependent hormonal fluctuations in the basal levels of hormones. We found that there were no significant differences in the levels of estradiol, which increased to 45.8±8.8 pg/mL and 48.9±8.1 pg/mL, in the main and control groups, respectively. The lack of difference is associated with the determination of basal levels of the hormone in the blood. There were also no significant differences when comparing prolactin levels in women of both groups ($p>0.05$). The AMH level in all patients was reduced and corresponded to 0.26±0.13 ng/mL, while in the control group, it amounted to 1.2±0.86 ng/mL.

Ultrasonographic criteria

Ultrasound scanning of the pelvic organs showed normal or reduced size of the uterus in patients. The total volume of the ovaries was 2.1±0.86 cm^3, indicating a poor prognosis for ovarian reserve according to ultrasound criteria. In the control group, this indicator corresponded to 6.1±2.3 cm^3, which was significantly different from the main group. In 16.7% of cases, one of the ovaries was not visualized. These ultrasound results were of patients that had undergone removal of a cyst larger than 8 cm in diameter, as well as two surgical interventions performed on one ovary.

Counting the number of antral follicles is a more accurate method for assessing ovarian reserve. A decrease in their number (i.e. less than 5) was recorded in 12 patients (28.6% of cases), a weakly expressed follicle count was registered in more than half of patients (26, or 61.9% of cases) and the absence of a follicle count was diagnosed in 4 patients (9.5%). The monotone pattern of the endometrium, which is when the anteroposterior size of the endometrium corresponds to 5 mm or less during the menstrual cycle, was observed in a third of patients (13 or 31.0% of cases). The absence of growth of the dominant follicle was recorded in the majority of women examined (37 or 88.1% of cases).

Discussion

There is a "theory of burnout" when there is an accelerated growth of follicles, with subsequent depletion in the cortical layer of the ovaries with endometriosis. At the same time, a decrease in the pool of early follicles is observed, which can occur due to various reasons such as exhaustion of the pool of primordial follicles, activation of the early development of follicles, an increase in the number of atresized follicles or dysregulation of the selection of follicles [10,12]. Thus, there is a violation of folliculogenesis in the ovaries of women with endometriosis, characterized by a decrease in the total number of follicles at all stages of development. The extent of decrease in the number of follicles depends on the stage of spread of the pathological process and the age of the patient [12]. It was found that patients with ovarian endometriosis of various stages of distribution have a low level of AMH, and lower values are observed in cases that have bilateral endometrioid ovarian formations compared to unilateral formations [7,13]. Therefore, ovarian endometriosis in combination with age is a significant risk factor for follicular reserve depletion.

Excisional surgery has been questioned as an ideal surgical approach for endometriomas because it is associated with potential reduction of ovarian reserve [6]. Another significant factor is ovarian apoplexy, both as a result of organ trauma and pathology leading to surgery – 28.6%. Currently, laparoscopic surgery in gynecology occupies a leading position among gynecological procedures. More than 70% of surgical interventions are performed by laparoscopic access. It is well known that it is necessary to differentially approach the use of high surgical energies when working on the ovaries. The goal of surgery should be effective hemostasis and reducing morbidity associated with exposure to tissues. Other gynecological pathologies in women included benign diseases of the cervix, endometrial polyps, uterine fibroids, adenomyosis, surgical interventions for ectopic pregnancy and postpartum hemorrhage. A study by V.A. Guriev showed that patients with low ovarian reserves underwent bilateral ovarian resection in 25.3% of cases, while a cystectomy was performed in 19.8% of cases – for the latter, the cystectomy was performed on the right, which increased the odds ratio of reducing the ovarian reserve since the right ovary is functionally more active and therefore its loss, or a decrease in the primordial pool due to surgical interventions, is more significant [8]. It is well known that surgical intervention may a major reason for the development of premature ovarian failure [1,6,7]. It has been found that uterine artery embolization increases the risk of premature ovarian failure [9].

Limitations of the study

The present study was conducted over a short period of time and had a small sample size. In future studies, a larger population size would be ideal.

Conclusions

In today's modern times, issues such as the increasing incidence of diseases and tendencies towards late reproductive periods requires the development of new criteria and an integrated approach to solving these problems. Early detection of LOOP syndrome, assessment of AMH after gynecological interventions and ultrasound criteria for ovarian reserve will allow timely diagnosis and appropriate treatment of hypergonadotropic states in women of late reproductive age.

References

1. Fraison E, Crawford G, Casper G, Harris V, Ledger W. Pregnancy following diagnosis of premature ovarian insufficiency: a systematic review. Reprod Biomed Online 2019; 39(3): 467–476.
2. Petrov YUA, Blesmanovich AE, Alekhina AG. Prezhdevremennaya ovarial'naya nedostatochnost' (obzor literatury) [Premature ovarian failure]. Tavricheskij mediko-biologicheskij vestnik 2018; 2(21): 207–212. (In Russian).
3. Bricaire L, Laroche E, Bourcigaux N, Donadille B, Christin-Maitre S. Insuffisances ovarienes prematures. Presse Med 2013; 42(11): 1500–1507. (In French).
4. Sharif K, Watad A, Bridgewood C, Kanduc D, Amital H, Shoenfeld Y. Insights into the autoimmune aspect of premature ovarian insufficiency. Best Pract Res Clin Endocrinol Metab 2019; 16: 2–13.

5. Hamoda H, British Menopause Society and Women's Health Concern. The British Menopause Society and Women's Health Concern recommendations on the management of women with premature ovarian insufficiency. Post Reprod Health 2017; 23(1): 22–35.
6. Candiani M, Ottolina J, Posadzka E, Ferrari S, Castellano L, Tandoi I, et al. Assessment of ovarian reserve after cystectomy versus 'one-step' laser vaporization in the treatment of ovarian endometrioma: a small randomized clinical trial. Hum Reprod 2018; 33(12): 2205–2211.
7. Kalampokas T, Kamath M, Kalampokas E. AMH after laparoscopic surgery of the ovaries: a review. Gynecol Endocrinol 2013 May; 29(5): 408–411.
8. Gur'yev V, Kurakina V. Otsenka faktorov, opredelyayushchikh ovarial'nyy rezerv u zhenshchin s narushennoy reproduktivnoy funktsiyey. Zhurnal akusherstva i ginekologii 2012; 6: 76–81. (In Russian).
9. Harlow S, Gass M, Hall J, Lobo R, Maki P, Rebar R, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. Menopause 2012 Apr; 19(4): 387–395.
10. Hwu Y, Wu F, Li S, Sun F, Lin M, Lee R. The impact of endometrioma and laparoscopic cystectomy on serum anti-Müllerian hormone levels. Reprod Biol Endocrinol 2011; 9: 80.
11. Hale G, Hughes C, Burger H, Robertson D, Fraser I. Atypical estradiol secretion and ovulation patterns caused by luteal out-of-phase (LOOP) events underlying irregular ovulatory menstrual cycles in the menopausal transition. Menopause 2009 Jan-Feb; 16(1): 50–59.
12. Sosnova EA. Embolizatsiya matochnykh arteriy pri miome matki u patsiyentok reproduktivnogo vozrasta i yee rol' v formirovanii autoimmunnogo ooforita. Arkhiv akusherstva i ginekologii im. V.F. Snegireva 2016; 3(2): 81–87. (In Russian).
13. Adamyan LV, Kurilo LF, Shulyak IYU. Follikulogenez yaichnikov zhenshchin s nekotorymi formami endometrioza. Problemy reproduktsii 2009; 15(1): 78–85. (In Russian).

Word count: 2585 • Tables: 1 • Figures: – • References: 13

Sources of funding:
The research was funded by the authors.

Conflicts of interests:
The authors report that there were no conflicts of interest.

Cite this article as:
Khvoryk NV, Aljazaa HA.
Hypergonadotropic ovarian insufficiency in women of late reproductive age.
MSP 2020; 14, 1: 10–14. Published online: 30 Mar 2020.

Correspondence address:
Hamed Asaad Aljazaa
Clinical Resident
Grodno State Medical University
290000, Grodno, Gorky Street, 80
Phone: +375 33 325 64 01
E-mail: kafedra2.bsmp@mail.ru

Received: 20.02.2020
Reviewed: 3.03.2020
Accepted: 9.03.2020

e-ISSN 2544-1620

Medical Science Pulse 2020 (14) 1

Original papers

Published online: 31 Mar 2020

DOI: 10.5604/01.3001.0014.0779

ORGANIZATIONAL FORMS AND METHODS OF EARLY DIAGNOSIS OF HEREDITARY TUMORS

Aleh Kuzniatsou[1,2 A–F]
• ORCID: 0000-0002-1348-8688
Andrei Shpakou[1 A,B,E,F]
• ORCID: 0000-0003-4340-5211

[1] Yanka Kupala State University of Grodno, Grodno, Belarus
[2] University of Medical Sciences in Bialystok, Bialystok, Poland

A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: With the development of genetic research in oncology, it has become possible to track and identify early and preclinical forms of hereditary oncological diseases, which allows timely and effective preventive and therapeutic measures in relation to relatives at risk.

Aim of the study: Assessment of genetically determined neoplasms in the region and the development of organizational forms and methods for early diagnosis.

Material and methods: 10,727 residents of the Belarus-Poland border region were examined. Clinical and medical history data of 2,054 patients with tumors of the breast (1406), ovaries (239), and colon (409) were analyzed. As a result of the questionnaire, three main observation groups were formed: "high risk of hereditary cancer", "hereditary cancer suspected", and "no risk of hereditary cancer".

Results: Register and hospital screenings were the most informative types of screening. Of the 149 HBC patients who underwent molecular genetic testing, BRCA1 gene mutations were found in 5.37%, 5382insC in all cases. Seven mutations were detected in 77 individuals with a diagnosis of HOC and in 6 cases 5382insC and in 2 – 4145delA. Signs of hereditary ovarian cancer and suspicion of it were found in 1.12%, including people who were found to have a high risk of hereditary ovarian cancer. By their effectiveness, register and hospital screenings significantly exceeded the population, $p<0.01$. 1.67% of women suffering from this disease met the high clinical risk criteria for hereditary ovarian cancer. A high clinical risk of hereditary tumor genesis was established in 0.73% of cases among patients with a diagnosis of colon cancer.

Conclusions: The results of assessing the clinical risk of hereditary cancer according to population screening indicates that approximately 1.2% of the population has an increased clinical risk of developing hereditary breast, ovarian, and colon cancer.

KEYWORDS: oncology, hereditary cancer, clinical risk, screening, risk, mutation, breast cancer, ovary cancer, colon cancer

Background

In connection with the development of genetic research in oncology, it has become possible to track and identify early and preclinical forms of hereditary oncological diseases, allowing timely and effective preventive and therapeutic measures in relation to relatives at risk. About 10% of diagnosed neoplasms are hereditarily determined and in the so-called "cancer families" up to 45% of relatives are affected by various forms of cancer [1–3].

The improper use of medical care for the timely detection and prevention of malignant neoplasms along with the lack of a scientifically based approach in the interaction of oncological and medico-genetic services amongst cancer patients is what led to this study [4,5].

Only half of blood relatives are carriers of mutations of a particular gene. However, the peculiarity of these genes is that they do not manifest themselves in any way before the onset of the tumor. Therefore, it is impossible to know in advance which family member is the carrier of the mutant gene and is predisposed to the development of cancer [6–9]. All members of such families have to be included in the high-risk group and subjected to expensive diagnostic tests. As a result, you may encounter a large number of healthy relatives with carcinophobia. This casts doubt on the need for unnecessary cardinal interventions, such as the currently used

prophylactic removal of the mammary glands in carriers of BRCA1 and BRCA2 [10–14]. At the same time, mammography self-monitoring and other diagnostic methods remain a prerequisite for early detection of cancer in the population [15].

After our experience with this contingent of the population, we recommend raising awareness and providing doctors, of both the oncological profile and the outpatient health department, about the role of the hereditary factor in the development of tumors of different localizations.

As we expand our knowledge about the problems of hereditary cancer, the medical community and health authorities are convinced of the need to introduce molecular genetic methods, into clinical practice. In particular for diagnosing hereditary predisposition to certain types of cancer and other forms of malignant neoplasms associated with the pathological BRCA1/2 genotype through the creation of hereditary tumor diagnostic centers. The main tasks are:

- hospital, population, and "register" screenings: compiling and studying pedigrees and identifying clinical signs of the presence of hereditary tumors among the population of the region;
- creation of a database for storing pedigrees obtained during population and hospital screenings and their analysis in order to calculate the risk of possible development of tumors in relatives of patients with cancer;
- dispensary registration: the organization and conduct of dispensary registration of relatives of cancer patients (first degree of kinship) for whom a high risk of tumors has been calculated (high risk group for the development of tumors);
- laboratory diagnostics: carrying out molecular genetic, immunological, and immunohistochemical studies in the case of a high probability of a hereditary predisposition;
- instrumental diagnostics: for the early diagnosis of tumors in groups of relatives with an increased oncological risk;
- educational and methodical work: with the aim of promoting knowledge and prevention.

Early detection of tumors is a very real goal, the achievement of which is seen in the screening of relatives of patients and "active monitoring" of patients with identified hereditary mutations. Patients who meet the criteria for hereditary cancer must be examined for mutations in the genes for the repair of tumor DNA [16–21].

Alternative methods of instrumental research can be magnetic resonance and computed spiral tomography for tumors of the mammary gland and ovaries and autofluorescence endoscopy and photodynamic diagnosis in combination with magnetic resonance imaging (MRI) for hereditary forms of colorectal cancer. Molecular genetic, immunological, and immunohistochemical methods are of great interest in the search for reliable criteria for the early diagnosis of cancer and its hereditary forms.

Aim of the study

The assessment of genetically determined neoplasms in the region and the development of organizational forms and methods for their early diagnosis.

Material and methods

Participants

A survey of 10,727 residents of the Belarus-Poland border region was conducted. The clinical and medical history of 2,054 patients with breast (1,406), ovarian (239 cases), and colon (409 cases) tumors was analyzed.

Study design

The study was conducted while the patient was seeking medical help in the clinic, during the treatment period in the hospital, or during preventive examinations. The survey contained questions to clarify the presence of cases of oncological pathology in the patient's family and the degree of kinship in the family [22]. As a result of the questionnaire, three main observation groups were formed: the group "at high risk of hereditary cancer", "hereditary cancer suspected", and "no risk of hereditary cancer". The distribution of probands was carried out according to three nosological forms of hereditary cancer tumors: breast (HBC), ovary (HOC), and colorectal cancer (HCC) (Tab. 1).

The main advantage of the system was its adaptability to the cancer register with the possibility of using register databases. The basis for identifying hereditary forms of oncological diseases is the screening method for examining the population; the results of which can be represented as:

- hospital screening: the study of the pedigree and the identification of clinical signs of the presence of hereditary tumors in people who seek medical help;
- screening of the register: based on the analysis of the data of the oncological register of patients whose tumors are highly likely to be associated with a hereditary predisposition, and surveys of their family members and relatives of the first and second level of kinship;
- population screening: questionnaire and genealogy of randomly selected individuals (visits to the clinic, to local doctors, home calls, etc.)

Statistical methods

The data obtained was analyzed statistically using Statistica v.10 software (Chi-squared test, Kruskal-Wallis test). The assumed level of significance was $p<0.05$.

Results

Of the 10,727 questionnaires, 762 individuals were selected based on the clinical risk of hereditary cancer. 47 respondents (0.44 ± 0.06%) had signs of high risk of

hereditary cancer and 715 (6.67 ± 0.24%) were assigned to the group "hereditary cancer suspected" (Tab. 2).

In 226 patients, 149 with a diagnosis of HBC and 77 with a diagnosis of HOC, venous blood was taken for molecular genetic (PCR method) studies for the presence of BRCA1 gene mutations (Exon 5382insC and 4145delA) [22].

The distribution of probands depending on the clinical risk of cancer and the type of screening study are presented in Tab. 3.

Table 1. Surveillance Groups ("high risk", "hereditary cancer suspected").

Clinical Risk Group	HBC or HOC	HCC
High Risk	– Three or more first-degree relatives suffer from HBC and/or HOC; – History of breast cancer in men present in the family; – HBC or HOC at any age in Ashkenazi Jewish women (Jewish, European)	– HCC or its associated tumors were diagnosed in 3 or more relatives of the 1st degree of kinship; – At least one relative under the age of 50 years
Hereditary Cancer Suspected	– HBC or HOC developed in a patient under the age of 40; – Two first-degree relatives suffer from HBC and/or HOC; – HBC or HOC in one patient present in family history; – A single case of HOC in a family history if the patient is from the genus Ashkenazi Jewish	– The presence of synchronous or metachronal colorectal cancer and associated tumors at any age; – The presence of pathological signs of high microsatellite instability (lymphocyte infiltration, Crohn's-like lymphocytic reaction, molecular growth pattern), established at 60 years of age; – HCC and associated tumors (cancer of the endometrium, stomach, ovaries, pancreas, etc.) diagnosed in at least one relative of the 1st degree of kinship under 50 years of age; – HCC or associated tumors diagnosed at any age in two relatives of 1st or 2nd degree of affinity

Table 2. Results of screening studies to identify among the population persons with clinical signs of hereditary forms of malignant neoplasms.

Clinical Risk Group	Nosological Form of Hereditary Cancer						Total	
	HBC		HOC		HCC			
	n	%	n	%	n	%	n	%
High Risk	32	0.30	7	0.065	8	0.07	47	0.44
Hereditary Cancer Suspected	461	4.60	113	1.05	141	1.31	715	6.67
Combination of Two Target Groups	493	4.60	120	1.12	149	1.39	762	7.10
No Risk of these Forms of Cancer	10,190	95.0	9,219	88.06	9446	88.06	9965	92.90
Total	10,727		10,727		10,727		10,727	

Table 3. Clinical risk assessment of hereditary breast cancer (HBC), hereditary ovarian cancer (HOC) and hereditary colorectal cancer (HCC) according to screening studies.

Clinical Risk Group	Type of Cancer	Type of Screening Study							
		Register		Hospital		Population		Total	
		n	%	n	%	n	%	n	%
High Risk	HBC	9	0.64±0.21	10	4.59±1.42	13	0.14±0.04	32	0.3±0.05
	HOC	4	1.67±0.83	3	3.13±1.78	0	0	7	0.07±0.03
	HCC	3	0.73±0.42	2	2.41±1.48	3	0.033±0.02	8	0.08±0.03
Hereditary Cancer Suspected	HBC	347	24.68±1.15	65	29.81±3.1	49	0.54±0.08	461	4.3±0.2
	HOC	82	34.31±3.07	24	25.0±4.42	7	0.077±0.03	113	1.05±0.1
	HCC	103	25.19±2.15	20	24.1±4.7	18	0.2±0.05	141	1.47±0.12
Combination of Two Target Groups	HBC	356	25.32±1.16	75	34.4±3.22	62	0.68±0.09	493	4.6±0.2
	HOC	86	36.0±3.1	27	28.13±4.59	7	0.077±0.03	120	1.12±0.1
	HCC	106	25.92±2.17	22	26.51±4.84	21	0.23±0.05	149	1.55±0.13
No Risk	HBC	1050	74.68±1.16	143	65.6±3.22	8997*	98.83±0.11	10190	95.0±0.21
	HOC	153	64.02±3.1	69	71.87±4.59	8997**	98.83±0.11	9219	85.9±0.34
	HCC	303	74.08±2.17	61	73.49±4.84	9082***	99.77±0.05	9446	98.4±0.13
Total	HBC	1406	100	218	100	9103*	100	10727	100
	HOC	239	100	96	100	9103**	100	10727	100
	HCC	409	100	83	100	9103***	100	9595	100

Note:
* included 36 cases of hereditary forms of cancer of a different localization and eight cases of "family congestion" which is classified as five or more episodes of cancer of different localization in three generations of the same family
** included 91 cases of hereditary forms of cancer of a different localization and eight cases of "family congestion"
*** included 36 cases of hereditary forms of cancer of a different localization and eight cases of "family congestion"

The most informative types of screening were register screening (25.32±1.16% of probands showed a high risk of HBC or suspected hereditary breast cancer) and hospital (34.4±3.22% of probands). In the population screening, only 0.68±0.11% of the respondents had a high risk of a hereditary breast tumor and/or suspicion of its development.

Of the 149 HBC patients who underwent molecular genetic testing, BRCA1 gene mutations were found in eight (5.37%), 5382insC in all cases. Among 77 examined with a diagnosis of HOC, mutations were detected in 7 people (9.09%), in 6 cases 5382insC, and in 2 - 4145delA (in 1 patient both mutations were found).

Out of 10,727 probands, signs of hereditary ovarian cancer and suspicion of it were found in only 120 people (1.12±0.1%), including 7 people who were found to have a high risk of hereditary ovarian cancer. By their effectiveness, register screening and hospital screening significantly ($p<0.01$) exceeded the population screening. 1.67% of women suffering from this disease met the high clinical risk criteria for hereditary ovarian cancer in the region's population. Among patients with a diagnosis of colon cancer, a high clinical risk of hereditary tumor genesis was established in 0.73% of cases.

When analyzing the relationship between the mutation frequency and the clinical risk group for hereditary cancer, it was found that, patients with a high risk of HBC and/or HOC, BRCA1 mutations were detected with the same frequency as in individuals with no clinical risk (Tab. 4).

Table 4. The results of molecular genetic analysis of patients with different clinical risks of hereditary ovarian and/or breast cancer.

Clinical Risk Group	Studies	Identified Patients with Mutations	%
High risk of hereditary breast cancer and/or ovarian cancer	28	2	7.14
Suspected hereditary breast cancer and/or ovarian cancer	90	5	5.55
No risk of hereditary breast cancer or ovarian cancer	108	8	7.41
Total	226	15	6.76

A low mutation rate was observed in the group with suspected hereditary HBC and/or HOC.

Discussion

The lack of a scientifically based approach in the interaction of oncological and medico-genetic services along with the lack of scientific work in this direction led to this study [4,5].

With the development of genetic research in oncology, it has become possible to track and identify early and preclinical forms of hereditary oncological diseases, which allows timely and effective preventive and therapeutic measures in relation to relatives at risk [1,2]. In "cancer families" up to 45% of relatives are affected by various forms of cancer [3]. 10% of diagnosed neoplasms are hereditarily determined.

Only half of blood relatives are carriers of mutations of a particular gene and the peculiarity of these genes is that they do not manifest themselves in any way before the onset of the tumor [6–8]. All members of such families have to be included in the high-risk group and subjected to expensive diagnostic tests. As a result, you may encounter a large number of healthy relatives with carcinophobia [9]. This casts doubt on the need for unnecessarily cardinal interventions, such as the currently used prophylactic removal of the mammary glands in carriers of BRCA1 and BRCA2 [10–14].

The expansion of knowledge about the problem of hereditary cancer convinces the medical community and health authorities of the need to introduce molecular genetic methods for diagnosing hereditary predisposition to certain types of cancer and other forms of malignant neoplasms associated with the pathological BRCA1/2 genotype through the creation of hereditary tumor diagnostic centers into clinical practice.

Early detection of tumors is a very real goal. This achievement is seen in the screening of relatives of patients and "active monitoring" of patients with identified hereditary mutations. Patients who meet the criteria for hereditary cancer must be examined for mutations in the genes for the repair of tumor DNA [16–21].

As a result of the studies, three main observation groups were formed: "at high risk of hereditary cancer" – "high risk", "hereditary cancer suspected", and "no risk of hereditary cancer". The distribution of probands was carried out according to three nosological forms of hereditary cancer tumors: breast (HBC), ovarian (HOC), and colorectal cancer (HCC).

The ability to obtain objective information about each proband and its family members from existing information databases and systems (a cancer registry, if available in the region), is crucial in identifying hereditary forms of the tumor, along with knowledge of the combination of the clinical and morphological characteristics of this syndrome and the information system of hereditary tumors (Patent of National Center for Intellectual Property of Belarus) [23].

In general, the results obtained are consistent with the data of European researchers, who established during hospital screening that 1.7% of patients diagnosed with breast cancer and 3.7% with a diagnosis of ovarian cancer meet the criteria for being assigned to the high clinical risk group as inherited breast cancer [2,24]. The frequency of hereditary colorectal cancer is 0.8% among the respondents while the suspicion of it is 1.47%. These results coincide quite accurately with the frequency of detection of mutations of the BRCA1 gene in cancer patients in Latvia, 3.7% for breast cancer and 10.7% for ovarian cancer [25]. With these results, it makes sense to propose the creation of special registers of hereditary tumors. This is possible both within the framework of territorial or hospital cancer registries with the introduction of the appropriate graphs, and within the framework of centers for the diagnosis of hereditary forms of cancer [26].

Conclusions

The results of assessing the clinical risk of hereditary cancer according to population screening indicate that approximately 1.2% of the population has an increased clinical risk of developing hereditary breast, ovarian, and colon cancer. During hospital screenings of patients whose diseases were first detected over the past two years, signs of a high clinical risk of hereditary cancer were detected in 4.5%.

Suspicion of the hereditary nature of cancer with the highest frequency (more than a third of the examined) was determined in the group of people with established ovarian cancer. Among those suffering from breast cancer and colorectal cancer, a quarter of the patients met the criteria for this clinical risk group.

The lack of a relationship between the degree of clinical risk determined by genealogy and the frequency of mutations of Exon 20 and Exon 11 of the BRCA1 gene most likely indicates that there are other genetic defects that play an etiological role in the development of HBC and/or HOC in the analyzed population. In order to identify these breakdowns, it seems appropriate to complete the sequencing of the BRCA1 gene in individuals with a high clinical risk of developing breast and/or ovarian cancer.

References

1. Aarnio M, Mecklin JP, Aaltonen LA, Nyström-Lahti M, Järvinen HJ. Life-time risk of different cancers in hereditary non-polyposis colorectal cancer (HNPCC) syndrome. Int J Cancer 1995 Dec 20; 64(6): 430–433.
2. Knerr S, West KM, Angelo FA. Organizational readiness to implement population-based screening and genetic service delivery for hereditary cancer prevention and control. J Genet Couns 2020 Jan 22. [Epub ahead of print].
3. Flaum N, Crosbie EJ, Edmondson RJ, Smith MJ, Evans DG. Epithelial ovarian cancer risk: a review of the current genetic landscape. Clin Genet 2020 Jan; 97(1): 54–63.
4. Kuznetcov OE, Gorchakova OV, Kuznetcova AA, Ianchevskii PN. Gruppy riska razvitiia nasledstvennykh opukholei tolstogo kishechnika. Materialy respublikanskoi s mezhdunarodnym uchastiem nauchno-prakticheskoi konferentcii, posviashchennoi 60-letiiu Grodnenskogo gosudarstvennogo meditcinskogo universiteta. Grodno: GrGMU; 2018: 451–454. (In Russian).
5. Thompson D, Easton DF, Breast Cancer Linkage Consortium. Cancer Incidence in BRCA1 mutation carriers. J Natl Cancer Inst 2002 Sep 18; 94(18): 1358–1365.
6. Narod SA, Feunteun J, Lynch HT, Watson P, Conway T, Lynch J, et al. Familial breast-ovarian cancer locus on chromosome 17q12-q23. Lancet 1991 Jul 13; 338(8759): 82–83.
7. Yamauchi H, Takei J. Management of hereditary breast and ovarian cancer. Int J Clin Oncol 2018 Feb; 23(1): 45–51.
8. Zheng G, Yu H, Kanerva A, Försti A, Sundquist K, Hemminki K. Familial ovarian cancer clusters with other cancers. Sci Rep 2018 Aug 1; 8(1): 11561.
9. Gori S, Barberis M, Bella MA, Buttitta F, Capoluongo E, Carrera P, et al. Recommendations for the implementation of BRCA testing in ovarian cancer patients and their relatives. Crit Rev Oncol Hematol 2019 Aug; 140: 67–72.
10. Bit-Sava EM, Belogurova MB. Hereditary breast cancer. Siberian journal of oncology 2013; 1(55): 75–81.
11. Mitelman F, Mertens F, Johansson B. A breakpoint map of recurrent chromosomal rearrangements in human neoplasia. Nat Genet 1997 Apr; 15 Spec No: 417–474.
12. Campacci N, de Campos Reis Galvão H, Garcia LF, Ribeiro PC, Grasel RS, Goldim JR, et al. Genetic cancer risk assessment: a screenshot of the psychosocial profile of women at risk for hereditary breast and ovarian cancer syndrome. Psychooncology 2020 Jan 26. [Epub ahead of print].
13. Pinsky PF. Recommendations related to genetic testing for breast cancer. JAMA. 2020 Jan 14; 323(2): 187–188.
14. Karamysheva TV, Matveeva VG, Shorina AR, Rubtsov NB. Clinical and molecular-cytogenetic analyses of a rare case of mosaicism for partial monosomy 3p and partial trisomy 10q in Man, Genetika (Moscow), 2001; 37(6): 811–816.
15. Burke W, Daly M, Garber J, Botkin J, Kahn MJ, Lynch P, et al. Recommendations for follow-up care of individuals with an inherited predisposition to cancer. II. BRCA1 and BRCA2. Cancer Genetics Studies Consortium. JAMA 1997 Mar 26; 277(12): 997–1003.
16. Yang S, Axilbund JE, O'leary E, Michalski ST, Evans R, Lincoln SE, et al. Underdiagnosis of hereditary breast and ovarian cancer in medicare patients: genetic testing criteria miss the mark. Ann Surg Oncol 2018 Oct; 25(10): 2925–2931.
17. Abul-Husn NS, Soper ER, Odgis JA, Cullina S, Bobo D, Moscati A, et al. Exome sequencing reveals a high prevalence of BRCA1 and BRCA2 founder variants in a diverse population-based biobank. Genome Med 2019 Dec 31; 12(1): 2.
18. Lynch HT, Smyrk T, Lynch JF. Molecular genetics and clinical-pathological features of hereditary nonpolyposis colorectal carcinoma (Lynch syndrome): historical journey from pedigree anecdote to molecular genetic confirmation. Oncology 1998 Mar-Apr; 55(2): 103–108.
19. Narod SA, Ford D, Devilee P, Barkardottir RB, Lynch HT, Smith SA, et al. An evaluation of genetic heterogeneity in 145 breast-ovarian cancer families. Breast Cancer Linkage Consortium. Am J Hum Genet 1995 Jan; 56(1): 254–264.
20. Olsen JH, Seersholm N, Boice JD, Krüger Kjær S, Fraumeni Jr JF. Cancer risk in close relatives of women with early-onset breast cancer – a population-based incidence study. Br J Cancer 1999 Feb; 79(3–4): 673–679.
21. Sachidanandam R, Weissman D, Schmidt SC, Kakol JM, Stein LD, Marth G, et al. A map of human genome sequence variation containing 1.42 million single nucleotide polymorphisms. Nature 2001 Feb 15; 409(6822): 928–933.
22. Struewing JP, Hartge P, Wacholder S, Baker SM, Berlin M, McAdams M, et al. The risk of cancer associated with specific mutations of BRCA1 and BRCA2 among Ashkenazi Jews. N Engl J Med 1997 May 15; 336(20): 1401–1408.
23. Informatcionnaia sistema ucheta i monitoringa onkologicheskikh zabolevanii: pat. No 675 Resp. Belarus O.E. Kuznetcov; zaiavitel Kuznetcov O.E. – S20140041; opubl.

20.06.2014 Afitcyiny biul. Natc. tcentr intelektual. Ulasnastci. (In Russian).
24. Rojas K, Stuckey A. Breast cancer epidemiology and risk factors. Clin Obstet Gynecol 2016 Dec; 59(4): 651–672.
25. Gardovski A. Clinical and molecular features of hereditary breast and ovarian cancer in Latvia. Riga: P. Stradin University; 2008.
26. Rodriguez-Bigas MA, Boland CR, Hamilton SR, Henson DE, Jass JR, Khan PM, et al. A national cancer institute workshop on hereditary nonpolyposis colorectal cancer syndrome: meeting highlights and Bethesda guidelines. J Natl Cancer Inst 1997 Dec 3; 89(23): 1758–1762.

Word count: 2740 • Tables: 4 • Figures: – • References: 26

Sources of funding:
The research was funded by the authors.

Conflicts of interests:
The authors report that there were no conflicts of interest.

Cite this article as:
Kuzniatsou A, Shpakou A.
Organizational forms and methods of early diagnosis of hereditary tumors.
MSP 2020; 14, 1: 15–20. Published online: 31 Mar 2020.

Correspondence address:
Andrei Shpakou PhD, MD
Yanka Kupala State University of Grodno
Belarus, Grodno, 230023, 22 Ozheshko str.
E-mail: shpakofff@tut.by

Received: 20.03.2020
Reviewed: 26.03.2020
Accepted: 26.03.2020

e-ISSN 2544-1620

Medical Science Pulse 2020 (14) 1

Original papers

Published online: 30 Mar 2020

DOI: 10.5604/01.3001.0014.0685

SOMATIC SYMPTOMS AND LEVEL OF ANXIETY AND DEPRESSION IN SELF-REFERRAL PATIENTS AT THE EMERGENCY DEPARTMENT

Ada Lisowska[1 A–G]
• ORCID: 0000-0002-1891-0788
Katarzyna Szwamel[2 D,E,G]
• ORCID: 0000-0001-8186-9979
Donata Kurpas[3 D,E,G]
• ORCID: 0000-0002-6996-8920

[1] Emergency Department, Opole University Hospital, Opole, Poland
[2] Opole Medical School, Opole, Poland
[3] Department of Family Medicine, Wrocław Medical University, Wroclaw, Poland

A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: Due to multiple morbidities, patients experience various symptoms that may be of psychogenic or somatic origin. Anxiety and depression can induce somatization and the feeling that ailments require urgent medical intervention.

Aim of the study: This study aimed to: (1) identify which symptoms self-referral patients most commonly report at the emergency department (ED) and which medical diagnoses they are discharged with; and (2) determine whether the type and severity of symptoms, as well as, sociodemographic variables are related to anxiety and depression levels.

Material and methods: The study included 110 patients who self-referred to the ED at the University Clinical Hospital in Opole. Diagnostic surveys and questionnaires were used, including the Hospital Anxiety and Depression Scale and an original questionnaire developed by the authors.

Results: Among those suffering from chronic diseases (n = 53; 48.62%), 12 patients (22.64%) did not complete a single visit to the PHCF (Primary Health Care Facility), and 30 patients (56.60%) did not complete a visit to OSC (Outpatient Specialist Care) during the previous 12 months. The most common cause of reporting to the ED were pain and a burning sensation in the chest (n = 29; 27.10%). During discharge, the most common diagnosis was "other chest pains" (n = 22; 20.00%). 82.73% (n = 91) of patients had clear anxiety disorders, and 68.18% (n = 75) had clear depressive disorders.

Conclusions: In case of somatic symptoms without a discernible cause in patients, it is necessary to implement comprehensive measures within PHCF, such as periodic measurements of anxiety and depression severity, psychological consultation, and an in-depth medical interview. These data also suggest that proper clinical monitoring should be implemented, including clinical parameters relevant for chronic diseases and the number of visits to the PHCF and OSC.

KEYWORDS: hospital emergency medical services, patients, anxiety, depression

Background

Over the last two decades, more and more patients have been seeking help in the emergency department (ED). The phenomenon of overload of these departments may be due, in part, to demographic aging of the population, an increase in the number of people suffering from chronic diseases, organizational problems at the level of primary care, and 24-hour availability of benefits in this department [1].

Nowadays, multiple morbidity is common among aging populations around the world [2]. Markun et al. report that over 30% of ED patients have two to four coexisting diseases [3]. Sarnaki et al. report that 19–42% of the population is living with three or more coexisting diseases [4].

Due to multiple morbidity, patients experience various symptoms that may be of psychogenic or organic origin. Patients with somatoform disorders currently

constitute a particular challenge for healthcare systems. These disorders are characterized by significant distress or functional impairment associated with one or more somatic symptoms or fear of a serious illness in the absence of somatic symptoms [5]. Patients affected by somatic symptom disorder suffer mainly from subjective physical complaints, most often including headache, abdominal pain, chest pain, back/neck complaints, gastrointestinal symptoms, kidney issues, seizures, vertigo, fibromyalgia, paresthesia, visual disturbances, or amnesia [6–9]. Symptoms such as those can affect any part of the body, and can range from minor occasional problems to severe and persistent symptoms resulting in functionally impaired states [10]. In addition to the term "somatoform disorders", researchers also use other terms, such as: functional somatic symptoms (FSS), medically unexplained symptoms (MUS), bodily distress syndromes (BDS), or somatic symptom disorder (SSD) [5].

MUS accounts for approximately 20% of new consultations in primary care and 20%–25% of all frequent attenders at medical clinics [10]. The ED is one of the services used the most by young people suffering from somatoform symptoms [11]. Alsma et al. (2017) showed that medically unexplained physical symptoms at the ED were present in 13.4% of all visits. These patients were often younger, frequent visitors reporting on their own, had fewer medications prescribed, and suffered from a psychiatric disease more often [9,12]. Across cultures, women are more likely to report somatoform disorders than men [13]. Somatoform disorders often coexist with depression and anxiety [14]. Moreover, Sporinova et al. (2019) claim that people with chronic disease show higher rates of mental health disorders, while people with mental health disorders have a greater risk of developing chronic diseases [15]. For example, in a Greek study, 19.1% of patients hospitalized with coronary disease experienced moderate depression, while 20% experienced severe depression [16]. Other researchers showed that 50% of the diabetic patients showed mild depression symptoms, with 20% showing symptoms [17]. The prevalence of clinical anxiety among COPD patients ranges between 13% and 46% [18].

It has been demonstrated that the prevalence of depression is significantly greater among patients in the ED as compared to the general population [13–14]. According to Hoyer and David, about 1 in 5 ED patients may be suffering from depression [19]. Other studies showed that the prevalence of depression among ED patients ranges from 27% to 42% [4,20]. On the other hand, anxiety most often occurs in patients experiencing pain and dyspnea [21–23]. In a study by Wells at al. (2018), 33% ED patients with pain reported anxiety [21]. Craven et al. (2013) enrolled 10,664 ED patients presenting with pain-related complaints and showed the following patient rates in terms of those reporting anxiety: 25.7%, none; 26.1%, mild; 23.7%, moderate; and 24.5%, severe [22]. Among patients with respiratory symptoms, 11% reported anxiety, 2.5% depression, and 4% reported both anxiety and depression [23].

One significant health policy challenge in many European countries at present is to develop strategies to deal with the increase in patient attendance to hospital EDs [5]. Patients with MUS may present frequently to hospital settings and receive potentially unnecessary investigations and treatments [24]. Many studies shown a strong relationship between somatization and excess healthcare costs resulting from high numbers of visits to healthcare facilities, repeated diagnostic testing, and costly treatments [8,25]. Having considered the foregoing, it is reasonable to carry out research focusing on the multiple morbidity of ED patients, concerning their somatic symptoms, as well as, anxiety and depression level in this group, in order to achieve the best possible understanding of this phenomenon.

Aim of the study

The present study aimed to: (1) demonstrate the chronic diseases for which ED patients are treated and the symptoms with which they most often report upon self-referral to the ED; (2) assess the level of anxiety and depression in this group; and (3) determine whether the type of symptoms, severity of symptoms, and/or sociodemographic variables determine levels of anxiety and/or depression.

Material and methods

Study design

A cross-sectional study was conducted in 2017. The study was started after obtaining permission from the Institutional Review Board at the Opole Medical School, No. 15/PI/2017. This study used diagnostic surveys and questionnaires.. The study was carried out in accordance with the requirements of the 1975 Helsinki Declaration (as amended in 2000) and Good Clinical Practice guidelines. ED patients received questionnaires after leaving the triage office. Initially, a group of 130 patients accepted the study invitation. 110 completed surveys were returned, so the maneuverability index was 84.61%. The ICD10 nomenclature was used to establish the diagnosis with which the patient was discharged from ED. These data were obtained from CGM Clininet computer system, version 7.69.8.

Settings

Participants in the study were enrolled from the ED at the University Clinical Hospital in Opole.

Participants

110 patients, who returned completed questionnaires were qualified for the study. The study included patients who met the following criteria: over 18 years of age; reported to the ED on their own without a medical referral; reported with internal complaints (e.g., cardiovascular, respiratory, related to gastrointestinal tract)

and without trauma or without cognitive disorders; in a state of health that allowed them to complete the study questionnaires; and expressed conscious consent to participate in the study. Exclusion criteria consisted of: under 18 years of age; submitted with a medical referral or were brought in by the emergency medical team; patients who were in a general severe condition that made it impossible to carry out the study; without logical contact; with injuries, and patients who did not agree to participate in the study.

Sociodemographic characteristics of study participants is showed in Tab. 1.

Table 1. Sociodemographic characteristics of ED patients of the University Clinical Hospital in Opole.

Trait		Value
Age [years]	M± SD	46.07±15.37
	median	43
	quartiles	34–59
Sex	Females	52 (47.27%)
	Males	58 (52.73%)
Marital status	In a relationship	82 (74.55%)
	Single	28 (25.45%)
Place of residence	Countryside	45 (40.91%)
	A city of up to 20,000 inhabitants	10 (9.09%)
	A city of 20–100,000 inhabitants	11 (10.00%)
	A city of 100,000–500,000 inhabitants	41 (37.27%)
	A city of over 500,000 inhabitants	3 (2.73%)
Education	Primary	8 (7.27%)
	Vocational	23 (20.91%)
	Secondary	38 (34.55%)
	Higher	41 (37.27%)
Status on the labor market	Employed	74 (67.27%)
	Unemployed	6 (5.45%)
	Retirees and pensioners	27 (24.55%)
	Students	3 (2.73%)
Self-reported financial situation	Very good	1 (0.91%)
	Rather good	9 (8.18%)
	Average	60 (54.55%)
	Rather poor	36 (32.73%)
	Poor	4 (3.64%)

Legend: M - mean, SD - standard deviation

Variables

The following groups of variables have been identified:

a. sociodemographic variables: age, gender, marital status, education, place of residence, labor market status, financial situation
b. anxiety level, depression level, number of visits to primary healthcare facilities (PHCF) in the previous 12 months, number of visits to outpatient specialist care clinics (OSC) in the previous 12 months
c. type of somatic symptoms: chest pain, elevated blood pressure, abdominal pain, other symptoms with which the patients have reported to the ED
d. the severity of the symptoms with which the patient reported to the ED. Symptoms were assessed on a 10-degree numerical scale, where 1 indicates weak intensity of a given symptom and 10 indicates the highest symptom intensity.

Data sources/measurement

The research was conducted using the *Hospital Anxiety and Depression Scale* (HADS), developed by Zigmond and Snaith [26], and an original questionnaire developed by the authors.

HADS was used to investigate the severity of anxiety and depression in patients. This questionnaire is a screening tool used to detect anxiety- and depression-related disorders. The study used the Polish version of HADS – M, which is a modification of HADS adapted by Majkowicz, de Walden-Gałuszko, and Chojnacka-Szawłowska. The tool consists of two subscales – depression and anxiety. A version consisting of 14 questions was used. Of note, this version does not include an aggression measurement. The following thresholds were used to analyze the prevalence of symptoms: 0–7 points – no disorders, 8–10 points – borderline states, more than 10 points – disorders are found (high level, appropriate for the disease) [27].

An original questionnaire developed by the authors was also used. This questionnaire consisted of items concerning: sociodemographic profile of the study subjects, chronic diseases treated in patients, the number of visits to PHCF and OSC outpatient clinics in the previous 12 months, the chronic use of medicines, the type of symptoms with which the patients reported to ED and their severity.

Statistical analyses

Statistical analyses used parametric or non-parametric tests as appropriate, depending on the departure of the variable of interest(s) from normality. Normality of variable distribution was tested using the Shapiro-Wilk test.

Comparison of the quantitative variable values in two groups was performed using Student's t-test or Mann-Whitney's test, as appropriate.

The comparison of the quantitative variable values in three and more groups was performed using ANOVA or the Kruskal-Wallis test, as appropriate.

Correlations between quantitative variables were analyzed using the Pearson's or Spearman's correlation coefficients, as appropriate. When the patient indicated more than one symptom to measure the strength of correlation between the level of anxiety and depression and the severity of symptoms, the calculations only included the symptom severity that was rated as the highest by the patient. The strength of

the relationship was interpreted according to the following scheme: $|r| \geq 0.9$ – very strong relationship, $0.7 \leq |r| < 0.9$ – strong relationship, $0.5 \leq |r| < 0.7$ – moderately strong relationship, $0.3 \leq |r| < 0.5$ – weak relationship, $|r| < 0.3$ – very weak relationship (i.e., negligible) [28].

If a patient reported several symptoms, the symptom with the greatest severity was taken into account to investigate the relationship between HADS and the severity of the symptoms that the patient reported with to ED.

Analyses assumed a significance level of 0.05. Analyses was performed in R software, version 3.6.1 [29].

Results

Chronic diseases of the subjects, symptoms with which patients most often reported upon self-referral to the ED, and medical diagnoses on the discharge report

Fifty-three (48.62%) survey respondents had chronic diseases, and 48 people (44.86%) took medication on a continuous basis because of these diseases. Self-referred ED patients were treated most often due to such coexisting diseases, such as: arterial hypertension (30; 56.60%), atrial fibrillation and flutter (10; 18.87%), thyroid disease (8; 15.09%), ischemic heart disease (6; 11.32%), and bronchial asthma (6; 11.32%) (Tab. 2).

Table 2. Chronic diseases in the study group.

Chronic diseases*	n	percentage
Arterial hypertension	30	56.60%
Atrial fibrillation and flutter	10	18.87%
Thyroid diseases	8	15.09%
Ischemic heart disease	6	11.32%
Bronchial asthma	6	11.32%
Atherosclerosis	5	9.43%
Gastrointestinal reflux	5	9.43%
Heart insufficiency	4	7.55%
Osteoarthritis	4	7.55%
Insulin-dependent diabetes	4	7.55%
Angina pectoris	3	5.66%
Urolithiasis	3	5.66%
Heart valve defects	2	3.77%
Osteoporosis	2	3.77%
Digestive ulcer	2	3.77%
Cholelithiasis	2	3.77%
Aneurysms	1	1.89%
Chronic obstructive pulmonary disease	1	1.89%
Bronchial dilatation	1	1.89%
Rheumatoid arthritis	1	1.89%
Chronic kidney failure	1	1.89%
Glomerulonephritis	1	1.89%
Adrenal insufficiency	1	1.89%

Legend: * - patients could indicate more than one chronic disease

Out of all the respondents, 41 patients (37.27%) reported visiting the PHCF facility in the previous 12 months, and a group of 23 patients (20.91%) had follow-ups concerning their chronic diseases in OSC at that time (Tab. 3). Among those suffering from chronic diseases, 12 people (22.64%) did not have a single visit to PHCF and 30 (56.60%) did not visit OSC at that time.

Table 3. Visits in the last 12 months due to chronic diseases in primary and specialist outpatient clinics.

Number of visits	N	%
Visits to a primary healthcare facility (PHCF)		
No visits	69	62.73%
1–3 visits	21	19.09%
4–6 visits	10	9.09%
7 visits and more	10	9.09%
Total	110	100.00%
Visits to a specialist doctor in an outpatient specialist care outpatient clinic (OSC)		
No visits	87	79.09%
1 visit	5	4.55%
2 visits	6	5.45%
3 visits	8	7.27%
4 visits	4	3.64%
Total	110	100.00%

The symptoms that were the most common cause of the report were: pain, chest burning (29; 27.10%), abdominal pain (26; 24.30%), high arterial blood pressure (17; 15.89%), palpitations (9; 8.41%), general malaise (7; 6.54%), headaches (4; 3.74%), dyspnea (3; 2.80%), diarrhea (3; 2.80%), fever above 38 degrees C – (3; 2.80%), coughing (2; 1.87%), vomiting (2; 1.87%), weakness, fatigue (1; 0.93%), and other symptoms (1; 0.93%).

The most common diagnoses made during the discharge from the ED were: other chest pain (R07.3) – 22 persons (20.00%), essential (primary) hypertension (I10) – 15 persons (13.64%), pain localized to upper abdomen including epigastric (R10.4) – 10 persons (9.09%), cardiac arrhythmia, unspecified (I49) – 6 (5.45%), functional dyspepsia (K30) – 6 (5.45%), and malaise and fatigue (R53) – 4 (3.64%) (Tab. 4).

Anxiety and depression levels and their determinants

Sten score analysis showed that 82.73% (91) of survey respondents had clear anxiety disorders (11–21 points in the HADS questionnaire), 14.55% (16) had borderline anxiety (8–10 points), whereas only 2.73% (3 persons) had no disorders (0–7 points).

The median intensity of depression was 11 points (min – max; 4–20 points). 68.18% (n = 75) of ED patients had a clear depressive disorder (11–21 points) and 30.00% (n = 33) had borderline depressive disorders (8–10 points). Only 1.82% (2 people) did not have depressive disorders (0–7 points).

There was no significant correlation between the age of patients and the severity of anxiety (rs =0.051,

Table 4. Medical diagnoses according to the ICD – 10 placed on patients upon discharge from the ED.

Diagnosis according to ICD – 10	n	Percentage
Other chest pain (R07.3)	22	20.00%
Essential (primary) hypertension (I10)	15	13.64%
Pain localized to upper abdomen. Incl.: Epigastric (R10.4)	10	9.09%
Cardiac arrhythmia, unspecified (I49)	6	5.45%
Functional dyspepsia (K30)	6	5.45%
Malaise and fatigue (R53)	4	3.64%
Angina pectoris, unspecified (I20.9)	4	3.64%
Unspecified renal colic (N23)	4	3.64%
Other and unspecified allergy (T78.4)	3	2.73%
Neuralgia and neuritis, unspecified [intercostal neuralgia] (M79.2)	3	2.73%
Hypertension (I10)	3	2.73%
Acute pharyngitis, unspecified [upper respiratory tract infection] (J02.9)	3	2.73%
Other disorders of electrolyte and fluid balance, not elsewhere classified (E87.8)	3	2.73%
Urinary tract infection, site not specified (N39.0)	3	2.73%
Congestive heart failure [acute chronic heart failure] (I50.0)	2	1.82%
Other soft tissue disorders, not elsewhere classified [soft tissue diseases related to overload] (M79)	2	1.82%
Gastritis (R29.7)	2	1.82%
Other viral enteritis [intestinal rhinitis] (A08.3)	2	1.82%
Acute biliary pancreatitis (K85)	1	0.91%
Intestinal colic (K92)	1	0.91%
Pneumonia, unspecified organism (J18.9)	1	0.91%
Bronchitis (J20)	1	0.91%
Pancreatitis (K85)	1	0.91%
Constipation (K59.0)	1	0.91%
Laryngitis (J04.0)	1	0.91%
Suspected perforation of the large intestine diverticulum (K63.1)	1	0.91%
Upper gastrointestinal bleeding (R04)	1	0.91%
Syncope (R55)	1	0.91%
Other unspecified headaches (G44.8)	1	0.91%
Dizziness (R42)	1	0.91%
Myocardial infarction (I21)	1	0.91%
Total	110	100.00%

p=0.599). Moreover, no correlation was found between the severity of anxiety and sex (p=0.287), marital status (p=0.167), place of residence (p=0.754), education (p=0.589), employment status (p=0.290) and financial situation of respondents (p=0.263) (Tab. 5).

The level of depressive disorders depended significantly only on the professional activity of the subjects. In particular, depression level was higher in subjects who did not work (Me= 12, min – max; 11–14) as compared to professionally active subjects (Me= 11, min – max; 10–12) (p<0.001). The other sociodemographic variables were not related to the severity of depressive disorders (Tab. 6).

Table 5. Analysis of the relationship between qualitative demographic variables and the intensity of anxiety.

Trait		HADS – anxiety [score]			p *
		M±SD	median	Quartiles	
Sex	Females (N=52)	13.15±3.16	13.5	10-15.25	0.287 P
	Males (N=58)	13.74±2.59	14	12-16	
Marital status	In relationship (N=82)	13.68±2.85	14	12-16	0.167 NP
	Single (N=28)	12.82±2.89	13	10.75-15	
Place of residence	Countryside (N=45)	13.8±2.53	14	12-16	0.754 NP
	City of up to 100,000 inhabitants (N=21)	13.43±2.98	14	12-15	
	City of more than 100,000 inhabitants. (N=44)	13.14±3.17	14	10.75-16	
Education	Primary, Vocational (N=31)	13.84±2.98	15	12.5-16	0.589 NP
	Secondary (N=38)	13.34±2.58	14	12-15	
	Higher (N=41)	13.29±3.09	13	11-15	
Employment status	Professionally active (N=77)	13.27±2.92	14	12-15	0.290 P
	Professionally inactive (N=33)	13.91±2.77	15	13-16	
Financial situation	Very good. Rather good. (N=10)	13.6±2.59	14	12.25-15.5	0.263 P
	Average (N=60)	13.83±2.73	14	12-16	
	Rather poor or poor (N=40)	12.88±3.11	13	10-15	

Legend: * P = Normal distribution in groups, Student t-test (for comparison of 2 groups) or ANOVA (for >2 groups); NP = No normal distribution in groups, Mann-Whitney test (for 2 groups) or Kruskal-Wallis test (for >2 groups), M – mean, SD – standard deviation.

Table 6. Analysis of the relationship between qualitative demographic variables and the severity of depression.

Trait		HADS - depression [score]			p *
		M±SD	median	Quartiles	
Sex	Females (N=52)	11.69±2.59	12	10-13	0.567 NP
	Males (N=58)	11.47±2.23	11	10-13	
Marital status	In relationship (N=82)	11.49±2.42	11	10-13	0.581 NP
	Single (N=28)	11.82±2.36	12	10-13	
Place of residence	Countryside (N=45)	11.6±2.24	12	10-13	0.999 NP
	City of up to 100,000 inhabitants (N=21)	11.48±1.4	11	11-12	
	City of more than 100,000 inhabitants. (N=44)	11.59±2.92	11	10-13	
Education	Primary, Vocational (N=31)	12.35±2.74	12	11-13	0.139 NP
	Secondary (N=38)	11.61±2.03	12	10-13	
	Higher (N=41)	10.95±2.31	11	10-12	
Employment status	Professionally active (N=77)	11.03±2.1	11	10-12	<0.001 NP
	Professionally inactive (N=33)	12.85±2.6	12	11-14	
Self – reported financial situation	Very good. Rather good. (N=10)	11.1±3	10	9-12.75	0.359 NP
	Average (N=60)	11.7±1.92	12	10.75-13	
	Rather poor. Poor. (N=40)	11.5±2.89	11	10-13	

Legend: * P = Normal distribution in groups, Student t-test (for comparison of 2 groups) or ANOVA (for >2 groups); NP = No normal distribution in groups, Mann-Whitney test (for 2 groups) or Kruskal-Wallis test (for >2 groups), M – mean, SD – standard deviation.

There were no significant relationships between the severity of symptoms reported by patients upon self-referral to the ED, and their anxiety level (r_S=0.107, p=0265). There was also no significant association between the severity of symptoms and the level of depression (r_S= 0.008, p=0. 933).

The mean level of severity of anxiety in patients with chest pain was 13.1±2.5; 13.53±3.69 in patients with high blood pressure; 13.35±3.19 in patients with abdominal pain; and 13.79±2.58 in patients with other symptoms. Severity of anxiety was not correlated with reporting to the ED due to chest pain, high blood pressure, abdominal pain, or other symptoms (p=0.807).

The median intensity of depression in the group of patients reporting to the ED due to chest pain was 12 (min–max; 10–13), 13 (min–max; 11–13) in patients with high BP, 11 (min–max; 9.25–12) in patients with abdominal pain, and 11 (min–max 10–13) in patients with other symptoms. There was no significant correlation between the severity of depression and reporting to ED due to the foregoing symptoms (p=0.142) (Tab. 7).

Discussion

Key results

Nearly half of the self-referred ED patients were treated due to chronic diseases. Some of the chronically ill patients did not have a single visit to the PHCF or OSC in the previous 12 months. The most frequent reasons for reporting to the ED were symptoms such as pain, burning sensation in the chest, stomachache, high blood pressure, and palpitations. The vast majority of the survey respondents had clear a anxiety or depressive disorder. None of the sociodemographic variables were associated with anxiety levels among patients. The level of depressive disorders was shown to differ based on the professional activity of the respondents, only.

Interpretation

Chronic diseases and patient symptoms among patients who self-referred to the ED

In our sample of 53 patients, patients indicated they had different chronic diseases 73 times. Thus, each patient reported suffering from more than one disease, on average. The respondents were most often affected by chronic diseases, such as: hypertension, atrial fibrillation and flutter, thyroid diseases, ischemic heart disease, and bronchial asthma. In a study by Dikme et al., 63% of patients indicated the presence of at least one coexisting disease [30]. Markun et al. demonstrated that 27.7% of patients reporting the simultaneous presence of 5–7 diseases, while 26.5% reported the presence of 8–10 diseases [3]. Of note, nearly half of the patients in their study with multiple morbidities were between the ages of 60 and 79 years [3]. In the present study, we found that of the patients with chronic diseases, 12 (22.64%) did not have a single visit to the PHCF and 30 (56.60%) did not visit OSC in the previous 12 months. Lack of reporting to OSC may result from the long waiting time for guaranteed services in Poland. According to the Watch Health Care Foundation (WHC) Barometer as of December/January 2019, the mean waiting time for a single guaranteed health service in Poland is 3.8 months. Long waiting times mainly concern OSC services. Patients encounter waiting lists for many months trying to schedule a visit to a specialist, a basic diagnostic examination, or a surgery [31]. However, it is difficult to explain the lack of visits of chronically ill patients to a PHCF doctor, as the availability of PHCF is assessed positively by the majority of Polish people (68%) [32]. Therefore, the reasons why patients with chronic diseases do not report to PHCFs require further investigation.

Anxiety and depression and their determinants

According to the World Health Organization (WHO), over 300 million people around the world suffer from depression and 264 million suffer from anxiety disorders [33]. Fogarty et al. also report that anxiety and depression are the two most common mood disorders, with a prevalence of 26.7% and 23.2%, respectively [34]. The results of our study showed that 82.73% (n = 91) of survey respondents had clear a anxiety disorder and 14.55% (n = 16) had a borderline case of an anxiety disorder. In addition, as many as 68.18% (n = 75) of patients had a clear depressive disorder, and 30.00% (n = 33) of patients had a borderline case of a depressive disorder. In Saudi Arabia, anxiety and depression were

Table 7. The level of severity of anxiety and depression and the type of symptoms that patients reported to ED.

HADS		Pain, burning sensation in the chest (N=29)	High blood Pressure (N=17)	Stomachache (N=26)	Other (N=38)	p *
Anxiety	M±SD	13.1±2.5	13.53±3.69	13.35±3.19	13.79±2.58	0.807 P
	Median	13	14	14	14	
	quartiles	11-15	11-16	12-15.75	12-16	
Depression	M±SD	11.86±2.29	12.41±2.53	10.92±2.08	11.42±2.56	0.142 NP
	Median	12	13	11	11	
	quartiles	10-13	11-13	9.25-12	10-13	

Legend: * P = Normal distribution in groups, ANOVA; NP = No normal distribution in groups, Kruskal-Wallis test, M – mean, SD – standard deviation.

observed in 27.2% and 23.0% of ED patients, respectively [35]. In a study conducted among ED patients in the USA, 33% of ED patients with pain reported anxiety [21]. In a study by Craven et al (2013), 48% of patients described moderate to severe anxiety at ED presentation [22]. Abar et al. showed that depression was relatively common in a sample of ED patients, with mean values in the "mild depression" range and 18% of patients reporting at least "moderate depression" [7]. As we can see, our own results concerning the prevalence of anxiety and depression among ED patients are much higher than those obtained by other authors. Such a large difference in percentages between our own study and the above-mentioned studies can be explained, in part, by the criteria for patient selection for the study sample; that is, our study sample consisted only of self-referred ED patients, whereas previous studies examined self-referred patients as well as surgically-referred patients. Further studies are needed to test the hypothesis that self-referred ED patients experience anxiety more frequently as compared to patients reporting to the surgical part of the ED. For example, further studies should be conducted on a larger test sample, in several EDs, and using other tools to measure anxiety and depression levels.

The presence of disease symptoms or the co-existence of other diseases in addition to the underlying disease may be associated with patient's anxiety concerning his or her condition. An analysis conducted by Nowicka-Sauer et al. in a group of patients with chronic diseases shows significantly higher levels of anxiety as compared to depression (i.e., 7 vs. 4 points in the HADS questionnaire). According to the authors, the disease most predisposing to the anxiety disorder presence was systemic lupus, with 55.6% of patients with lupus reporting anxiety. In contrast, anxiety symptoms were reported by 50% of patients with RA, 31.4% of patients with myocardial infarction, and 20% of patients with stroke [36].

The literature shows that patients with a diagnosis of group F-45 in the ICD 10 classification ('somatic disorders') are often diagnosed with coexisting diseases such as anxiety disorders and depression. A study by Leutgeb et al. compared the percentage of pain symptoms in two study groups: "F-45 patients" and "non-F45-patients". They found that back pain was present in 4.99% of patients with a diagnosis of F-45 and 3.29% without such diagnosis. Similarly, abdominal pain was present in 4.56% vs. 2.97%, and throat and chest pain in 1.58% vs. 0.99% [5]. On the other hand, Abar et al. observed somatization among patients with depression and anxiety disorders in the form of chest pain (16% for depression and 23% for anxiety) and abdominal pain (14% for depression and 23% for anxiety) [7]. A study in Brazil reports that chest pain in patients reporting to ED is correlated with anxiety (33.9%) and depression (30.5%) [37]. Similar results were reported in a study from India, wherein depressive and anxiety disorders in patients reporting to ED for chest pain were identified in 23% [38]. In our study, there were no significant correlations between the severity of anxiety and reporting to ED due to chest pain, high blood pressure, abdominal pain, or other symptoms (p=0.807). There was also no significant correlation between the severity of depression level and reporting to ED due to the foregoing symptoms.

Patients may interpret their ailments as requiring a visit to ED because of their perceived anxiety [30]. Many patients with somatic symptoms are frequently subjected to invasive diagnostic tests; however, psychological factors are not sufficiently analyzed [39]. Shindhaye et al. suggest a strong association between somatoform disorders and depression/anxiety (with odds ratios ranging from 2.5–3.5) [13]. Research by Hsia and Niedźwiecki shows that mood disorders such as anxiety and depression were diagnosed in 6.8% of non-urgent ED visits, i.e. those which were not caused by the patient's health- or life-threatening condition and did not require tests and diagnostics [40]. According to Lubszczyk et al., 28.37% of patients in the ED seek help because of cardiovascular problems, and 18.86% seek help because of symptoms and abnormal test results [41]. It is worth noting that many researchers associate the presence of non-cardiac chest pain with somatization of anxiety and depression. In our study, 27.10% of survey respondents reported to the ED due to chest pain, and 20% were subsequently discharged from the ED with a diagnosis of "other chest pains" (R07.3 according to ICD-10). As mentioned by Croicu & Chwiastiak, somatization can occur among patients with chronic medical conditions, such as cardiovascular disease or chronic obstructive pulmonary disease [39].

One of the aims of the present study was to determine whether sociodemographic variables determine the level of anxiety and depression. The level of depressive disorders in our study varied significantly only on the professional activity of the respondents; with higher levels of depression reported in inactive patients relative to active ones. This result may have been due to the relatively limited number of patients who qualified for this study. However, in our study, severity of anxiety was not significantly correlated with age, sex, marital status, place of residence, employment status, nor self-reported financialsituation of the respondents. In a study by Salsberry et al., anxiety disorders were reported in 80% (48) of women and 20% (12) of men, and the age group from 45 to 54 years old was the most numerous for this diagnosis [42]. In a study by Dark et al., women constituted 62% of anxiety-related ED visits compared with all-cause ED visits, with visits related to anxiety disorders being more frequent in non-urban areas [43]. A study by Weiss et al. also did not find a significant correlation between sociodemographic variables (such as sex and age) and the presence of mood disorders. Indeed, according to Weiss et al., the number of visits to the ED that were associated with depression, anxiety, and acute responses to stress increased by 49.7% among both women and

men across the years 2006–2013 [44]. However, a relationship between the incidence of mood disorders and gender was not reported in a study by Fogarty et al., in which patients were divided according to the type of mental disorder they had. In the category of depressive disorders, women constituted 24.5% of the surveyed population, compared to 21.2% of men. In the category of anxiety disorders, in contrast, woman constituted 19.8% of the surveyed population as compared to 21.3% of me [34]. Uchmanowicz and Gobbens who conducted studies in a population of individuals over 60 years of age using the HADS scale. The researchers found relatively high levels of anxiety and depression, with levels at 9.5 and 8.8, respectively [45].

The level of depressive disorders in the present study depended significantly only on the professional activity of the respondents, with higher levels reported in the inactive patients as compared to the active ones. The other sociodemographic variables did not differentiate the level of depressive disorders. In the aforementioned study by Nowicka-Sauer, the level of depression and anxiety among women than men (i.e., 5 vs. 4 points for depression and 8 vs. 5.5 points for anxiety, respectively) [36].

Patients with anxiety and depression may perceive their health in a different way than medical personnel. Dikme et al. analyzed the assessment of condition severity made by the patients themselves and also by doctors. 14.1% of respondents described their condition as "not very serious" (38.5% according to doctors), 39.7% as "not serious" (32.7%), 27.9% as "normal" (26%), 15.8% as "serious" (2.7%), and 2.5% as "very serious" (0.1%). Among patients classified as "not serious" by ED doctors, 96.7% were discharged, while 37.5% of patients classified as "serious" were discharged. Also, the study by Dikme et al. found that 17.6% of respondents believed that their condition required hospital admission [30]. These data suggest a subjective approach to the patient as early as at the level of outpatient care, and highlights the critical need to identify the influence of mental factors on the general condition of the patient [46]. At the level of this care, any barriers to access to health services (e.g., care for a sick family member, lack of transport means, shame of the disease) should be determined and help should be provided to eliminate these barriers [7]. This allows for a quicker diagnosis of mental problems to prevent potential consequences, such as job loss, or financial and family problems [39].

Generalizability

The study examined the prevalence of anxiety and depression among self-referred ED patients and found high levels of these disorders. These data suggest that, in case of somatic symptoms in patients with no apparent cause, the patient's history should be broadened each time with questions about the occurrence of severe stress, anxiety symptoms, and deteriorating mood. We recommend the use of tools that can assist with diagnosing the most common mental disorders, such as the Patient Health Questionnaire (PHQ) – 9 or the Generalized Anxiety Disorder (GAD-7). These questionnaires show a high level of sensitivity, and can allow medical providers to determine the risk of their occurrence as early as the patient's first visit, which is important for the context of a primary healthcare physician's office [47].

Limitations of the study

The study was limited by focusing on only one ED and a relatively small group of patients. The latter limitation resulted from the fact that not all patients met the inclusion criteria during the observation period. Therefore, the results have limited generalizability to a wider population. Another limitation of the study was the use of only one standardized tool to measure levels of anxiety and depression. In the future, other tools should be used, such as the Beck Depression Inventory, the Spielberger State Anxiety Inventory (SSAI), and the Trait (STAI) Anxiety Inventory [48,49].

Conclusions

1. Self-referred ED patients most often report due to thoracic pain and/or a burning sensation. During discharge, these patients are most often diagnosed with "other chest pains." In addition, nearly half of the patients were diagnosed with chronic diseases, and most patients had clear anxiety or depression disorder. Taken together, these data suggest that comprehensive measures should be taken for this group of patients at the primary healthcare level.
2. In case of a patient's somatic symptoms without an apparent cause, we suggest that: (1) the PHCF physician should broaden the interview with questions about the presence of severe stress, anxiety symptoms, and mood deterioration; (2) trained PHCF nurses should periodically assess the severity of anxiety and depression using standardized tools; and (3) the patient should be referred for psychological consultation. Only the results of all the foregoing actions should form the basis for a PHCF doctor to make further therapeutic decisions concerning the patient (e.g., extension of diagnostics, psychiatric consultation, psychotherapy).
3. Self-referred ED patients with various somatic symptoms and who do not work may demonstrate high levels of depressive disorders. The ED doctor should take this potential risk into account when making a diagnosis. Moreover, after discharge from the ED, in addition to the implementation of appropriate treatment for such patients, it is recommended that the doctor coordinates actions between the PHCF facility and social services, as patients may require social support.

References

1. Newton MF, Keirns CC, Cunningham R, Hayward RA, Stanley R. Uninsured adults presenting to US emergency departments: assumptions vs data. JAMA 2008 Oct 22; 300(16): 1914–1924.
2. Moffat K, Mercer SW. Challenges of managing people with multimorbidity in today's healthcare system. BMC Family Practice 2015; 16: 129.
3. Markun S, Holzer B, Rodak R, Kaplan V, Wagner C, Battegay E, et al. Therapeutic conflicts in Emergency Department Patients with multimorbidity: a cross sectional study. Plos One 2014; 9(10): 1–9.
4. Sarnak D, Ryan J. How high-need patients experience the health care system in nine countries. The Commonwealth Fund 2016: 1–14 [online] [cit. 27.12.2019]. Available from URL: https://www.commonwealthfund.org/publications/issue-briefs/2016/jan/how-high-need-patients-experience-health-care-system-nine.
5. Leutgeb R, Berger S, Szecsenyi J, Laux G. Patients with somatoform disorders: more frequent attendance and higher utilization in primary Out-of-Hours care? PLoS ONE 13(8): e0202546 [online] [cit. 27.12.2019]. Available from URL: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0202546.
6. Cozzi G, Barbi E. Facing somatic symptom disorder in the emergency department. J Paediatr Child Health 2019 Jan; 55(1): 7–9.
7. Abar B, Hong S, Aaserude E, Holub A, DeRienzo V. Access to care and depression among emergency department patients. Emerg Med 2017; 53(1): 30–37.
8. Rodriguez González AM, Ramírez Aranda JM, de Los Santos Reséndiz H, Lara Duarte MY, Pazaran Zanella SO, Méndez López JF, et al. Health care utilization of Mexican patients with medically unexplained physical symptoms. Colomb Med (Cali) 2016 Sep 30; 47(3): 155–159.
9. Poloni N, Ielmini M, Caselli I, Ceccon F, Bianchi L, Isella C, et al. Medically unexplained physical symptoms in hospitalized patients: a 9-year retrospective observational study. Front Psychiatry 2018 Nov 23; 9: 626 [online] [cit. 27.12.2019]. Available from URL: https://www.frontiersin.org/articles/10.3389/fpsyt.2018.00626/full.
10. Jadhakhan F, Lindner OC, Blakemore A, Guthrie E. Prevalence of medically unexplained symptoms in adults who are high users of health care services: a systematic review and meta-analysis protocol. BMJ Open 2019 Jul 2; 9(7): e027922 [online] [cit. 27.12.2019]. Available from URL: https://bmjopen.bmj.com/content/9/7/e027922.
11. Marzilli E. Somatoform symptoms in adolescents who visit the emergency department: alexithymia and defensive strategies. EpSBS 2017; 24: 257–266.
12. Alsma J, Wouw JV, Jellema K, Coffeng SM, Tobback E, Delesie L, et al. Medically unexplained physical symptoms in patients visiting the emergency department: an international multicentre retrospective study. Eur J Emerg Med 2019 Aug; 26(4): 249–254.
13. Shindhaye R, Mendenhall E, Sumathipala K, Sumathipala A, Patel V. Association of somatoform disorders with anxiety and depression in women in low and middle income countries: a systematic review. Int Rev Psychiatry 2013 Feb; 25(1): 65–76.
14. Lieb R, Meinlschmidt G, Araya R. Epidemiology of the association between somatoform disorders and anxiety and depressive disorders: an update. Psychosom Med 2007; 69: 860–863.
15. Sporinova B, Manns B, Tonelli M, Hemmelgarn B, Macmaster F, Mitchell N, et al. Association of mental health disorders with healthcare utilization and costs among adults with cronic disease. JAMA Netw Open 2019; 2(8): e199910 [online] [cit. 27.12.2019]. Available from URL: https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2748662.
16. Polikandrioti M, Gouvenos I, Michalis L, Patsilinakos S, Nikolaou V, Olympios C, et al. The effects of anxiety and depression on the needs of patients hospitalized with coronary disease. Arch Hell Med 2012; 29: 33–34.
17. Rekleiti M, Roupa Z, Kyriazis I, Wozniak G, Kyloydis P, Souliotis K. Self-assessment of depression in patients with diabetes mellitus and its correlation with complications. Arch Hell Med 2012; 29: 599–605.
18. Willgoss TG, Yohannes AM. Anxiety disorders in patients with COPD: a systematic review. Respir Care 2013; 58: 858–866.
19. Hoyer D, David E. Screening for depression in emergency department patients. J Emerg Med 2012 Nov; 43(5): 786–789.
20. Beiser DG, Ward CE, Vu Ma M, Leiteerapong N, Gibbons R. Depression in emergency department patients and association with healthcare utilization. Acad Emerg Med 2019; 26(8): 878–888.
21. Wells K, Craven P, Steenblik J, Carlson M, Cooper C, Madsen T. Prevalence and treatment of anxiety among emergency department patients with pain. Am J Emerg Med 2018 Jul; 36(7): 1315–1317.
22. Craven P, Cinar O, Madsen T. Patient anxiety may influence the efficacy of ED pain management. Am J Emerg Med 2013 Feb; 31(2): 313–318.
23. Leander M, Lampa E, Rask-Andersen A, Franklin K, Gislason T, Oudin A, et al. Impact of anxiety and depression on respiratory symptoms. Respir Med 2014 Nov; 108(11): 1594–1600.
24. Lee K, Johnson MH, Harris J, Sundram F. The resource utilization of medically unexplained medical symptoms. SAGE Open Med 2016; 4: 2050312116666217.
25. Andersen NL, Eplov LF, Andersen JT, Hjorthoj CR, Birket-Smith M. Health care use by patients with somatoform disorders: a registered-based follow up study. Psychosomatics 2013 Mar-Apr; 54(2): 132–141.
26. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983; 67: 361–370.
27. Majkowicz M. Praktyczna ocena efektywności opieki paliatywnej – wybrane techniki badawcze. In: de Walden-Gałuszko K, Majkowicz M. Ocena jakości opieki paliatywnej w teorii i praktyce. Gdańsk: Akademia Medyczna; 2000: 21–42. (In Polish).
28. Hinkle DE, Wiersma W, Jurs SG. Applied statistics for the behavioral sciences. 5th ed. Boston: Houghton Mifflin; 2003.
29. R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria [cit. 27.12.2019]. Available from URL: https://www.r-project.org/index.html.
30. Sadillioglu S, Topacoglu H, Dikme O, Erdede MO, Ozyuvaci E, Dikme O. Patients do actually know? Evaluation of patients perception regarding their disease severity in the Emergency Department. International Medical Journal 2013; 20(6): 1–4.
31. Barometr WHC. Raport na temat zmian w dostępności do gwarantowanych świadczeń zdrowotnych w Polsce nr 19/15/02/2019. Stan na grudzień/styczeń 2019 r. Warszawa [online] 2019

[cit. 24.12.2019]. Available from URL: http://www.korektorzdrowia.pl/wp-content/uploads/barometr_whc_xii_i_2019_final.pdf. (In Polish).
32. CBOS. Komunikat z badań Nr 89/2018. Opinie na temat funkcjonowania opieki zdrowotnej [online] 2018 [cit. 24.12.2019]. Available from URL: https://cbos.pl/SPISKOM.POL/2018/K_089_18.PDF. (In Polish).
33. World Health Organization. Depression and other common mental disorders. WHO/MSD/MER/2017.2: 1–24 [online] [cit. 27.12.2019]. Available from URL: https://apps.who.int/iris/bitstream/handle/10665/254610/WHO-MSD-MER-2017.2-eng.pdf.
34. Fogarty C, Sharma S, Chetty V, Culpepper L. Mental health conditions are associated with increased health care utilization among urban family medicine patients. J Am Board Fam Med 2008; 21(5): 398–407.
35. Al Aseri Z, Suriya MO, Hassan HA, Hasan M, Sheikh SA, Al Tamimi A, et al. Reliability and validity of the hospital anxiety and depression scale in an emergency department in Saudi Arabia: a cross-sectional observational study. BMC Emerg Med 2015 Oct 12; 15: 28.
36. Nowicka-Sauer K, Pietrzykowska M, Staśkiewicz I, Ejdys M, Czuszyńska Z, Molisz A, et al. Lęk u pacjentów z chorobami przewlekłymi: istotny a marginalizowany problem. Fam Med and Prim Care Rev 2015; 17(2): 120–123. (In Polish).
37. Soares-Filho GL, Freire RC, Biancha K, Pacheco T, Volschan A, Valenca AM, et al. Use of hospital anxiety and depression scale (HADS) in a cardiac emergency room chest pain unit. Clinics 2009; 64: 209–214.
38. Srinivasan K, Joseph W. A study of lifetime prevalence of anxiety and depressive disorders in patients presenting with chest pain to emergency medicine. Gen Hosp Psychiatry 2004; 26: 470–474.
39. Croicu C, Chwastiak L, Katon W. Approach to the patient with multiple somatic symptoms. Med Clin North Am 2014; 98: 1079–1095.
40. Hsia R, Niedzwiecki M. Avoidable emergency department visits: a starting point. International for Quality in Health Care 2017; 29(5): 642–645.
41. Lubszczyk M, Pietrus M, Sulewski M, Gajecki K, Styka L. Emerytura na SORze – analiza przyczyn hospitalizacji osób po 65 roku życia w szpitalnym oddziale ratunkowym. Geriatria 2014; 8: 93–101. (In Polish).
42. Salsberry PJ, Chipps E, Kennedy C. Use of general medical services among patients with severe and persistent mental illness. Psychiatr Serv 2005; 56(4): 458–462.
43. Dark T, Flynn H, Rust G, Kinsell H, Harman J. Epidemiology of emergency department visits for anxiety in the United States: 2009–2011. Psychiatr Serv 2017; 68(3): 238–244.
44. Weiss A, Barrett ML, Heslin KC, Stocks C. Trends in emergency department visits involving mental and substance use disorders 2006–2013. HCUP Statistical Brief Nr 216 [online] 2016 Dec [cit. 27.12.2019]. Available from URL: https://hcup-us.ahrq.gov/reports/statbriefs/sb216-Mental-Substance-Use-Disorder-ED-Visit-Trends.pdf.
45. Uchmanowicz I, Gobbens RJJ. The relationship between frailty, anxiety and depression and health-related quality of life in elderly patients with heart failure. Clinical Interventions in Aging 2015; 10: 1595–1600.
46. Aoun A, Al Hayek S, El Jabbour F. The need for new model of the physician – patient relationship" a challenge for modern medical practice. Fam Med and Prim Care Rev 2018; 20(4): 379–384.
47. Pfizer. Patient Health Questionnaire (PHQ) Screeners (online) (cit. 27.12.2019). Available from URL: https://www.phqscreeners.com/select-screener.
48. Parnowski T, Jernajczyk W. Inwentarz Depresji Becka w ocenie osób zdrowych i chorych na choroby afektywne (ocena pilotażowa). Psychiatr Pol 1977; 11: 417–421. (In Polish).
49. Sosnowski T, Wrześniewski K. Research with the Polish form of the State-Trait Anxiety Inventory. In: Spielberger CD, Diaz-Guerrero R, eds. Cross-cultural anxiety. New York: Hemisphere/Harper and Row; 1986.

Word count: 5704 • Tables: 7 • Figures: – • References: 49

Sources of funding:
The research was funded by the authors.

Conflicts of interests:
The authors report that there were no conflicts of interest.

Cite this article as:
Lisowska A, Szwamel K, Kurpas D.
Somatic symptoms and level of anxiety and depression in self-referral patients at the emergency department.
MSP 2020; 14, 1: 21–30. Published online: 30 Mar 2020.

Correspondence address:
Ada Lisowska
Uniwersytecki Szpital Kliniczny w Opolu
al. Wincentego Witosa 26, 45-401 Opole
E-mail: ada.lisowska@o2.pl

Received: 21.01.2020
Reviewed: 23.03.2020
Accepted: 30.03.2020

e-ISSN 2544-1620

Medical Science Pulse 2020 (14) 1

Original papers

DOI: 10.5604/01.3001.0014.1208

ANTINEOPLASTIC AGENTS AND THE USE OF PERSONAL PROTECTIVE EQUIPMENT: NURSING STAFF AWARENESS

Katarzyna Szwamel[1 A,D–G]
• ORCID: 0000-0001-8186-9979
Żaneta Dębicka[2 A–D,G]

Marta Gawlik[1 E–G]
• ORCID: 0000-0001-9849-9134

[1] Department of Medical Sciences, Opole Medical School, Opole, Poland

[2] Department of Hematology and Hematological Oncology, Voivodeship Hospital in Opole, Opole, Poland

A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: Along with an increasing number of cancer patients, the need for cytostatic drugs is also increasing. Nursing staff are the largest professional group exposed to the potential dangers of these substances.

Aim of the study: Assess the awareness of nursing staff who have direct contact with cytostatic drugs in the use of personal protective equipment (PPE).

Material and methods: The research group consisted of 101 nurses routinely exposed to cytostatic drugs. A diagnostic survey and questionnaire technique were used along with the author's original questionnaire.

Results: Of the respondents, 58.42% (n=59) never used protective shoes while dealing with cytostatics, while 53.4% (n=54) never used long-sleeved, waterproof uniforms; 49.50% (n=50) did not apply half masks, and 34.65% (n=35) failed to protect their eyes with protective glasses. The most common cause of not using the protective equipment was identified as lack of time (72; 71.29%). Deficiency of training on protective measures while working with hazardous cytostatics was cited by 37.62% (n=38) as the reason for their behavior, while almost 22% of them claimed that their employer did not provide them with a sufficient amount of protective equipment for individual use. The older, more experienced and higher-educated the staff, the higher awareness among them about the need for using PPE.

Conclusions: Higher-educated and more experienced nursing staff should constitute the source of 'good practices' and educate younger undergraduate colleagues theoretically and practically. Employers and management staff should provide employees with more training on the correct application of protective measures and increase the intensity of control of the use of personal protective equipment.

KEYWORDS: antineoplastic agents, nursing, awareness

Background

Despite continuous progress in diagnostics and therapies, the treatment of neoplastic diseases is one of the most challenging issues in medicine [1]. Cancer is a leading cause of death worldwide, accounting for an estimated 9.6 million deaths in 2018 [2]. In 2018, an estimated 1,735,350 new cases of cancer were diagnosed in the United States [3], and 185,630 new cases in Poland [4]. The most common cancers are breast, lung and bronchus, prostate, and colorectal cancer [3,4].

Along with an increasing number of cancer patients, the need for cytostatic drugs is also increasing. Cytostatics are substances used in chemotherapy to destroy or damage the cells which are cancerously altered. One of the side effects is damaging healthy cells which are not cancerously affected [1,5]. Most of these drugs have been classified as dangerous to humans because of their mutagenic, clastogenic, and carcinogenic properties [6]. Nurses, doctors and pharmacists, as well as cleaning staff, are potentially exposed to negative effects of cytostatics' activity through their direct care of patients who receive the drugs, but also by being in the rooms where the drugs are stored [7].

Nurses belong to the group of professionals most frequently exposed to antineoplastic agents [8]. Tompa et al. (2016) showed that in nurses exposed to cyto-

statics, a significantly increased frequency of chromosome aberrations and sister chromatid exchanges were observed when compared with those in the controls. Genotoxicological and immunotoxicological changes, as well as iron deficiency, anemia and thyroid diseases increased among cytostatic exposed subjects [6]. Polovich showed that the incidence of leukemia among exposed nurses was 10 times higher, and the incidence of non-Hodgkin lymphoma among pharmacy technicians was 3.7 times higher, than in the control [9]. Cieślicka et al. (2016) found that staff working in cytostatic environments noted excessive lacrimation, dry eye, redness and itchy eyes, skin and mucous membrane irritation, increased eyebrow and eyelash prolapse, abnormalities of the heart rate, and nausea [10]. Exposure to cytostatics may also evoke allergies, hair loss, liver or kidney damage as well as respiratory diseases such as asthma, allergic rhinitis and nasal ulceration. Additionally, fertility issues, carrying pregnancy to term, severe fetal defects, non-neoplastic hematopoietic system diseases, leukemia and lymphomas may occur [10–13].

Cytostatics most frequently enter the human body through the respiratory system and the skin [14]. Exposure to the drugs may take place during such nursing procedures as assigning and administering cytostatics in the form of pills or tablets, opening ampoules, bleeding syringes, and applying and ceasing intravenous infusions. During these activities cytostatics diffuse into the air and enter the respiratory system. Exposure at work may also occur while cleaning surfaces used for preparing cytostatic drugs [15–17]. Touching patients who receive the drugs, contact with their bodily fluids, as well as every day bed linen change (which comes in contact with these fluids) can all be hazardous [12,18–20].

The negative exposure of nurses to cytostatic drugs may be minimized by following safety measures and work hygiene practices while preparing, administering, and storing them. These regulations must be applied to the process of equipping the rooms for preparation of cytostatics properly, controlling the equipment used while preparing and administering the drugs, disposable PPE use by all employees, prohibiting any food and drink consumption and smoking in the premises, and proper processing of contaminated areas, patients' underwear and their bed linen [20,21]. Previous studies showed that nurses, despite negative effects of these drugs on the human body, not always obey work safety regulations [22–25]. Taking into consideration the above, this study aims to assess the awareness of nursing staff, who come into direct contact with cytostatic drugs professionally, on the use of PPE.

The results collected in this study may have a positive impact on work safety conditions among nurses who have a direct contact with cytostatic drugs by identifying the areas requiring educational intervention. The results will also determine the degree of negligence and the reasons of insufficient usage of the PPE by staff.

Aim of the study

The aim of the study was to evaluate the awareness of nursing staff in direct contact with cytostatic drugs on the use of personal protective equipment, in particular determining: (1) the measures undertaken by the employer to minimize the risk of exposure to cytostatic drugs, (2) the frequency of PPE use by staff, and possible reasons for not using them, (3) the frequency of applying alternative methods aimed at minimizing the negative effects of antineoplastic agents. The study also sought to determine whether or not a correlation exists between variables such as age, level of education, work experience, and applying safety measures while working with cytostatics.

Material and methods

Study design

Observational research was carried out among the nursing staff who have direct contact with cytostatics at work.

Settings

The research was conducted between 2018–2019 in five hospitals throughout Poland which used cytostatics, including four hospitals in the Opolskie Region and one in the Greater Poland Region. Approval was granted by The Bioethics Committee at Opole Medical School (NR 114/PI/2018). The study was carried out in the spirit of the Declaration of Helsinki dated on 1975 and amended in 2013 as well as *Good Clinical Practice*.

Participants

The research surveyed 101 nurses who have direct contact with cytostatics at work and knowingly approved of taking part in the procedure; completing the questionnaire implied approval of participation.

Data sources/measurement

The research was conducted according to a diagnostic survey method with the use of the author's original questionnaire which consisted of 21 closed questions. Questions 1 to 7 concerned socio-demographic data, work experience, and form of employment. Questions 8 and 9 concerned the usage of cytostatic drugs at work and the frequency of their administration. Other questions dealt with professional training organized by the employer, supervision of the staff while at work, and providing staff with PPE (questions 11–15). To enter the data on the protection of nurses, the following questions were used: Do you properly protect yourself against the exposure to cytostatics? (q. 10), Do you or your colleagues eat or drink in the rooms where cytostatics are prepared or stored? (q. 16), How often do you use listed means of PPE while working with cytostatics? (q. 17). Question 17 included 10 different means of PPE and the respondent could choose between four levels indicating the frequency of their usage (always, often, sometimes, never).

Questions 16 and 20 examined the methods of minimizing the negative effects of cytostatics applied by the respondents. Question 19 probed the degree of awareness of the risks and possible complications while working with antineoplastic agents among the nursing staff. Responses to three statements were gathered using a 5-point Likert scale (I definitely agree, I rather agree, I don't have an opinion, I don't agree, I definitely disagree). Furthermore, the respondents were asked to list the activities during which, in their opinion, the exposure takes place (q. 21).

Statistical methods

For quantitative variables, normal distribution was obtained, whereas, for qualitative ones, numbers and percentages were calculated. The quantitative variables such as age, overall work experience and current work experience (the duration of cytostatic drug exposure) did not follow normal distribution, which was verified with the use of Shapiro – Wilk's test. For the variables which did not display normal distribution, median, maximum and minimum values were shown. The verification of the hypothesis was conducted with the use of Chi-squared test, Fisher's test, Spearman's rank correlation coefficient and adjusted contingency factor Pearson's chi-squared test.

Microsoft Excel 2010 and online calculators were used to calculate the data such as Rho-Spearman's correlation coefficient [26], Chi-squared test [27] and Shapiro – Wilk's test [28].

Results

Descriptive data

The median age of the respondents' was 45 (min-max; 22–63), the vast majority of whom were female (98; 97.03%). Regarding educational qualifications, most respondents were university graduates (60; 59.40%), 41 (40.59%) had completed a 3-month professional course in oncology, 23 (22.77%) had done a fully-qualifying course, and 18 nurses completed a 2-year specialization in this field. A substantial majority of all the nurses (77; 66.33%) had worked in their profession for more than 16 years prior to examination. Most of them worked with cytostatic drugs from 6–15 years (34; 33.66%), with a significant majority of them using the drugs on an everyday basis, at each shift (64; 63.37%). They also added that drip infusion is the most common route of drug administration (98; 97.03%) for their patients (Tab. 1).

Table 1. Characteristics of respondents n=101.

Variables		N	%	Me (min-max)
Age, years	18–30	15	14.85	45 years (22–63)
	31–40	14	13.86	
	41–50	46	45.54	
	more than 50	26	25.74	
Gender	Woman	98	97.03	
	Men	3	2.97	
Education	secondary vocational	41	40.59	
	higher – undergraduate studies	38	37.62	
	higher education – master's degree	22	21.78	
	PhD degree	0	0.00	
Postgraduate education	specialist course in oncology	41	40.59	
	qualification course in the field of oncology	23	22.77	
	oncological specialization	18	17.82	
	no training	31	30.69	
Work experience in the profession	0–5 years	17	16.83	22 years (6 months – 42 years)
	6–15 years	17	16.83	
	16–25 years	31	30.69	
	more than 25 years	36	35.64	
Work experience in the current workplace	0–5 years	28	27.72	13 years (6 months – 40 years)
	6–15 years	34	33.66	
	16–25 years	23	22.77	
	more than 25 years	16	15.84	
Frequency of using cytostatics at work	at each duty	64	63.37	
	several times a month	29	28.71	
	twice a month	2	1.98	
	once a month	6	5.94	
The form of the most frequently administered cytostatics in the current workplace	drip infusion	98	97.03	
	Injection	22	21.78	
	drug for oral administration	29	28.71	
	Other	0	0.00	

Legend: Me – median, min – minimum, max – maximum

Employer's activities aimed at minimizing the risk associated with the exposure to cytostatic drugs

Most employees (63; 62.38%) claimed to be provided with a sufficient training on protective measures against the harmful effects of cytostatics; 37.62% of the respondents (n=38) noticed some shortages in this matter. Responses regarding supervision of staff on the use of protective measures at work appeared to be very much alike – 65.35% (n=66) confirmed that supervision in their workplaces worked well, but 34.65 % (n=35) claimed it did not exist at all. The majority of respondents (79; 78.22%) believed that their employers provided them with a sufficient number of the PPE. However, 22 of them (21.78%) claimed quite the opposite (Tab. 2).

Application of PPE by nurses

The examinees (89; 88.12%), in general, agreed that being exposed to harmful cytostatics as a nurse constitutes a serious issue at work. They also confirmed that coming into contact with these drugs creates a real risk of health complications among nurses (85; 84.16%). According to the staff, the activities which endanger them the most are physical contact with patients' bodily fluids (69; 68.32%) as well as preparing and administering the drugs (62; 61.39%). The least dangerous activities were identified as transportation of drugs to the ward (9; 8.91%) and discarding contaminated clothing (19; 18.81%).

Table 2. Employer's activities aimed at minimizing the risk associated with exposure to cytostatic drugs.

	N	%	95% CI	
Provision of sufficient training by the employer for nursing staff on issues related to protection against the harmful effects of cytostatics				
Yes	63	62.38	52.93	71.82
No	38	37.62	28.18	47.07
Total	101	100.00		
Supervising nursing staff regarding their use of personal protective equipment				
Yes	66	65.35	56.07	74.63
No	35	34.65	25.37	43.93
Total	101	100.00		
Ensuring by the employer sufficient number of all types of personal protective equipment for nursing staff				
Yes	79	78.22	70.17	86.27
No	22	21.78	13.73	29.83
Total	101	100.00		
Encouraging nursing staff to use personal protective equipment during their work				
Yes	79	78.22	70.17	86.27
No	22	21.78	13.73	29.83
Total	101	100.00		

Legend: n – number, CI – confidence interval

Uniform was "always" used by 34.65% of respondents (35), waterproof apron with long sleeves – 15.84% (n=16), gloves – 89.11% (n=90), two pairs of gloves – 14.85% (n=15), thicker plastic gloves intended for work with cytostatics – 41.58% (n=42), cap – 29.70% (n=30), safety glasses – 23.76% (n=24), surgical mask – 31.68% (n=32), half-mask – 10.89% (n=11) and safety shoes – 25.74% (n=26). Safety shoes were "never" worn by 58.42% (n=59) of respondents while working with cytostatic drugs, long-sleeved waterproof uniforms – 53.47% (n=54), a half mask – 49.50 (n=50), safety glasses – 34.65% (35), two pairs of gloves – 33.66% (n=34), special thicker plastic gloves recommended at work with cytostatic drugs – 31.68% (n=35) and, finally, the same number of the examinees never used any head protection in the form of caps.

The most common reason for not using PPE was lack of time (72; 71.29%). Some other significant findings appeared to be the discomfort using PPE (48; 47.52%), inaccessibility of PPE (39; 38.61%) and patients' anxiety while using PPE (37; 36.63%) (Fig. 1).

Alternative prophylactic activities aimed at minimizing the risk associated with exposure to cytostatics

Alternative procedures aimed at minimizing the risk associated with exposure to cytostatic drugs included frequent, regular airing of patients' rooms (72; 71.29%), avoiding any food and drink consumption in the areas where cytostatics are prepared and stored (64; 63.37%), and checking prepared cytostatic solution containers for any leakage or tightness (55; 54.46%). Respondents also noted the following, less frequent, activities: taking a shower after a shift (22; 21.78%), and consuming a significant volume of liquids during shifts (29; 28.71%) (Tab. 3).

Table 3. Alternative methods used by the staff in order to minimize the negative impact of antineoplastic agents on their bodies.

	Alternative activities	n	%	95% CI	
1.	Frequent airing of the patients' rooms	72	71.29	62.46	80.11
2.	Avoiding any food and drink consumption in the area where cytostatic drugs are prepared and stored	64	63.37	53.97	72.76
3.	Checking prepared solution containers for any damage or leakage	55	54.46	44.74	64.17
4.	Checking infusive apparatuses used for cytostatic infusions for any damage or leakage	52	51.49	41.74	61.23
5.	Washing contaminated hospital clothing in the hospital laundry	50	49.50	39.75	59.26
6.	Frequent airing of cytostatics' preparation rooms	45	44.55	34.86	54.25
7.	Changing disposable gloves at least every 30 min. while working with cytostatics	37	36.63	27.24	46.03
8.	Daily change of hospital uniforms	35	34.65	25.37	43.93
9.	Drinking a lot of fluids during shifts	29	28.71	19.89	37.54
10.	Showering after shifts	22	21.78	13.73	29.83

Legend: n – number, CI – confidence interval

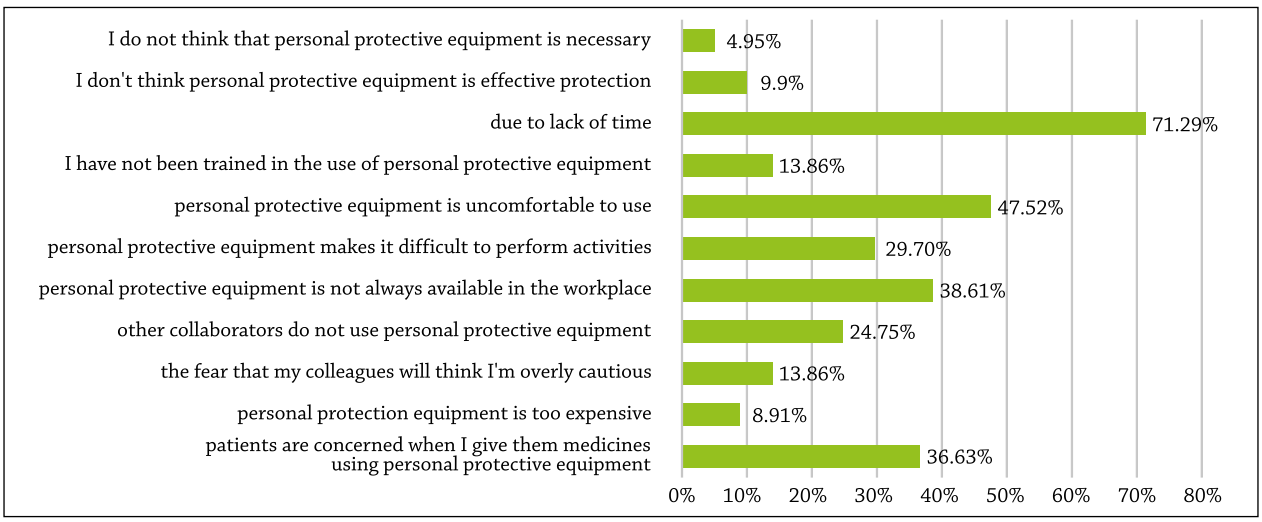

Figure 1. Reasons for not using PPE by nursing staff while working with cytostatics.

Undertaking protective measures while working with cytostatics vs. age, level of education and work experience of the staff

As age of respondents increased:

- self-assessment of the correct use of PPE during exposure to cytostatics increased (C=0.60, p<0.001)
- the frequency of eating meals in rooms with cytostatics decreased (C=0.43, p=0.013)
- the frequency of using PPE during exposure to cytostatics increased (r_s= 0.27, p=0.032) (Tab. 4).

As the level of education increased, self-assessment on the proper use of PPE during exposure to cytostatics decreased (C=0.38, p<0.001) (Tab. 4).

As the number of years of work in nursing increased:

Table 4. Selected variables versus nursing staff activities related to occupational exposure to cytostatics.

The age of respondents and self-assessment of the proper use of personal protective equipment during occupational exposure to cytostatics								
Age	Yes		No		Sum (n)	Chi²	P value	*Adjusted contingency factor Pearson's C. /**Spearman's rho correlation coefficient
	N	%	n	%				
18–30 years	6	40	9	60	15	22.98	<0.001	0.60*
31–40 years	10	71	4	29	14			
41–50 years	43	93	3	7	46			
>50 years	23	88	3	12	26			
Sum (n)	82		19		101			
Age of respondents and eating in rooms with cytostatics								
Age	Yes		No		Sum(n)	10.79	0.013	0.43*
	N	%	n	%				
18–30 years	5	33	10	67	15			
31–40 years	4	29	10	71	14			
41–50 years	6	13	40	87	46			
>50 years	0	0	26	100	26			
Sum (n)	15		86		101			
Age of respondents and frequency of using PPE during work exposure to cytostatics								
Age	Never	sometimes	often	always	Sum (n)	18.25	0.032	0.27**
	n (%)	n (%)	n (%)	n (%)				
18–30 years	8 (53)	5 (33)	1 (7)	1 (7)	15			
31–40 years	3 (21)	9 (64)	2 (14)	0 (0)	14			
41–50 years	6 (13)	18 (39)	18 (39)	4 (9)	46			
>50 years	4 (15)	11 (42)	8 (31)	3 (12)	26			
Sum (n)	21	43	29	8	101			
The level of education and self-assessment of the proper use of personal protective equipment during occupational exposure to cytostatics								
Level of education	Yes		No		Sum(n)	9.46	<0.001	0.38*
	N	%	n	%				
secondary education	37	90	4	10	41			
bachelor degree	32	84	6	16	38			
master degree	13	59	9	41	22			
Sum (n)	82		19		101			
Educational level and eating meals in rooms with cytostatics								
Level of education	Yes		No		Sum(n)	5.46	0.065	0.29*
	N	%	n	%				
secondary education	2	5	39	95	41			
bachelor degree	8	21	30	79	38			
master degree	5	23	17	77	22			
Sum (n)	15		86		101			
Work experience and self-assessment of proper protection against the negative effects of cytostatics								
Work experience	Yes		No		Sum(n)	21.46	<0.001	0.532*
	n	%	n	%				
0–5 years	7	41	10	59	17			
6–15 years	15	88	2	12	17			
16–25 years	28	90	3	10	31			
more than 25 years	32	89	4	11	36			
Sum (n)	82		19		101			
Work experience and the frequency of eating meals and drinks at the place of preparation and administration of cytostatics								
Work experience	Yes		No		Sum (n)	9.75	0.02	0.377*
	n	%	n	%				
0–5 years	6	35	11	65	17			
6–15 years	4	24	13	76	17			
16–25 years	3	10	28	90	31			
more than 25 years	2	6	34	94	36			
Sum (n)	15		86		101			

Legend: * Corrected Pearson C contingency coefficient, ** Spearman rho correlation coefficient.

– staff self-assessment in terms of proper protection against the negative effects of cytostatics increased (C=0.532, p<0.001)
– the frequency of eating meals and drinks at the place of preparation and administration of cytostatics decreased (C=0.377, p=0.002) (Tab. 4).

Discussion

Key results

This study shows that the older, more educated, and more experienced the nursing staff, the more frequently they use all the protective measures while working with cytostatics and, consequently, the higher their awareness of using PPE. Staff did not use PPE mainly because of lack of time for such procedures during their shifts, some discomfort resulting from using PPE or, finally, because of not being provided with sufficient PPE by their employer. Although staff were highly self-aware of proper self-protection against exposure to cytostatics, it was observed that usage of PPE was incomplete or improper e.g. staff used interlining uniforms or surgical masks.

Interpretation

It is employers' responsibility to inform their employees about sources of exposure to agents which have cancerous or mutagenic properties, familiarizing them with potential health consequences, hygiene requirements critical to minimizing exposure to dangerous substances, informing them about the necessity of using PPE, as well as providing them with appropriate PPE in order to minimize the risk of the exposure to these agents [19,29]. However, this study demonstrated that approximately 38% of respondents noticed some shortages in training on protective measures while working with harmful substances, and almost 22% claimed that their employers does not provide them with sufficient PPE. Kyprianou et al. (2010) found that only 33% nurses reported having received specialized training [23]. Boiano et al. (2014) indicated that the main reasons for not using PPE while administering antineoplastic drugs included not being provided with a sufficient amount of specialized gloves (31%), lack of waterproof uniforms (13%) and lack of masks protecting the airways (15%) [25]. Coupled with this, education on the usage of cytostatics is essential; this was highlighted by Rai et al. (2015) who applied two tests (pre and post training of nurses) to illustrate the importance of education. The mean participant score on the safe handling of cytotoxic drugs was 35.3 in the pre-test, significantly increasing to 83.7 in the post-test after an educational intervention (p<0.001) [30].

In this study, despite high awareness surrounding the use of proper protection against exposure to cytostatic drugs, many respondents appeared to have used PPE in an incomplete or inappropriate way. Most of them (90; 89.11%) used gloves most frequently. Although an interlining uniform does not provide proper protection, as it does not have liquid-proof properties, it was declared to have been used by 34.65% (n=35) of the nurses at any time. In contrast, only 15.84% (n=16) claimed to have always used a long-sleeved, waterproof uniform designed specifically to work with cytostatics while working in hazardous environments. Despite the fact that a surgical mask does not protect against gases, fumes and sprays, it was always used by 31.68% (n=32) of the surveyed. On the contrary, a half mask, recommended for such tasks, was worn by only 10.89% (n=11) of the respondents. Cieślicka et al (2016), in their research among nurses in hospitals in Lubelskie Province, found that during the administration of cytostatic drugs, staff used disposable gloves (83%; n=66), disposable interlining uniforms (64%; n=51), and face masks (61%; n=49). They less frequently used PPE such as protective glasses (36%; n=29), head caps (33%; n=26) and two pairs of disposable gloves (20%; n=16). Only 11% (n=9) declared to have used disposable uniforms [10]. Kim et al. (2019) found that only 24.1% of nurses showed high adherence to standard guidelines, while 58.3% and 17.7% reported moderate and low adherence, respectively. Nurses reported very low adherence to 'wearing protective eye gear' (6.7%) and 'wearing protective clothing' (13.3%). In this study, protective clothing was always worn by 116 (13.3%) of the nurses, hand protective equipment was used by 683 (78.3%) of the respondents, eye protection gear by 58 (6.7%) of them, and a group of 390 nurses (44.7%) declared to have always worn protective respiratory gear [31]. Research conducted in Cyprus showed that most participants reported high levels of compliance with the use of personal protective equipment such as gloves and protective gowns (95.4%, and 84.5%) during reconstitution of antineoplastic agents, respectively [23]. In contrast, Colvin et al. (2016) compared questionnaire responses to their own observations and observed that 75% of them used two pairs of gloves while applying chemotherapy to their patients. The researchers also noted that other indicators of protective behaviors were lower than declared during the survey [24]. The results clearly demonstrate the need for constant supervision of staff in order to increase safety during chemotherapy procedures. Our research shows that 34.65% (n=35) of respondents highlighted the existence of any supervision during cytostatic procedures. The study did not include questions on the form of monitoring. Therefore, further studies should likely concentrate on this aspect.

This research showed that, during the exposition to cytostatics, respondents never used protective footwear (59; 58.42%), long-sleeved, waterproof uniforms (54; 53.47%), half masks (50; 53.47%) or protective glasses (35; 34.65%); lack of time was identified as the main reason for not applying PPE. Krzemińska et al. (2016) found haste (36; 38%) and duty overload (45; 48%) as the most frequent reasons for it, while a group of 16 nurses (17%) indicated the disregard of

danger as the main cause [11]. Such factors as duty overload, shortages of staff, haste, exhaustion, and disregard of dangers were also found as the reasons for not using the PPE in Bilski's study [22]. Their research, along with ours, also mentioned patients' anxiety as the reason for not using the PPE. To conclude, patients need to be educated on the necessity of using such measures by nursing staff.

The study also asked the respondents to identify other methods used to minimize the influence of cytostatic drugs on their bodies. They most often mentioned frequent airing of the patients' rooms (72; 72.29%). A group of 63.7% (n=64) of respondents followed the legal regulations regarding the prohibition of any food and drink consumption in the rooms where cytostatic drugs are prepared, administered or stored. In order to protect themselves, 51.49% (n=52) of them checked infusion apparatuses for their leakage properties. It is highly concerning that only 49.5% (50) of the nurses decided to wash their contaminated uniforms and clothing in the hospital laundry, which suggests that the rest of them took them to their homes. The research by Cieślicka et al. (2016) found that 86% of staff (n=83) frequently performed airing of the chemotherapy preparation and patients' rooms, while 82% (n=80) of them checked preparations for any leakage or damage. However, a much smaller group, in comparison to our study, declared washing contaminated clothing at home (12%) [10]. Boiano's study was similar to Cieślicka's in this aspect [10,25]; this suggests that this study yielded poorer results than those previously reported.

In our study, we asked the nurses to identify the activities, which in their opinions, are the most dangerous when the staff might be exposed to cytostatics. They most frequently indicate that contact with patients' bodily fluids (69; 68.32%), preparing and administering the drugs (62; 61.39%) and, finally, administering tablets (46; 45.54%). In the study performed by Krzemińska et al. (2016), only 6% of the respondents indicated the direct contact with patients' bodily fluids, whereas they named the most dangerous procedures as drug preparation (60%) and starting intravenous infusions (55%) [11]. In contrast, Jeong et al. (2015) found switching cytostatic infusions (92; 21.6%) and discarding cytostatic waste (88; 20.7%) as the most hazardous procedures [32].

Generalizability

The results obtained in this study suggest that not only lack of time can be blamed for not using PPE. Incomplete and improper usage of PPE among staff suggests some shortcomings in their knowledge on work safety measures and work hygiene while preparing, administering, and storing cytostatic drugs. These knowledge deficits may result in discrepancies between suggested standards of proceeding, and methods of work used at work. As a result, the number of dangerous situations may be increasing. Incomplete knowledge of risky situations leads to disregard of issues like this. Therefore, there is a need for constant training of nursing staff and supervision of the employers in terms of providing PPE to their employees. It is, however, comforting that the number of nurses following safety measures while working with cytostatic drugs is increasing with age, work experience and the level of education. Highly educated and experienced staff set an example, and can be the source of valuable knowledge for younger and less educated colleagues.

Limitations of the study

The limitations of the study fall into a small research sample and a non-standard tool used to collect data. However, conducting research in five different hospitals and taking into consideration multiple aspects (employer's actions, frequency of using the PPE, reasons for not using the PPE, other prophylactic activities to minimize the risks of exposure to cytostatics) in the research tool are its great asset.

Conclusions

Despite the high level of self-assessment regarding adequate protection against exposure to cytostatic drugs, most nursing staff did not fully apply PPE. It was observed that respondents used PPE in an incomplete and improper way. The awareness of using PPE increased with age, work experience and the level of education. Higher educated and experienced nurses should constitute the source of 'good practices' and ought to provide their younger and less experienced and less educated colleagues with theoretical and practical knowledge. Accordingly, employers and management staff should provide employees with more training on the correct application of protective measures and increase the intensity of control of the use of personal protective equipment. The lack of time and the reduced comfort of tasks performed after the use of PPE were the most common reasons why nursing staff did not apply PPE. The response "lack of time for use PPE" may indicate that nurses are overloaded with the work, but this phenomenon requires further research. Nursing staff cannot identify all situations during which exposure to cytostatic drugs may occur. In addition, it omits the use of many important methods that ensure safety at work, such as avoiding washing contaminated clothing at home. The above information confirms the need to increase the intensification of training of nursing staff on the safe handling of cytostatic drugs.

References

1. Gorczyca M. Chemioterapia chorób nowotworowych. Leki przeciwnowotworowe. In: Zejc A, Gorczyca M, ed. Chemia leków. Podręcznik dla studentów farmacji i farmaceutów. Warszawa: PZWL; 2009: 757–758. (In Polish).

2. World Health Organization. Cancer [online] [cit. 14.03.2020]. Available from URL: https://www.who.int/news-room/fact-sheets/detail/cancer.
3. National Cancer Institute. Cancer statistics [online] [cit. 14.03.2020]. Available from URL: https://www.cancer.gov/about-cancer/understanding/statistics.
4. International Agency for Research on Cancer. World Health Organization. Poland 2018 [online] [cit. 14.03.2020]. Available from URL: http://gco.iarc.fr/today/data/factsheets/populations/616-poland-fact-sheets.pdf.
5. Schmid B, Strub P, Studer A. Farmakologia dla zawodów pielęgniarskich. Prandota J. [red wyd pol]. Wrocław: MedPharm: 2013. (In Polish).
6. Tompa A, Biró A, Jakab M. Genotoxic Monitoring of Nurses Handling Cytotoxic Drugs. Asia Pac J Oncol Nurs 2016 Oct-Dec; 3(4): 365–369.
7. Shahrasbi AA, Afshar M, Shokraneh F, Monji F, Noroozi M, Ebrahimi-Khojin M, et al. Risks to health professionals from hazardous drugs in Iran: a pilot study of understanding of healthcare team to occupational exposure to cytotoxics. EXCLI J 2014; 13: 491–501.
8. Bilski B. Leki cytostatyczne i leki niebezpieczne w środowisku pracy personelu pielęgniarskiego. In: Bilski B, ed. Higiena pracy w pielęgniarstwie. Wybrane zagadnienia. Poznań: Wydawnictwo Naukowe Akademii Medycznej 2009; 96–109. (In Polish).
9. Polovich M. Minimizing occupational exposure to antineoplastic agents. J Infus Nurs 2016; 39(5): 307–313.
10. Cieślicka A, Gębka M, Rząca M, Kocka K, Pietraszek A, Bartoszek A, et al. Następstwa zdrowotne pracy w narażeniu na leki cytostatyczne w grupie zawodowej pielęgniarek i pielęgniarzy. J Educ Health Sport 2016; 6(9): 566–574. (In Polish).
11. Krzemińska S, Pośniak M, Szewczyńska M. Stosowanie środków ochrony indywidualnej w warunkach zawodowego narażenia na cytostatyki. Med Pr 2016; 67(4): 499–508. (In Polish).
12. Connor TH, Lawson CC, Polovich M, Mc Diarmid MA. Reproductive health risks associated with occupational exposures to antineoplastic drugs in health care settings: a review of the evidence. J Occup Environ Med 2014 Sep; 56(9): 901–910.
13. Połaska K. Zagrożenia zawodowe w pracy pielęgniarki onkologicznej pediatrycznej. In: Pasek M, Dębska G, ed. Interdyscyplinarna opieka nad pacjentem z chorobą nowotworową. Kraków: Krakowskie Towarzystwo Edukacyjne; 2011: 159–172. (In Polish).
14. Chaudhary R, Karn BK. Chemotherapy – knowledge and handling practice of nurses working in a Medical University of Nepal. J Cancer Ther 2012; 3: 110–114.
15. Roussel C, Connor TH. Chemotherapy: current and emerging issues in safe handling of antineoplastic and other hazardous drugs. Oncology Pharmacy 2014; 7(3): 1,8–11.
16. Świątkowska B. Zagrożenia zawodowe pracowników opieki zdrowotnej: Co wiemy i co możemy zrobić? Probl Hig Epidemiol 2010; 91(4): 522–529. (In Polish).
17. Connor TH, Mc Diarmid MA. Preventing occupational exposures to antineoplastic drugs in health care settings. CA Cancer J Clin 2006 Nov-Dec; 56(6): 354–365.
18. Walton AL. Doing the dirty work: who handles antineoplastic drug contaminated excreta and do they do it safely? Asia Pac J Oncol Nurs 2017; 4(2): 120–121.
19. Bilski B. Higiena pracy z lekami cytostatycznymi. In: Bilski B, ed. Higiena pracy dla pielęgniarek. Wybrane zagadnienia. Poznań: Wydawnictwo Naukowe Akademii Medycznej; 2004: 80–102. (In Polish).
20. Rozporządzenie Ministra Zdrowia i Opieki Społecznej z 1996 w sprawie bezpieczeństwa i higieny pracy przy przygotowywaniu, podawaniu i przechowywaniu leków cytostatycznych w zakładach opieki zdrowotnej, Dz. U. 2000 Nr 80, poz. 376 z późn. zm. (In Polish).
21. Rozporządzenie Ministra Zdrowia z 2000, zmieniające rozporządzenie w sprawie bezpieczeństwa i higieny pracy przy przygotowywaniu, podawaniu i przechowywaniu leków cytostatycznych w zakładach opieki zdrowotnej, Dz. U. 2000 Nr 79, poz. 897. (In Polish).
22. Bilski B. Postępowanie personelu pielęgniarskiego z lekami cytostatycznymi – wstępne wyniki badań. Med Pr 2004; 55(3): 243–247. (In Polish).
23. Kyprianou M, Kapsou M, Raftopoulos V, Soteriades ES. Knowledge, attitudes and beliefs of Cypriot nurses on the handling of antineoplastic agents. Eur J Oncol Nurs 2010; 14(4): 278–282.
24. Colvin CM, Karius D, Albert NM. Nurse adherence to safe-handling practices: observation versus self-assessment. Clin J Oncol Nurs 2016; 20(6): 617–622.
25. Boiano JM, Steege AL, Sweeney MH. Adherence to safe handling guidelines by health care workers who administer antineoplastic drugs. J Occup Environ Hyg 2014; 11(11): 728–740.
26. Kalkulator korelacji [online] [cit. 1.04.2020]. Available from URL: http://www.naukowiec.org/kalkulatory/korelacja.html. (In Polish).
27. Kalkulator testu chi-kwadrat [online] [cit. 1.04.2020]. Available from URL: http://statpages.info/chisq.html. (In Polish).
28. Shapiro-Wilk Test Calculator [online] [cit. 1.04.2020]. Available from URL: http://www.statskingdom.com/320ShapiroWilk.html.
29. Rozporządzenie Ministra Zdrowia z 2012 w sprawie substancji chemicznych, ich mieszanin, czynników lub procesów technologicznych o działaniu rakotwórczym lub mutagennym w środowisku pracy, Dz. U. 2012, poz. 890. (In Polish).
30. Rai DK, Lama S, Badu A, Mandal GN. Impact of educational intervention on knowledge regarding safe handling of cytotoxic drugs among the nursing personnel working in BPKIHS. Health Renaissance 2015; 13(1): 13–22.
31. Kim O, Lee H, Jung H, Jang HJ, Pang Y, Cheong H. Korean nurses' adherence to safety guidelines for chemotherapy administration. Eur J Oncol Nurs 2019; 40: 98–103.
32. Jeong KW, Lee BY, Kwon MS, Jang JH. Safety management status among nurses handling anticancer drugs: nurse awareness and performance following safety regulations. Asian Pac J Cancer Prev 2015; 16(8): 3203–3211.

Word count: 4654 • Tables: 4 • Figures: 1 • References: 32

Sources of funding:
The research was funded by the authors.

Conflicts of interests:
The authors report that there were no conflicts of interest.

Cite this article as:
Szwamel K, Dębicka Ż, Gawlik M.
Antineoplastic agents and the use of personal protective equipment: nursing staff awareness.
MSP 2020; 14, 1: 31–39.

Correspondence address:
Katarzyna Szwamel
Państwowa Medyczna Wyższa Szkoła Zawodowa w Opolu
ul. Katowicka 68, 45-060 Opole, Poland
E-mail: k.szwamel@interia.pl

Received: 29.03.2020
Reviewed: 31.03.2020
Accepted: 31.03.2020

e-ISSN 2544-1620

Medical Science Pulse 2020 (14) 1

Case reports

Published online: 30 Mar 2020

DOI: 10.5604/01.3001.0014.0264

PHYSIOTHERAPEUTIC MANAGEMENT OF A PATIENT AFTER CRANIOCEREBRAL TRAUMA IN THE INTENSIVE CARE UNIT – A CASE REPORT

Klaudia Kałużа[A,B,D–F]

Opole Medical School, Opole, Poland

Antonina Kaczorowska[A,E,F]
• ORCID: 0000-0002-0488-8583

A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: Craniocerebral injuries are one of the most common causes of mortality and disability in Poland. The treatment of patients who are in an intensive care unit is based primarily on stabilizing the patient's general condition as well as basic duties according to the patient's functioning.

Aim of the study: The aim of this study is to demonstrate the importance of early rehabilitation and the role of physiotherapy in recovery after craniocerebral trauma.

Case report: The subject was an 18-year-old patient who suffered craniocerebral trauma as a result of a road accident. After losing consciousness, he was in the intensive care unit, where he was placed on a medical ventilator. A properly selected physiotherapeutic procedure was performed. Passive exercises, contracture correction and appropriate positioning were used. To prevent pressure sores, anti-bedsore prophylaxis was implemented. Respiratory therapy played a key role. The goal of respiratory physiotherapy was to improve respiratory function by maintaining proper lung ventilation, increasing chest and diaphragm mobility along with maintaining the efficiency of respiratory muscles, as well as stimulating effective coughing and evacuation of secretions. The NDT-Bobath concept was used as therapy for spastic tension. The goal of the therapy was to get rid of pathological movement patterns and replace them with physiological patterns. The PNF method, classical and lymphatic massage, polysensory stimulation and music therapy were also used.

Conclusions: Early and comprehensive rehabilitation in a patient after craniocerebral trauma is extremely important and determines therapeutic effectiveness. Comprehensive therapy and care are able to prevent a number of complications that threaten the patient as a result of immobilization.

KEYWORDS: craniocerebral trauma, coma, rehabilitation

Background

Craniocerebral trauma is an important cause of mortality and disability in Poland. The development of diagnostics and therapies for craniocerebral trauma, whose incidence rises along with the development of communication, industry, as well as with increased gunshot wounds and recreational sports practitioners, leads to the most difficult rehabilitation problems. People who have been seriously injured are hospitalized [1]. In highly developed countries, craniocerebral injuries are the most common cause of death among the population in the first four decades of life. Treatment of trauma patients requires accurate decision-making and high professional qualifications. Patients with multi-organ injuries are managed by a multi-disciplinary team composed of specialists from various fields of medicine [2,3].

Treatment of patients who are in the intensive care unit is initially based on stabilizing the patient's general condition and restoring basic physical performance. For patients who have limited contact, rehabilitation therapy should additionally combine sensory channel stimulation and advanced functional mobilization using neurophysiological methods, in addition to the use of posture positions, passive exercises and respiratory mobilization. The goal is also to improve basic life functions such as breathing and swallowing [4,5].

Returning to the best possible fitness involves organizational, psychological, medical, social and educational activities. The whole range of physiotherapeutic activities is aimed at supporting the process of natural regeneration, as well as the elimination of mental and physical effects of the disease [6].

Aim of the study

The aim of this study is to demonstrate the importance of early rehabilitation and the role that physiotherapy plays in the recovery of patients after craniocerebral and multiorgan injuries.

Case report

The subject of this study is an 18-year-old patient who suffered a craniocerebral trauma secondary to a road accident. As a result of this incident, he was sent to the Hospital Emergency Department of the University Clinical Hospital in Opole, where he lost consciousness and was transferred to the intensive care unit. The coma lasted for about six weeks. At that time, the patient was intubated and then put on a medical ventilator (respirator). During the full loss of consciousness, he was under the care of many specialists. Intensive pharmacological treatment was implemented. In addition, specialist rehabilitation was carried out throughout this period to support basic life processes.

Due to open fractures in both femurs, external stabilization was required (Fig. 1–2).

Later, anastomosis with the intramedullary nail was performed (Fig. 3–4).

There was also a fracture of the left ninth rib accompanied by bilateral lung contusion. In addition, an ocular

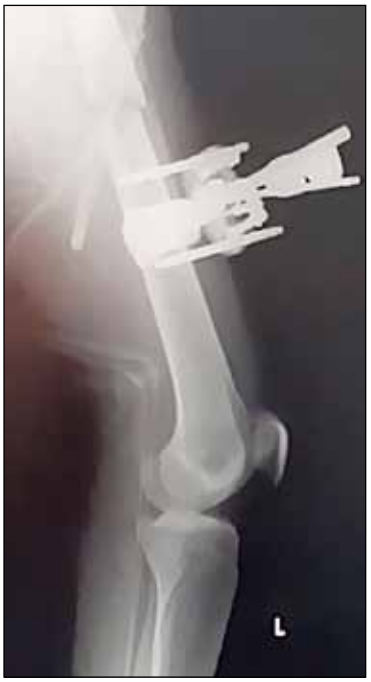

Figure 1. X-ray of the femur after external stabilization [authors' image].

Figure 2. External stabilization after bilateral femoral fracture [authors' image].

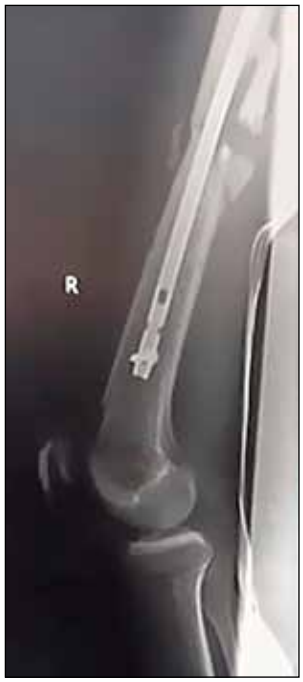

Figure 3. An X-ray of the femur after surgery with intramedullary nail [authors' image].

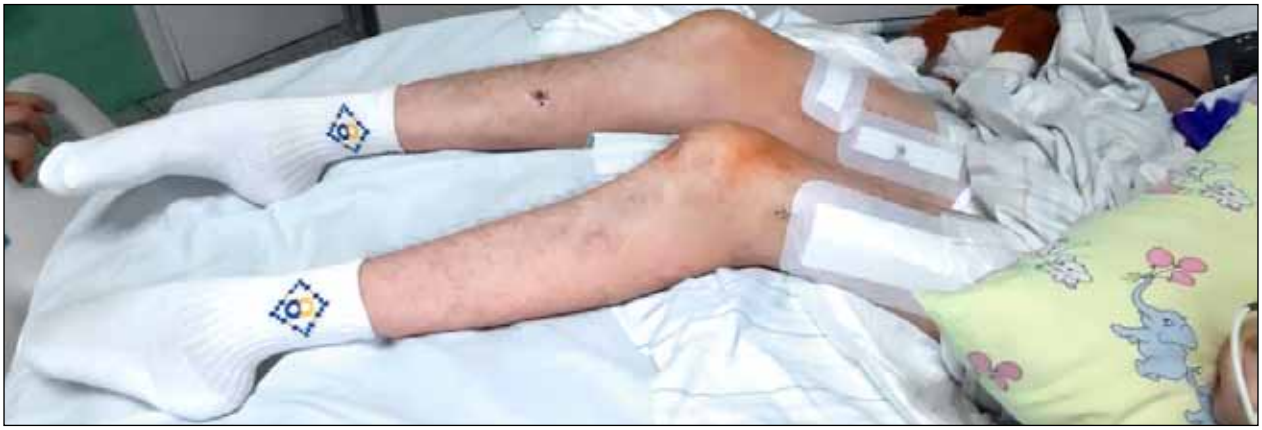

Figure 4. The condition of the lower extremities after surgery using an intramedullary nail [authors' image].

hematoma of the left eye was present. A tracheostomy was also required.

The patient developed spastic tension affecting the upper and lower limbs (Fig. 5–6).

Figure 5. Spastic right upper limb [authors' image].

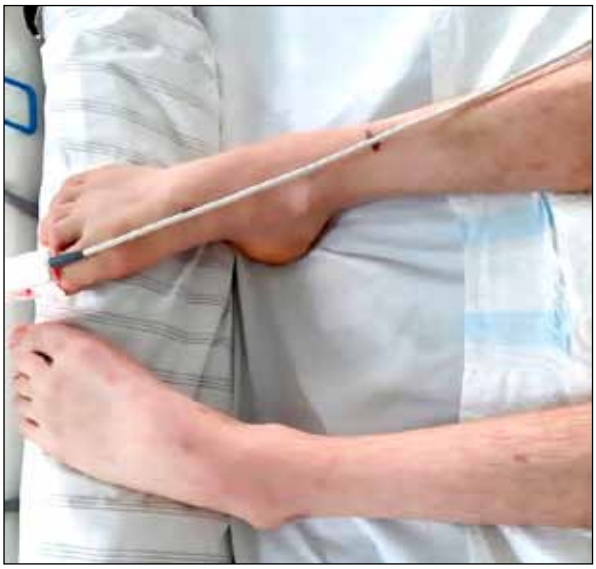

Figure 6. Spastic tension in the feet [authors' image].

A properly selected physiotherapeutic procedure has been implemented. Passive exercises, contracture correction and appropriate positioning were used. This prevented the development of muscle contractures and paresis. During passive exercises, it was important not to exceed the current range of motion, as dislocation of joints could occur. Passive exercises were performed several times a day in two series of 12 movements. The physiotherapist performed elbow, shoulder, wrist and hand exercises. Then, ankle and toe exercises were performed. They were also one of the basic anticoagulant exercises required for comatose patients. In addition, a higher position of the lower limbs was used to protect the patient from thrombosis, so that they were above the level of the heart.

To prevent pressure sores, anti-bedsore prophylaxis was used. Every two hours the patient was given a change of position. It was possible thanks to appropriately designed wedges and rollers and the use of anti-bedsore discs protecting elbows, buttocks, hips, knees, ankles and heels. In addition, the patient was placed on an anti-bedsore mattress, which prevented excessive pressure on the areas most vulnerable to pressure sores. The patient was monitored daily in areas prone to pressure sores. The whole-body toilet, maintaining high hygiene standards, keeping the patient's bed clean and ventilating the room was also very important. Due to such care, bedsores were fully prevented.

The bronchial toilet was another aspect of the treatment process. The patient's lungs were patted in individual segments. This was followed by suction and removal of residual secretion by an electric suction device. The frequent bronchial toilet provided airway patency, optimal gas exchange conditions, and acted as infection prevention.

Respiratory therapy played a key role [7]. The goal of respiratory physiotherapy was to improve respiratory function by maintaining proper lung ventilation, increasing chest and diaphragm mobility along with maintaining the efficiency of respiratory muscles, as well as stimulating effective coughing and evacuation of secretions. The patient worked on increasing three dimensions of the chest: upper-lower by lowering the diaphragm, anteroposterior through contraction of the external intercostal muscles located between successive ribs from I to V, as well as transverse, causing contraction of intercostal muscles located between successive ribs from VI to X.

Chest springing was applied, which consisted of compression of the lower part of the chest during exhalation and sudden release of the pressure at the beginning of inspiration (Fig. 7).

Figure 7. Chest springing technique [authors' image].

By introducing the forced exhalation technique, secretions from the upper respiratory tract were removed. Effective exhalation was also worked upon.

Turning the diaphragm movement on by blocking it was a great technique (Fig. 8). The therapist placing

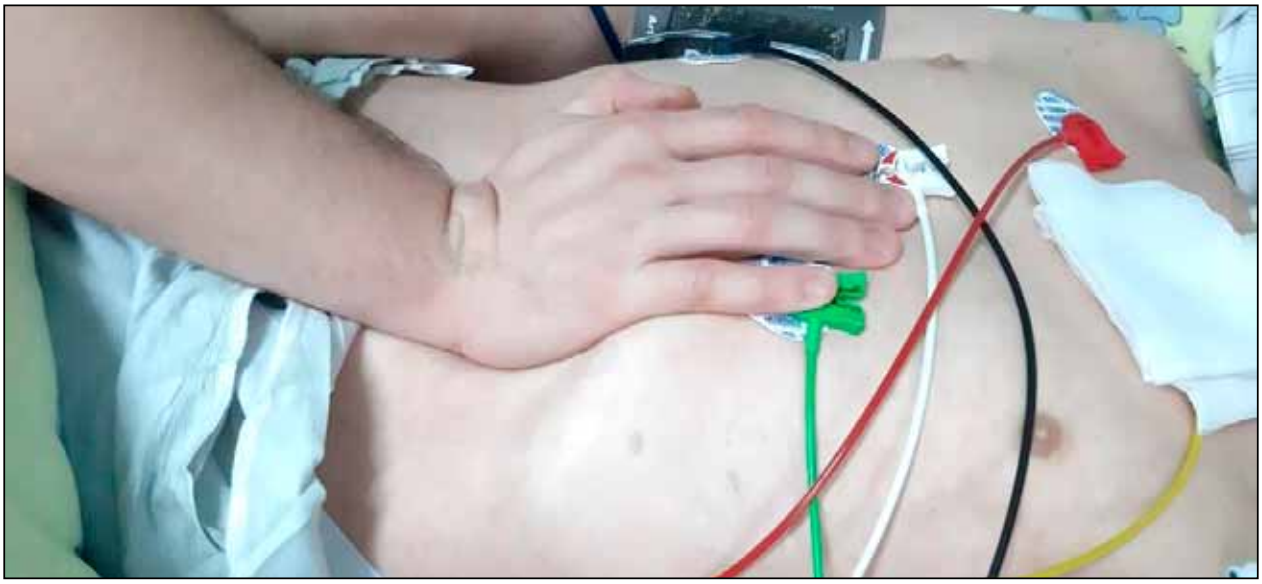

Figure 8. Mobilization of the diaphragm – the initial stage [authors' image].

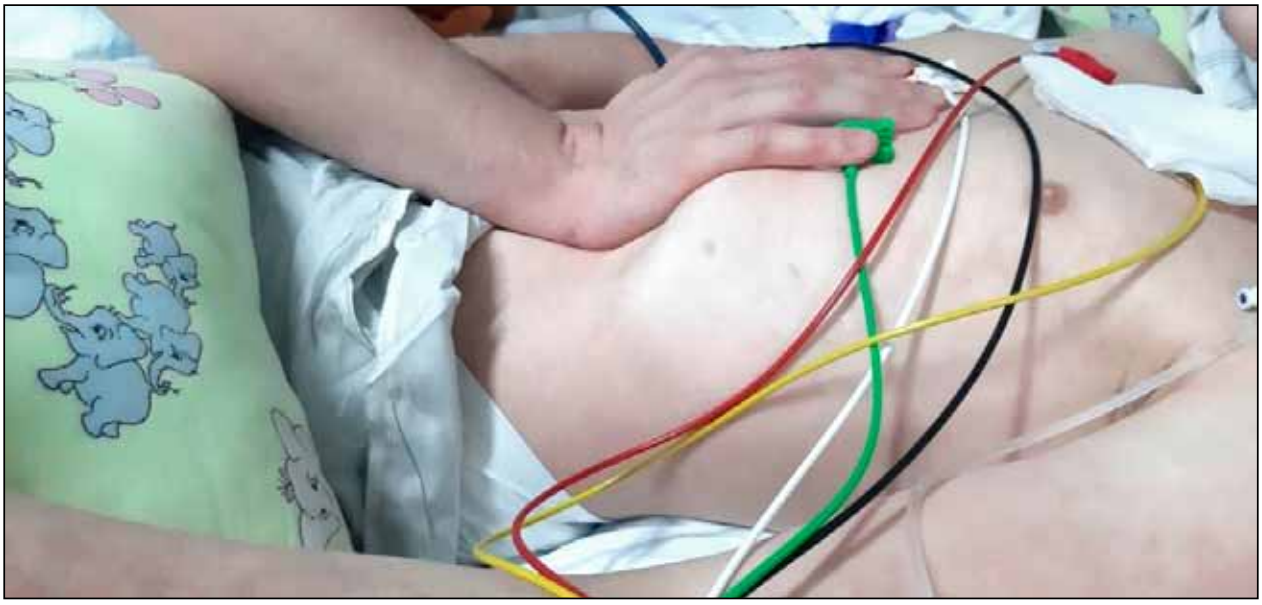

Figure 9. Mobilization of the diaphragm - the final stage [authors' image].

the patient's wrist on the diaphragm blocked the diaphragm when he inhaled. Then during exhalation, it was still maintained. With each breath, the range of movement increased (Fig. 9).

Then, the rib part of the diaphragm was mobilized. The chest opening technique was performed in a lying position backwards or lying sideways (Fig. 10). Following the chest opening technique, the chest closing technique was used (Fig. 11).

Figure 10. The chest opening technique while lying on its side [authors' image].

Figure 11. The chest closing technique [authors' image].

The patient did not have serious respiratory complications due to chest physiotherapy. Classic massage was also used in the therapy. The aim of the massage was to improve the blood supply and nutrition of tissues, accelerate the removal of unnecessary metabolism products, relax excessively contracted muscles, improve muscle flexibility, stimulate flaccid muscles as well as reduce and eliminate tissue adhesions and scars.

Alternately with classical massage, lymphatic massage was used. It improved the outflow of lymph, thanks to which edema of the upper and lower limbs was reduced.

The patient's upright standing required special caution. It started in a bed with high support, gradually increasing the angle of inclination and at the same time extending the duration of the vertical position. The next and more advanced stage involved sitting with the lowered lower limbs (Fig. 12). The moment of uprighting required continuous monitoring of pulse and blood pressure as well as a careful observation of the patient.

It was important to carry out global, complex movements, involving all components, which was achieved by the usage of PNF patterns. Early rehabilitation using the PNF method is effective in patients with neurological disorders, including patients in a coma and in the intensive care unit [4,8]. Before implementing this type of therapy, it was very important to know the range of mobility of individual joints to avoid later complications. Due to femoral fractures, the lower limb and pelvic patterns were not used, only the upper limb and torso patterns.

The NDT-Bobath concept was used as a therapy for spastic tension. The goal of the therapy was to get rid of pathological movement patterns and replace them with physiological patterns. Basic activity was monitored by mobilizing the sternum in bed, which prepared the extensors of the pelvis and lower limbs for fulfilling their body support function. The derotation of the lower trunk is one of the methods inhibiting lower limb spasticity. It was performed by stretching the spine extensor and multifiber muscles. The patient was then prepared to move from lying on their back to lying on their side and then sitting. This therapy improved abdominal oblique muscle control while silencing the overactive torso extensors. The therapist mobilized the greater round muscle in both upper limbs to prevent these muscles from working properly. An inhibition technique was also used to fight the spastic muscles of the wrist flexors and flexor digitorum longus. Hand therapy was conducted in order to inhibit finger flexor spasticity while preparing the hand for opening. The work of the upper limbs on supportive activity in closed chains also played a key role in the process of recovery. In addition, the physiotherapist activated the patient's torso [9]. Thanks to NDT-Bobath therapy, contractures did not consolidate and muscle spasticity decreased.

Rehabilitation also involved the use of polysensory stimulation. Stimulation through auditory, olfactory, visual, gustatory and tactile stimuli provided the possibility of global and multi-sensory shaping of the given concept image. The patient's relatives were also involved in rehabilitation. The family tried to talk about

Figure 12. Patient during upright positioning – sitting down with lower limbs down [authors' image].

moments spent together and motivating the patient to fight for life. Ensuring a calm, supportive environment was of great importance: talking to the patient in a gentle voice, reading, informing him about every activity performed on the patient. Music therapy was also used by playing music he was known to like.

The patient, being comatose, did not show any activity or any ability to perceive. He did not respond to any stimuli. This condition lasted for about six weeks. After this time, small but noticeable signs of consciousness began to appear. Then we managed to make contact with the patient. He opened his eyes, began to show his first limb movements, and understood the questions asked, and articulated short, slow answers.

The positioning, exercises and neurophysiological methods still played an important role in the rehabilitation, which helped to avoid large distortions in the musculoskeletal system and assisted in the appropriate response. It was important to work in higher positions such as sitting down due to reduction of muscle tone, coordination and body posture. The key role was to work on endurance.

After the patient regained consciousness, prevention of breathing, swallowing and speech disorders became important. Starting early speech therapy was crucial as it helped to avoid the development of abnormal movement habits of the articulatory apparatus and non-physiological speaking habits. It also helped to eliminate drooling as well as lockjaw that could be a threat to the patient.

The next focus of the therapy was stimulation of memory, attention, perception, thinking and work on the emotional and motivational sphere. Short, simple instructions were directed to the patient to avoid situations where excessive information flow into the patient would result in confusion and gradual withdrawal from social interactions.

The patient is currently in the Opole Rehabilitation Center in Korfantów, where further rehabilitation was undertaken. Kinesiotherapy, physical therapy and rehabilitation pool exercises were introduced. Thanks to systematic rehabilitation, the patient has already started to take the first steps with the help of crutches. In addition, the patient attends occupational therapy and speech therapy classes.

Discussion

The described patient underwent early comprehensive rehabilitation, taking into account the patient's condition after multi-organ trauma. Various physiotherapy methods were used, such as passive exercises, positioning, respiratory therapy, classical and lymphatic massage, PNF method, the Bobath concept, and polysensory stimulation. In addition, music therapy was used. The patient's condition has improved significantly thanks to early and appropriate rehabilitation.

According to Arias-Fernandes et al., early rehabilitation in the intensive care unit is associated with an increase in functional fitness and muscle strength, improved walking distance and a better perception of the quality of life related to health [10].

Mandel et al. believe that whilst undertaking physiotherapy during the time of regeneration and compensation, the type of therapy introduced and its intensity should be selected appropriate to the patient's current condition and the etiology of the disease. In order to achieve improvement in the functioning of the patient, rehabilitation should be carried out systematically. At a later stage, in addition to early management elements such as passive exercises and respiratory, special methods in physiotherapy, e.g., PNF and NDT Bobath methods, should be successively introduced. In the fight against spasticity, music and art therapies are widely used. Relaxation exercises are also important elements of therapy [11]. During work with the presented patient, therapists focused on multifaceted action and used most of the available methods in such cases.

The patient's big problem was muscle spasticity. Therefore, various physiotherapeutic and neurophysiological methods were used in therapy. Kalinowska and Kułak observed that in the fight against spasticity biomechanical aspects including movement therapy or kinesiotherapy, physical factors or physical therapy, chemical factors offered by pharmacotherapy as well as surgical methods should be taken into account. Such a large number of therapeutic methods ensures an individual therapeutic approach to each patient struggling with spasticity [12].

Music had a beneficial effect on the described patient. He heard his favorite songs. Bukowska and Konieczna in their research have proved that music therapy through its multifaceted activity is increasingly used in many branches of medicine, including neurology. It very effectively supports basic therapy in diseases or disorders resulting from damage to the nervous system and in the treatment of cognitive, movement and sensory disorders [13].

For a patient in a coma, it is important to connect with the environment, speak to him in a calm voice and inform about the activities performed. The case study presented by Tapson et al. shows the great power of conversation with an unconscious patient and proves that the sense of hearing functions in comatose patients [14].

Conclusions

Early and comprehensive rehabilitation undertaken in a patient after craniocerebral trauma is extremely important and determines the effectiveness of therapy.

Comprehensive therapy and care are able to prevent a number of complications that threaten the patient as a result of immobilization.

The assumption that a comatose patient is unable to contact the outside world, but responds to stimuli, is fully correct. This concept allows the patient's family to be involved in the healing process.

References

1. Kaźmierczak K, Majchrzycki M, Stryła W. Rozkład zaleconych zabiegów w rehabilitacji pacjentów po urazie czaszkowo-mózgowym w zależności od stopnia urazu wg Glasgow Coma Scale. Now Lek 2011; 80(4): 288–294. (In Polish).
2. Radek A, Radek M. Urazy czaszkowo-mózgowe. Neurol Dypl 2016; 1: 8-13. (In Polish).
3. Çakmak A, İnce Dİ, Sağlam M, Savcı S, Yağlı NV, Kütükcü EÇ, et al. Physiotherapy and rehabilitation implementation in intensive care units: a survey study. Turk Thorac J 2019; 20(2): 114–119.
4. Kwiecień-Jaguś K, Zwoliński T, Szamotulska J, Hansdorfer-Korzon R. Wczesna rehabilitacja na oddziale intensywnej terapii z wykorzystaniem metody PNF. Anest Ratow 2016; 10: 86–96. (In Polish).
5. Monti MM, Vanhaudenhuyse A, Coleman MR, Boly M, Pickard JD, Tshibanda L, et al. Willful modulation of brain activity in disorders of consciousness. N Eng J Med 2010; 362: 579–589.
6. Corner EJ, Murray EJ, Brett SJ. Qualitative, grounded theory exploration of patients' experience of early mobilization, rehabilitation and recovery after critical illness. BMJ Open 2019 Feb 24; 9(2): e026348.
7. Pozuelo-Carrascosa DP, Torres-Costoso A, Alvarez-Bueno C, Cavero-Redondo I, López Muñoz P, Martínez-Vizcaíno V. Multimodality respiratory physiotherapy reduces mortality but may not prevent ventilator-associated pneumonia or reduce length of stay in the intensive care unit: a systematic review. J Physiother 2018; 64(4): 222–228.
8. Gruszczyk D, Kaczorowska A, Katan A. Application of various physiotherapeutic methods in a conservative treatment of neurogenic scoliosis in a comatose patient – a case report. Med Sci Pulse 2017; 11(4): 46–53.
9. Półtorak M, Tokarz M, Bilińska M, Biliński G, Ciesielski T, Fuchs M, et al. Wykorzystanie koncepcji Bobath w zwalczaniu spastyczności. Rehabil Prakt 2013; 2: 14–18. (In Polish).
10. Arias-Fernández P, Romero-Martin M, Gómez-Salgado J, Fernández-García D. Rehabilitation and early mobilization in the critical patient: systematic review. J Phys Ther Sci 2018; 30(9): 1193–1201.
11. Mandel SE, Davis BA, Secic M. Effects of music therapy and music-assisted relaxation and imagery on health-related outcomes in diabetes education: a feasibility study. Diabetes Educ 2013; 14: 37–41.
12. Kalinowska AK, Kułak W. Wpływ muzyki na organizm ludzki. Fizjoterapia 2010; 18(4): 77–82. (In Polish).
13. Bukowska A, Konieczna L. Neuromuzykoterapia w pracy muzykoterapeutów, fizjoterapeutów, logopedów i terapeutów zajęciowych. Wrocław: Wydawnictwo Akademii Muzycznej im. K. Lipińskiego; 2010. (In Polish).
14. Tapson K, Sierotowicz W, Marks-Maran D, Thompson TM. 'It's the hearing that is last to go': a case of traumatic head injury. Br J Nurs 2015; 24(5): 277–281.

Word count: 2306 • Tables: – • Figures: 12 • References: 14

Sources of funding:
The research was funded by the authors.

Conflicts of interests:
The authors report that there were no conflicts of interest.

Cite this article as:
Kałuża K, Kaczorowska A.
Physiotherapeutic management of a patient after craniocerebral trauma in the intensive care unit – a case report.
MSP 2020; 14, 1: 40–46. Published online: 30 Mar 2020.

Correspondence address:
Antonina Kaczorowska
Państwowa Medyczna Wyższa Szkoła Zawodowa w Opolu
ul. Katowicka 68
45-060 Opole
Phone: (+48) 692 639 634
E-mail: t.kaczorowska@op.pl

Received: 29.01.2020
Reviewed: 2.03.2020
Accepted: 9.03.2020

e-ISSN 2544-1620

Medical Science Pulse 2020 (14) 1

Case reports

Published online: 31 Mar 2020

DOI: 10.5604/01.3001.0014.0926

THE CHANGES IN PROPORTION AND BODY COMPOSITION OF A WOMAN PRACTICING GROUP FITNESS TRAINING FOR THREE MONTHS

Agata Mroczek[A,D–F]
• ORCID: 0000-0002-5246-0792
Magdalena Chawałek[B,D–F]

Opole Medical School, Opole, Poland

A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: Physical activity is an excellent form of prevention of modern diseases. The most popular form of physical activity chosen by women is group fitness activities. Women are most likely to focus on exercises for the lower parts of the body (thighs, buttocks, abdomen). In recent years, dance classes (e.g. Zumba) or exercises on mini trampolines have become very popular. Regular fitness training contributes to positive changes in the proportions and body composition.

Aim of the study: The aim of the study was to assess the proportions and body composition of a woman via a 3-month group fitness training program.

Case report: The study involved a woman aged 26, participating in fitness classes three times a week for a period of three months. The woman participated in the following training cycle: twice a week (Monday and Wednesday) in the Jumping Frog interval training on a trampoline; twice a week (Monday and Friday) in ZUMBA® classes; and once a week (Wednesday) in ABT classes (abdomen, buttocks, thighs). Her height and weight, waist and hips circumference, and the thickness of three skinfolds (subscapular, triceps, abdominal) were measured. Body mass index (BMI) and waist to hip ratio (WHR) were calculated and body composition analysis (% of body fat, lean body mass) was performed. Two measurements were made: the first at the beginning of the training cycle, the second on completion. After three months of training, there were a decrease in body weight (2.2 kg), BMI (0.77 kg/m^2), waist circumference (4 cm), hip circumference (2 cm), WHR (0.03), subscapular, abdominal and triceps skinfold (1 mm, 3 mm, 3 mm), body fat (2.6%) and perimeters, and an increase in lean body mass (1 kg).

Conclusions: This study shows a positive effect of fitness training on body proportions and body composition.

KEYWORDS: body composition, group fitness training, woman

Background

Regular physical activity is an important element in the prevention of modern diseases [1–5]. During physical exertion, blood pressure is reduced, oxygen transport to tissues increases, and venous blood flow to the heart is facilitated [6].

The World Health Organization (WHO) recommend that healthy people aged 18–64 do a minimum of 150 minutes a week of moderate aerobic physical activity, or a minimum of 75 minutes of high-intensity aerobic activity. Additional benefits may be obtained with 300 minutes a week of activity [7]. The motivations for undertaking physical activity vary. This is not only for health, but in the case of women, systematic training can contribute to positive changes in body composition and proportions, including a reduction of fat mass and an increase in lean body mass, and thus improve the aesthetics of the body [8–10].

The most popular form of physical activity chosen by women is group exercise activities. These include ABT exercises (abdomen, thighs, buttocks) that not only improve the condition and shape of the figure, but also help in getting rid of excess body fat, especially from the lower parts of the body [11]. A relatively new form of fitness classes use mini trampolines for general development training that burns adipose tissue, shapes the body and improves the condition and releases a large dose of endorphins. Contraindications for these classes include pregnancy, discopathy, osteoporosis, cardiovascular diseases (hypertension), as well as balance and

movement coordination disorders. In turn, ZUMBA® is a dance class combined with aerobics, which improves condition and also shapes the figure [12].

Aim of the study

The aim of the study was to assess the proportions and body composition of a woman via a 3-month group fitness training program.

Case report

The study involved a 26-year-old woman, an office worker, who attended five training sessions, three times a week, for three months. Each training session lasted 55 minutes. The fitness classes took place at the Calypso Fitness Opole Turawa Park club. Diet control was not implemented. The woman participated in the following training sessions: twice a week (Monday and Wednesday) in a Jumping Frog interval training class on the trampoline; twice a week (Monday and Friday) in ZUMBA® classes; once a week (Wednesdays) in ABT classes (abdomen, buttocks, thighs).

The following somatic measurements were carried out at the Opole Medical School in Opole: height and weight, and waist and hip circumference. Body mass index (BMI) and waist to hip ratio (WHR) were calculated. Three skinfolds were measured using an electronic skinfold caliper: subscapular skinfold, below the inferior angle of the scapula; triceps skinfold, on the posterior midline of the upper arm; and abdominal skinfold. Body composition was assessed as a percentage of body fat and lean body mass.

Two measurements were made: the first measurement at the beginning and the second after three months, at the end of the training cycle. Prior to the study, the participant was informed about the principles and purpose of the study and gave their written consent to participate in the study. The approval of the Bioethical Commission at the Opole Medical School in Opole was obtained (Nr 20/2017) for conducting the research.

Results

Tab. 1 shows that after three months of fitness training there was a 2.2 kg weight loss, and thus a BMI reduction of 0.77 kg/m^2. Waist and hip circumference were reduced by 4cm and 2 cm, respectively, and thus the WHR index was reduced by 0.03. The skinfolds decreased as follows: subscapular by 1 mm, and abdominal and triceps by 3 mm. There was also a 2.6% reduction in body fat and an increase in lean body mass by 1 kg.

Table 1. Characteristics of somatic features and body composition of a woman before the beginning of the training cycle and after its completion.

Variables	Before the beginning of the training cycle	After the end of the training cycle	Difference
Body mass [kg]	59.5	57.3	2.2
BMI [kg/m2]	20.83	20.06	0.77
Waist circumference [cm]	75	71	4
Hip circumference [cm]	102	100	2
WHR	0.74	0.71	0.03
Subscapular skinfold [mm]	11	10	1
Abdominal skinfold [mm]	16	13	3
Triceps skinfold [mm]	22	19	3
Fat [%]	20.2	17.6	2.6
LBM [kg]	47	48	1

Discussion

There is growing awareness of the impact of physical activity on health, and so women increasingly use the services of fitness clubs and spend their free time actively [13]. Physical inactivity is a primary contributor to the obesity epidemic but this may be promoted or hindered by environmental factors [14]. Understanding the etiology of obesity and identifying prevention mechanisms are a public health priority [15]. The causes of obesity are multifactorial: genetics [15] and family history [16], dietary intake [17,18] and physical activity [18].

Processed foods contribute to obesity [19,20]. Increasingly, the role of the ambient environment has been recognized as a critical element in the obesity epidemic [21]. Recent studies show numerous environmental associations with obesity [22–25]. These factors are all likely operating in tandem, creating a complex set of conditions in which obesity persists.

This study showed a positive effect of fitness training on body composition and proportions, including the reduction of body weight and body fat, BMI, waist and hip circumference, and the WHR index. There was an increase in lean body mass. Similar results were presented by So et al., who conducted research on middle-aged women. After twelve weeks of aerobic exercise the participants showed a reduction in body weight and fat, waist and hip circumference, and BMI [26]. In a study of 30 women and two types of training, aerobics or aerobics combined with peripheral training, there was a significant reduction in body fat in both groups. However, the women who undertook aerobic exercise with peripheral training experienced a greater difference compared to the aerobic-only group [27]. A study by Stachoń et al. showed that female students who undertook the highest physical activity (four times a week) had the least-thick skin-fat folds. In addition, students who were physically inactive had the highest body fat content, as well as the lowest lean body mass [28]. Other studies have shown that the content of adipose tissue decreased in both women and men partici-

pating in Crossfit® functional high-intensity training five times a week for two months [29].

According to the WHO recommendations, adults aged 18–64 should do at least 150 minutes of moderate intensity aerobic activity, or at least 75 minutes of vigorous intensity aerobic physical activity, per week. Additional health benefits can be achieved with moderate intensity aerobic physical activity of 300 minutes or 150 minutes of vigorous intensity aerobic physical activity, per week. Muscle-strengthening activities should be done, involving major muscle groups on two or more days a week. These recommendations are relevant to all healthy adults unless they have specific medical conditions. Adults who currently do not meet the recommendations for physical activity should aim to increase duration, frequency and finally intensity [30]. Moderate or vigorous physical activity performed three times per week for at least 150 minutes gives an additional health benefit and has a positive effect on body composition. In future research, attention should be paid to changing the body composition of overweight and obese people via physical activity [30].

Conclusions

This study has shown a positive effect on changing body composition, of systematic physical training three times a week, for at least 150 minutes. After three months of training, there was a decrease in body weight, BMI, WHR, waist and hip circumference, skinfolds, body fat and perimeters, and an increase in lean body mass.

References

1. Nowak P. Motywy zdrowotne w hierarchii wartości kobiet ćwiczących w klubach fitness. Med Og Nauk Zdr 2012; 18(4): 387–392. (In Polish).
2. Blomstrand A, Bjorkelund C, Ariai N, Lissner L, Bengtsson C. Effects of leisure-time physical activity on well-being among women: a 32-year perspective. Scand J Public Health 2009 Sep; 37(7): 706–712.
3. Nies MA, Motyka CL. Factors contributing to women's ability to maintain a walking program. J Holistic Nurs 2006; 24(1): 7–14.
4. Ritvanen T, Louhevaara V, Helin P, Halonen T, Hänninen O. Effect of aerobic fitness on the physiological stress responses at work. Int J Occup Med Environ Health 2007; 20(1): 1–8.
5. Rotem M, Epstein L, Ehrenfeld M. Does the conservation of resources motivate middle-aged women to perform physical activity? West J Nurs Res 2009; 31(8): 999–1013.
6. Makowiec-Dąbrowska T. Wpływ aktywności fizycznej w pracy i życiu codziennym na układ krążenia. Forum Med Rodz 2012; 6(3): 130–138. (In Polish).
7. Global Strategy on Diet, Physical Activity and Health (online) 2004 (cit. 01.03.2020). Available from URL: https://www.who.int/ncds/prevention/global-strategy-diet-physical-activity-2004-goals/en/.
8. Wojtasik W, Szulc A, Kołodziejczyk M, Szulc A. Wybrane zagadnienia dotyczące wpływu wysiłku fizycznego na organizm człowieka. J Educ Health Sport 2015; 5(10): 350–372. (In Polish).
9. Janiszewska R, Bornikowska A, Gawinek M, Makuch R. Skład ciała i jego zmiany pod wpływem 3-miesięcznego treningu zdrowotnego u dorosłych kobiet. Probl Hig Epidemiol 2013; 94(3): 484–488. (In Polish).
10. Sanabria JC, Hernández-Elizondo J. Effect of high-intensity and concurrent training in body composition in Costa Rican overweight and obese women. Arch Sports Med 2017; 1(2): 65–74.
11. Hyun-Joo K, Yang L, Doo-Soon P, Duk-Ho K. Effects of 12-week circuit weight training and aerobic exercise on body composition, physical fitness, and pulse wave velocity in obese collegiate women. Soft Computing – A Fusion of Foundations, Methodologies & Applications 2012; 16(3): 403–410.
12. Ljubojević A, Jakovljević V, Popržen M. Effects of Zumba Fitness Program on body composition of women. SportLogia 2014; 10(1): 29–33.
13. Kalińska M, Milde K. Efektywność grupowego i indywidualnego treningu fitness w redukcji tkanki tłuszczowej u kobiet. Zeszyty Naukowe WSKFiT 2015; 10: 57–62. (In Polish).
14. Gray ChL, Messer LC, Rappazzo KM, Jagai JS, Grabich SC, Lobdell DT. The association between physical inactivity and obesity is modified by five domains of environmental quality in U.S. adults: a cross-sectional study. PLoS One 2018; 13(8): e0203301.
15. Locke AE, Kahali B, Berndt SI, Justice AE, Pers TH, Day FR, et al. Genetic studies of body mass index yield new insights for obesity biology. Nature 2015; 518(7538): 197–206.
16. van der Sande MA, Walraven GE, Milligan PJ, Banya WA, Ceesay SM, Nyan OA, et al. Family history: an opportunity for early interventions and improved control of hypertension, obesity and diabetes. Bull World Health Organ 2001; 79(4): 321–328.
17. Swinburn BA, Caterson I, Seidell JC, James WP. Diet, nutrition and the prevention of excess weight gain and obesity. Public Health Nutr 2004; 7(1A): 123–146.
18. World Health Organization. Obesity and Overweight [online] 2016 [cit. 25.01.2016]. Available from URL: http://www.who.int/mediacentre/factsheets/fs311/en/.
19. Popkin BM. Agricultural policies, food and public health. EMBO Rep 2011; 12(1): 11–18.
20. Stuckler D, Nestle M. Big food, food systems, and global health. PLoS Med 2012; 9(6): e1001242.
21. Thayer KA, Heindel JJ, Bucher JR, Gallo MA. Role of environmental chemicals in diabetes and obesity: a National Toxicology Program workshop review. Environ Health Perspect 2012; 120(6): 779–789.
22. Holtcamp W. Obesogens: an environmental link to obesity. Environ Health Perspect 2012; 120(2): 62–68.
23. Kelishadi R, Poursafa P, Jamshidi F. Role of environmental chemicals in obesity: a systematic review on the current evidence. J Environ Public Health 2013; 2013: 896789.
24. Ghosh-Dastidar B, Cohen D, Hunter G, Zenk SN, Huang C, Beckman R, et al. Distance to store, food prices, and obesity in urban food deserts. Am J Prev Med 2014; 47(5): 587–595.
25. Wen M, Kowaleski-Jones L. The built environment and risk of obesity in the United States: racial-ethnic disparities. Health Place 2012; 18(6): 1314–1322.

26. So R, Eto M, Tsumijoto T, Tanaka K. Acceleration training for improving physical fitness and weight loss in obese women. Obes Res Clin Pract 2014; 8(3): 238–248.
27. Park SK, Park JH, Kwon YC, Kim HS, Yoon MS, Park HT. The effect of combined aerobic and resistance exercise training on abdominal fat in obese middle-aged women J Physiol Anthropol Appl Human Sci 2003; 22(3): 129–135.
28. Stachoń A, Pietraszewska J, Burdukiewicz A, Andrzejewska J. Wpływ aktywności fizycznej na poziom otłuszczenia młodych kobiet. Med Og Nauk Zdr 2013; 19(2): 188–192. (In Polish).
29. Cieślik B, Rutkowski T, Kuligowski T. Wpływ 8-tygodniowego treningu według metodyki Crossfit® na skład ciała osób dorosłych. PNAJD Kultura Fizyczna 2016; 15(4): 169–179. (In Polish).
30. Kahlmeier S, Wijnhoven TMA, Alpiger P, Schweizer C, Breda J, Martin BW. National physical activity recommendations: Systematic overview and analysis of the situation in European countries. BMC Public Health 2015; 15: 133.

Word count: 1261 • Tables: 1 • Figures: – • References: 30

Sources of funding:
The research was funded by the authors.

Conflicts of interests:
The authors report that there were no conflicts of interest.

Cite this article as:
Mroczek A, Chawałek M.
The changes in proportion and body composition of a woman practicing group fitness training for three months.
MSP 2020; 14, 1: 47–50. Published online: 30 Mar 2020.

Correspondence address:
Agata Mroczek
Państwowa Medyczna Wyższa Szkoła Zawodowa w Opolu
ul. Katowicka 68, 45-060 Opole
Phone: (+48) 609 742 070
E-mail: agata_mroczek@wp.pl

Received: 10.03.2020
Reviewed: 30.03.2020
Accepted: 30.03.2020

e-ISSN 2544-1620

Medical Science Pulse 2020 (14) 1

Reviews

Published online: 30 Mar 2020

DOI: 10.5604/01.3001.0013.9718

EXTRACORPOREAL SHOCK WAVE THERAPY (ESWT) IN CHRONIC LOW BACK PAIN: A SYSTEMATIC REVIEW OF RANDOMIZED CLINICAL TRIALS

Karolina Walewicz[A-G]
• ORCID: 0000-0002-4272-8978

Opole Medical School, Opole, Poland

A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: Extracorporeal Shock Wave Therapy (ESWT) has become a popular tool to treat musculoskeletal disorders and chronic low back pain.

Aim of the study: To review the current scientific literature and assess the utility of ESWT in treating chronic low back pain.

Material and methods: This systematic review was conducted from November 2019 to January 2020. Its purpose was to determine what the effectiveness is of the various forms of ESWT for the treatment of chronic low back pain. The critical review of the literature on the use of ESWT in chronic low back was made using the scientifically recognized medical databases PubMed, MEDLINE, Physiotherapy Evidence Database (PEDro) and Web of Science Core Collection. There was no restriction by date. Exclusion criteria were experimental, in vitro, animal, review, case reports, non-randomized clinical trials or studies with healthy participants. All articles written in languages other than English have also been excluded.

Results: Six studies were included in the final analysis. According to the applied PEDro classification, the average scoring for the studies was 4.83, which indicates overall low quality of the presented reports. However, this result appeared closer to the moderate (acceptable) quality range (6-8 points) than to the unacceptable range (0-2 points).

Conclusions: Based on the findings in the analyzed articles, ESWT promises to be an efficient and useful procedure in chronic low back pain treatment. Unfortunately, the level of evidence is relatively weak because there are a limited number of published studies related to ESWT and the final score in the PEDro classification was low. Together, these results indicate the need for further high quality randomized clinical trials.

KEYWORDS: low back pain, ESWT, shock waves, treatment

Background

Extracorporeal Shock Wave Therapy (ESWT) has emerged as a popular tool for treatment of musculoskeletal disorders such as lateral epicondylitis [1–3], painful shoulder syndrome [4–6] and plantar fasciitis [7,8]. Additionally, it has been used to treat lymphedema [9,10], chronic unhealed wounds [11] and muscle spasticity [12–14]. Some reports also indicate there is significant utility and clinical efficacy in applying ESWT to cases of low back pain.

The two primary types of shock waves are the Focused Extracorporeal Shock Wave (fESW) and the Radial Extracorporeal Shock Wave (rESW). They differ in terms of the manner and extent of the acoustic energy propagation, the shape of the beam and its physical properties. The fESW was initially used in lithotripsy devices, which are devices used in interventional urology or abdominal surgery as a non-invasive procedure for crushing urinary or gallstones. The devices emitting this type of wave are usually generated from an electromagnetic, electrohydraulic or piezoelectric method. The wave physically manifests as pressure, which increases rapidly to 100-1000 bars (10-100 MPa) in less than 10 ns, which absorbs soft tissue at a depth of up to 12 cm. The standard wave beam is characterized by a focused propagation shape of the focal length, or the place with the highest energy density over a relatively small area, located 4-6 cm deep.

The rESW, in contrast to the fESW, is generated by the pneumatic (ballistic) technique. This wave is characterized by a slow increase in pressure, reaching 1–10 bars (0.1–1 MPa) in more than 5 μs; it absorbs at a depth of up to 3 cm with a typically diffused (unfocused) beam shape [15,16].

Aim of the study

The purpose of this paper was to assess the utility of ESWT for chronic lower back pain treatment by performing a thorough review of the current, relevant scientific literature.

Material and methods

This systematic review was conducted from November 2019 to January 2020. Its purpose was to determine how effective the various forms of ESWT are for the treatment of chronic low back pain. The study was conducted in accordance with the Preferred Reporting System Items for Systematic Reviews and Meta-analyses (PRISMA) statement.

Search strategy

The critical review of the literature on the use of ESWT in chronic low back was made using the following scientifically recognized medical databases: PubMed, MEDLINE, Physiotherapy Evidence Database (PEDro) and Web of Science Core Collection. The search criteria used were as follows: (efficacy OR management OR effectiveness) AND (low back OR lumbar changes OR coccydynia OR disc pathology OR pain) AND (ESWT OR shock wave OR extracorporeal). These keywords were identified after preliminary literature searches. There was no restriction by date. Exclusion criteria were experimental, in vitro, animal, review, case reports, non-randomized clinical trials or studies with healthy participants. All articles written in languages other than English have also been excluded.

The risk of bias

The articles were analyzed using the Physiotherapy Evidence Database (PEDro) Scale checklist for randomized clinical trials (Tab. 1). Using the criteria in the PEDro checklist, each paper was scored as "high quality, low risk of bias", "acceptable quality, moderate risk of bias", "low quality, high risk of bias", or "unacceptable quality" which resulted in rejection. For each criterion on the checklist, a value of 0 or 1 was assigned for each "no" or "yes" response, respectively. The checklist was comprised of ten items and final quality scores were assigned as follows: high quality, low risk of bias, 9-10; acceptable quality, moderate risk of bias, 6-8; low quality, high risk of bias, 3-5; unacceptable (reject), 0-2.

Table 1. The PEDro scale.

Items	Score: Yes (1 point), No (0 points)
1. Eligibility criteria*	
2. Random allocation	
3. Concealed allocation	
4. Baseline comparability	
5. Blind subjects	
6. Blind therapists	
7. Blind assessors	
8. Adequate follow-up	
9. Intention-to-treat analysis	
10. Between-group comparisons	
11. Point estimates and variability	

* Does not contribute to total score.

Data extraction

The data resulting from the collected articles were analyzed by only one researcher and focused on the characteristics of the material and methods, main outcomes and final conclusions. The primary parameters were pain scales and questionnaires, range of motion measurements and quality of life aspects.

Results

The flowchart of randomized clinical trials at all stages of the systematic review is shown in Fig. 1. In total, six studies were included in the final analysis. The characteristics of the included articles are outlined in Tab. 2 and 3. The average quality score for the studies was 4.83, which indicates a general low quality. However, this result was closer to the moderate (acceptable) quality range (6-8 points) than to the unacceptable range (0-2 points).

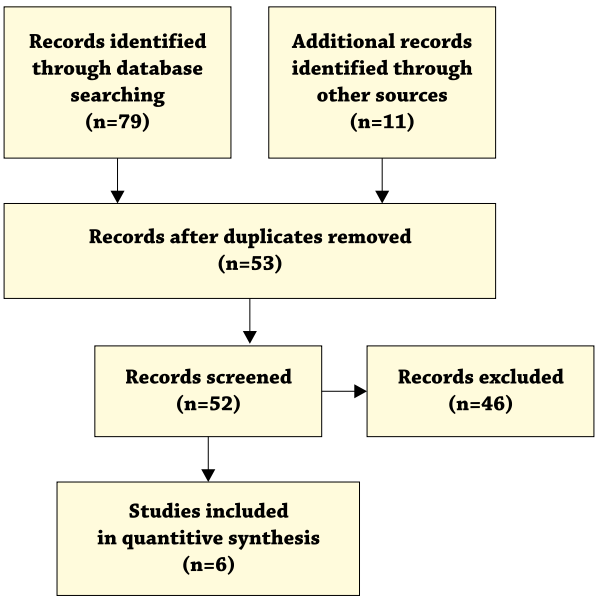

Figure 1. The Prisma flowchart.

Discussion

The following studies show that ESWT may be an effective tool in managing chronic low back pain. Additionally, the literature review illustrates the potential therapeutic mechanisms of ESWT. Basic science studies have well-documented in vitro and animal experiments that demonstrate the pro-angiogenic and anti-inflam-

Table 2. Characteristics of included articles.

	Methods	Results	Conclusions
Han et al. [17]	30 chronic low back pain patients were divided into an extracorporeal shock wave therapy group (ESWTG, n=15) and a conservative physical therapy group (CPTG, n=15). The ESWTG received extracorporeal shock wave therapy (1000 shock waves-7 times per sec were applied at 2.5 Hz at low energy flux densities of 0.01–0.16 mJ/mm2 using a 17 mm head) and the CPTG received general conservative physical therapy two times per week for six weeks. Pain was measured using a visual analog scale (VAS), the degree of disability of the patients was assessed using the Oswestry Disability Index (ODI), and their degree of depression was measured using the Beck depression index (BDI).	In intra-group comparisons, ESWTG and CPTG showed significant decreases in VAS, ODI, and BDI scores. Intergroup comparisons revealed that these decreases in VAS, ODI, and BDI scores were significantly larger in ESWTG than in CPTG.	Extracorporeal shock wave therapy is an effective intervention for the treatment of pain, disability, and depression in chronic low back pain patients.
Schneider [18]	Eligible patients were adults seeking physiotherapeutic treatment. They were randomly allocated to either six treatments of MT (myofascial training) or to six treatments of combined MT and vibro treatment with ESWT. Outcome parameters were pain intensity, pain days, pain duration, and quality of life.	The pain relieving effects of the combined treatment were very large (d=1.6). It clearly outperformed MT and considerably improved patients' health related quality of life.	Combining MT with ESWT enhances the physiotherapeutic effectiveness of treating chronic back pain.
Moon et al. [19]	30 patients with low back pain were assigned randomly to ESWT (n=15) and sham control (n=15) groups. The ESWT group received 2000 shockwaves with energy set to the maximum level tolerable by the patient (energy density=0.09 to 0.25 mJ/mm2). The probe was oriented perpendicular to the posterior lumbar line and moved up and down along the joint line. The sham control group received 2000 shockwaves with the probe oriented parallel to the posterior lumbar line. A 10-cm numeric rating scale (NRS) and the Oswestry Disability Index (ODI) scores were assessed before the intervention, and 1- and 4-weeks post intervention.	In the ESWT group, NRS decreased significantly at post-treatment week 4 (3.64 (95% confidence interval 2.29 to 4.99)) compared to baseline (6.42 (5.19 to 7.66); $p < 0.05$). ODI improved at 1 and 4 weeks compared to baseline, but not significantly. In the sham group, NRS and ODI did not differ at any post-treatment time point. There was a significant group difference in NRS at week 4 post-treatment (3.64 (2.29 to 4.99) in the ESWT group versus 6.18 (5.34 to 7.02) in the sham control group; $p<0.05$), but this was not the case for ODI.	ESWT represents a potential therapeutic option for decreasing chronic low back pain.
Notarnicola et al. [20]	30 patients affected by low back pain were treated with ESWT (shockwave group) or a standard protocol characterized by rehabilitative exercises (control group).	At one and three months, the patients treated with shockwave therapy showed clinical improvement measured by VAS scales (p=0.002; p=0.02), and disability evaluated with Roland scales (p=0.002; p=0.002) and Oswestry (p=0.002; p=0.002). At three months, the patients treated with shock waves showed a significant improvement in terms of values of amplitude of the sensory nerve conduction velocity (SNCV) of the plantar medialis nerve (left: p=0.007; right: p=0.04), the motor nerve muscular conduction (MNCV) of the deep peroneal nerve (left: p=0.28; right: p=0.01) and recruitment of motor units of finger brevis extensor (left: p=0.02; right: p=0.006). In the control group, there was a trend to increase the clinical and electromyographic results without statistical significance.	The results suggest a good applicability of shockwave therapy in the treatment of low back pain, in accordance with the anti-inflammatory, antalgic, decontracting effects and remodeling of the nerve fiber damage verified in previous studies conducted on other pathological models.
Lee et al. [21]	28 patients with chronic low back were divided into an extracorporeal shockwave therapy group (ESWTG – 2000 shocks, 7 times per sec shockwave impulses 5 Hz at an energy flux density of 0.10 mJ/mm2 were delivered using a 17-mm head; n=13) and a conservative physical therapy group (CPTG; n=15). An exercise program that included Williams' exercises and McKenzie's exercises was performed by both groups. The program was implemented twice a week for six weeks. The visual analog scale (VAS) was used to measure the chronic low back pain of the patients. Their dynamic balance ability was measured with BioRescue.	The within-group comparison of the VAS of the ESWTG and the CPTG showed significant improvements after the intervention. In the VAS comparison between the groups after the treatment, the ESWTG showed a significantly larger improvement. In the within-group comparison of dynamic balance ability, the ESWTG showed significant improvements after the intervention in balance control.	The exercise program combined with the ESWT relieved chronic back pain more than the exercise program combined with the CPT.
Walewicz et al. [22]	40 patients with low back pain were randomized into group A (n=20) treated with ESWT (2000 pulses; 2.5 bars; 5 Hz, 7 mins) performed twice a week for five weeks (10 sessions) and stabilization training, as well as group B (n=20) treated with sham ESWT and stabilization training. To analyze the therapeutic progress, the following tests were performed (before and after therapy; 1- and 3-months follow-up) to assess pain and functional efficiency: (1) Visual Analog Scale (VAS), (2) Laitinen Pain Scale (LPS), and (3) Oswestry Disability Index (ODI).	The control group had a statistically significant advantage over the ESWT group (4.4 vs. 3.1 points on the VAS; p=0.039). However, in long-term observations, group A gradually experienced more pain relief than group B (2.7 vs. 3.5 points, $p>0.05$, at one month and 2.0 vs. 4.4 points at three months after treatment; $p<0.0001$). Similar findings can be seen in the analysis of changes in pain sensations measured with the LPS. The functional state (ODI) was better in ESWT group, especially in follow-up observation (9.3 vs. 14.6 points, p=0.033, at one month and 9.3 vs. 17.8 points, p=0.004, at three months after treatment).	The ESWT combined with stabilization training is particularly effective in the long-term and achieves a stable beneficial effect for patients with LBP. The use of ESWT has a significant long-term influence on the reduction of pain and the improvement of the general functional state in relation to the conventional motor improvement program.

Table 3. Quality of included articles.

	Score	Limitations
Han et al. [17]	3/10	no sham therapy, no placebo, no blinded participants, therapists and assessors, no follow-up, no intention to treat
Schneider [18]	6/10	no blinded therapists and assessors
Moon et al. [19]	7/10	no blinded assessors, no intention to treat
Notarnicola et al. [20]	3/10	no sham therapy, no placebo, no blinded participants, therapists and assessors, no follow-up, no intention to treat
Lee et al. [21]	3/10	no sham therapy, no placebo, no blinded participants, therapists and assessors, no concealed allocation, no intention to treat
Walewicz et al. [22]	7/10	no blinded assessors, no intention to treat

matory effects of ESWT. Hatanaka et al. [23] performed in vitro single exposure experiments with a low energy wave (800 beats, frequency 1 Hz, dose 0.03 mJ/mm^2) on cultured human vascular endothelial cells. They measured a significant increase in mRNA expression and activity of Vascular Endothelial Growth Factor (VEGF) and of nitric oxide synthase. In addition, the researchers observed enhanced cellular signal transduction due to increased caveolin 1 and integrin β1 activity. These phenomena are hallmarks of blood vessel reconstruction.

Yahata et al. [24] used low-energy ESWT three times a week for three consecutive weeks in Sprague-Dawley rats with damaged spinal cords. The authors noted increased cellular VEGF as well as initiation of nerve regeneration and angiogenesis at the site of injury.

Kang et al. [25] also conducted an interesting rESWT experiment in Sprague-Dawley rats. They induced brain ischemia in 105 rats and randomly assigned them to three comparative groups. For the first group (n=45), rESWT was applied (200 beats, frequency 10 Hz, dose 1 bar). The second group (n=15) received an additional treatment compared to group 1 using the same parameters (200 beats, frequency 10 Hz, dose 2 bars). Finally, the third group (n=45) was not subjected to any physical treatment and served as the control. After a single exposure to the shockwave, a significant improvement in blood flow was observed in cerebral vessels compared to the control group irrespective of dose. In addition, enhanced VEGF activity and stimulation of the neovascularization process were detected in rats from the groups exposed to rESWT.

In another experiment, Kisch et al. [26] assigned 18 Sprague-Dawley rats into two groups that were either stimulated with a series of eight high-energy ESWT (1000 pulses, 10 J output energy) or were subjected to eight quasi-ESWT (sham therapy). Procedures were applied to the dorsal side of the hind limbs. Ten minutes after the end of each procedure, laser Doppler flowmetry measurements were taken within the skin capillaries both on the limb subjected to physical treatments and on the opposite side. Cutaneous blood flow increased by 152.8% in the first group compared to the placebo group (p=0.01), and the average oxygen pressure was 12.7% higher than in the control group (p=0.02).

There are reports promoting the theory that ESWT increases nerve fiber regeneration and prevents muscular atrophy. Lee and Cho [27] studied the effectiveness of low-energy waves (300 impulses, frequency 3 Hz, dose 0.09 mJ/mm^2) in mice in relation to a single-blind placebo group. A one-time application of low-energy waves was applied to the sciatic nerve of mice damaged by induced mechanical ischemia Therapeutic progress was evaluated by measuring the change in weight of the gastrocnemius and soleus calf muscles before and 14 days after the injury and analyzed using the Sciatic Functional Index (SFI). In all measured parameters, the ESWT group showed a statistically significant difference compared to the placebo-treated group.

Many researchers additionally emphasize that ESWT can be applied to stimulation of osteogenesis. Schnurrer-Luke-Vrbanić et al. [28] measured the rate of bone tissue regeneration in response to ESWT in Wistar rats. Forty-eight animals were randomly divided into two groups. In the first group (n=36), a radial wave (0.15 mJ/mm^2, 300 pulses) was used. The second group (n=12) served as the control and received no therapeutic intervention. After three weeks, a biopsy was performed, and they measured cross-sectional areas of bone beams from 0.04 mm^2 in the cartilage to 1.7 mm^2 in the bone trabeculae. Overall, the bone tissue was significantly greater in the ESWT-treated group compared to the control group.

Conclusions

Based on the findings in the analyzed articles, ESWT promises to be an efficient and useful procedure in chronic low back pain treatment. Unfortunately, the level of evidence is relatively weak because there are a limited number of published studies related to ESWT and the final score in the PEDro classification was low. Together, these results indicate the need for further high quality randomized clinical trials.

References

1. Köksal İ, Güler O, Mahiroğulları M, Mutlu S, Çakmak S, Akşahin E. Comparison of extracorporeal shock wave therapy in acute and chronic lateral epicondylitis. Acta Orthop Traumatol Turc 2015; 49(5): 465–470.
2. Król P, Franek A, Durmała J, Błaszczak E, Ficek K, Król B, et al. Focused and radial shock wave therapy in the treatment of tennis elbow: a pilot randomised controlled study. J Hum Kinet 2015; 14(47): 127–135.
3. Razavipour M, Azar MS, Kariminasab MH, Gaffari S, Fazli M. The short term effects of shock-wave therapy for tennis elbow: a clinical trial study. Acta Inform Med 2018; 26(1): 54–56.

4. Chou WY, Wang CJ, Wu KT, Yang YJ, Cheng JH, Wang SW. Comparative outcomes of extracorporeal shockwave therapy for shoulder tendinitis or partial tears of the rotator cuff in athletes and non-athletes: retrospective study. Int J Surg 2018; 51: 184–190.
5. Circi E, Okur SC, Aksu O, Mumcuoglu E, Tuzuner T, Caglar N. The effectiveness of extracorporeal shockwave treatment in subacromial impingement syndrome and its relation with acromion morphology. Acta Orthop Traumatol Turc 2018; 52(1): 17–21.
6. Frassanito P, Cavalieri C, Maestri R, Felicetti G. Effectiveness of extracorporeal shock wave therapy and kinesio taping in calcific tendinopathy of the shoulder: a randomized controlled trial. Eur J Phys Rehabil Med 2018; 54(3): 333–340.
7. Hocaoglu S, Vurdem UE, Cebicci MA, Sutbeyaz ST, Guldeste Z, Yunsuroglu SG. Comparative effectiveness of radial extracorporeal shockwave therapy and ultrasound-guided local corticosteroid injection treatment for plantar fasciitis. J Am Podiatr Med Assoc 2017; 107(3): 192–199.
8. Hsu WH, Yu PA, Lai LJ, Chen CL, Kuo LT, Fan CH. Effect of extracorporeal shockwave therapy on passive ankle stiffness in patients with plantar fasciopathy. J Foot Ankle Surg 2018; 57(1): 15–18.
9. Bae H, Kim HJ. Clinical outcomes of extracorporeal shock wave therapy in patients with secondary lymphedema: a pilot study. Ann Rehabil Med 2013; 37(2): 229–234.
10. Cebicci MA, Sutbeyaz ST, Goksu SS, Hocaoglu S, Oguz A, Atilabey A. Extracorporeal shock wave therapy for breast cancer-related lymphedema: a pilot study. Arch Phys Med Rehabil 2016; 97(9): 1520–1525.
11. Dymarek R, Halski T, Ptaszkowski K, Słupska L, Rosińczuk J, Taradaj J. Extracorporeal shock wave therapy as an adjunct wound treatment: a systematic review of the literature. Ostomy Wound Manage 2014; 60(7): 26–39.
12. Daliri SS, Forogh B, Emami Razavi SZ, Ahadi T, Madjlesi F, Ansari NN. A single blind, clinical trial to investigate the effects of a single session extracorporeal shock wave therapy on wrist flexor spasticity after stroke. NeuroRehabilitation 2015; 36(1): 67–72.
13. Dymarek R, Taradaj J, Rosińczuk J. Extracorporeal shock wave stimulation as alternative treatment modality for wrist and fingers spasticity in poststroke patients: a prospective, open-label, preliminary clinical trial. Evid Based Complement Alternat Med 2016; 2016: 4648101.
14. Dymarek R, Taradaj J, Rosińczuk J. The effect of radial extracorporeal shock wave stimulation on upper limb spasticity in chronic stroke patients: a single-blind, randomized, placebo-controlled study. Ultrasound Med Biol 2016; 42(8): 1862–1875.
15. Connors BA, Schaefer RB, Gallagher JJ, Johnson CD, Li G, Handa RK, et al. Preliminary report on stone breakage and lesion size produced by a new extracorporeal electrohydraulic (sparker array) discharge device. Urology 2018; 116: 213–217.
16. Foldager CB, Kearney C, Spector M. Clinical application of extracorporeal shock wave therapy in orthopedics: focused versus unfocused shock waves. Ultrasound Med Biol 2012; 38(10): 1673–1680.
17. Han H, Lee D, Lee S, Jeon C, Kim T. The effects of extracorporeal shock wave therapy on pain, disability, and depression of chronic low back pain patients. J Phys Ther Sci 2015; 27(2): 397–399.
18. Schneider R. Effectiveness of myofascial trigger point therapy in chronic back pain patients is considerably increased when combined with a new, integrated, low-frequency shock wave vibrotherapy (Cellconnect Impulse): a two-armed, measurement repeated, randomized, controlled pragmatic trial. J Back Musculoskelet Rehabil 2018; 31(1): 57–64.
19. Moon YE, Seok H, Kim SH, Lee SY, Yeo JH. Extracorporeal shock wave therapy for sacroiliac joint pain: a prospective, randomized, sham-controlled short-term trial. J Back Musculoskelet Rehabil 2017; 30(4): 779–784.
20. Notarnicola A, Maccagnano G, Gallone MF, Mastromauro L, Rifino F, Pesce V, et al. Extracorporeal shockwave therapy versus exercise program in patients with low back pain: short-term results of a randomised controlled trial. J Biol Regul Homeost Agents 2018; 32(2): 385–389.
21. Lee S, Lee D, Park J. Effects of extracorporeal shockwave therapy on patients with chronic low back pain and their dynamic balance ability. J Phys Ther Sci 2014; 26(1): 7–10.
22. Walewicz K, Taradaj J, Rajfur K, Ptaszkowski K, Kuszewski MT, Sopel M, et al. The effectiveness of radial extracorporeal shock wave therapy in patients with chronic low back pain: a prospective, randomized, single-blinded pilot study. Clin Interv Aging 2019; 14: 1859–1869.
23. Hatanaka K, Ito K, Shindo T, Kagaya Y, Ogata T, Eguchi K, et al. Molecular mechanisms of the angiogenic effects of low-energy shock wave therapy: roles of mechanotransduction. Am J Physiol Cell Physiol 2016; 311(3): C378–85.
24. Yahata K, Kanno H, Ozawa H, Yamaya S, Tateda S, Ito K, et al. Low-energy extracorporeal shock wave therapy for promotion of vascular endothelial growth factor expression and angiogenesis and improvement of locomotor and sensory functions after spinal cord injury. J Neurosurg Spine 2016; 25(6): 745–755.
25. Kang N, Zhang J, Yu X, Ma Y. Radial extracorporeal shock wave therapy improves cerebral blood flow and neurological function in a rat model of cerebral ischemia. Am J Transl Res 2017; 9(4): 2000–2012.
26. Kisch T, Sorg H, Forstmeier V, Knobloch K, Liodaki E, Stang F, et al. Remote effects of extracorporeal shock wave therapy on cutaneous microcirculation. J Tissue Viability 2015; 24(4): 140–145.
27. Lee JH, Cho SH. Effect of extracorporeal shock wave therapy on denervation atrophy and function caused by sciatic nerve injury. J Phys Ther Sci 2013; 25(9): 1067–1069.
28. Schnurrer-Luke-Vrbanić T, Avancini-Dobrović V, Sosa I, Cvijanovic O, Bobinac D. Effect of radial shock wave therapy on long bone fracture repair. J Biol Regul Homeost Agents 2018; 32(4): 875–879.

Word count: 2659 • Tables: 3 • Figures: 1 • References: 28

Sources of funding:
The research was funded by the author.

Conflicts of interests:
The author reports that there were no conflicts of interest.

Cite this article as:
Walewicz K.
Extracorporeal Shock Wave Therapy (ESWT) in chronic low back pain:
a systematic review of randomized clinical trials.
MSP 2020; 14, 1: 51–56. Published online: 30 Mar 2020.

Correspondence address:
Karolina Walewicz; PT, PhD
Opole Medical School
Katowicka 68 Street, 45-060 Opole
E-mail: karolina.w101@wp.pl

Received: 29.01.2020
Reviewed: 2.03.2020
Accepted: 9.03.2020

e-ISSN 2544-1620

Medical Science Pulse 2020 (14) 1

Opinion paper

Published online: 30 Mar 2020

DOI: 10.5604/01.3001.0014.0266

HOW TO WRITE A GOOD ABSTRACT FOR A BIOMEDICAL PAPER

Mark Jeremy Hunt[1 E,F]
• ORCID: 0000-0001-7741-2191
Klaudia Raflik[1,2 E,F]
• ORCID: 0000-0002-4453-259X
Dawid Wesołowski[1,3 E,F]
• ORCID: 0000-0003-1306-1139
Agata Sibilska-Woźniacka[1 E,F]
• ORCID: 0000-0002-7397-2826
Dorota Eliza Sakowska-Hunt[1 E,F]
• ORCID: 0000-0002-1325-5681

[1] eCORRECTOR Ltd, Newton, Cambridge, UK
[2] Adam Mickiewicz University in Poznan, Poznan, Poland
[3] Jagiellonian University in Cracow, Cracow, Poland

A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Although a relatively short text, the abstract of a paper summarizes the most important issues raised in the main text. The abstract is, at least initially, the key text on which journal editors, reviewers and eventually readers form their initial judgement on the overall quality of the full manuscript. Therefore, it is essential to execute this step of the writing process well. In this article, we discuss the purpose of an abstract, why it is important, and how to write a good abstract. Increasingly, journal abstracts are structured to follow the IMRAD format (Introduction, Methods, Results, and Discussion). We provide examples of well written and badly written abstracts, with explanatory notes, to help readers understand the key points that need to be addressed and mistakes that should be avoided. Since international abstracts are generally written in English, preparing an abstract can be especially challenging for researchers who are not native speakers of English. We close this article with general linguistic advice, paying particular attention to key terms and word choice than can meaningfully express an author's intention in a concise way. The points raised in this article will help authors improve their scientific writing and enable their findings to be expressed with clarity.

KEYWORDS: scientific writing, writing advice, abstract, IMRAD

What is an abstract?

All researchers will have written an abstract for journal submissions or conference proceedings. The abstract is essentially a mini version of the full paper. The slightly unusual origin of the word, abstract, actually sums up its purpose very nicely. Abstract, in the context of academic articles, comes from the Latin *abstractus* – meaning to draw away. In relation to writing, this means that the central points of the paper are extracted into the form of a very short version of the full manuscript. This text, the abstract, is then a self-contained text that can be understood on its own, including all of the key aspects of the study that is being described. The abstract is drawn away from the main text and is presented at the beginning of the paper. Its purpose is to help readers decide whether or not the study is of sufficient interest for them to read the full manuscript.

Why is an abstract important?

You may think your abstract is of the same importance as the text in the main body of the paper. In fact, as I will show, the abstract and title are the most important part of your written work. This is best understood in terms of who the readers of your work are. As a general rule, a good abstract indicates a good paper, whereas a bad abstract – a weak one.

Potential Readers. The most obvious targets are other scientists. Many scientists may read the abstract but far fewer read the paper. There needs to be enough information so that readers can decide whether or not to read the full paper.

Reviewers. Before your paper is even considered for publication it needs to be reviewed. Typically, 2-3 reviewers will read and evaluate your manuscript for its strengths and weaknesses. Based on this, they will accept or reject the publication or recommend minor/

major revisions. When reviewers are invited to review a text the only information they have to go on is the title and abstract (the full text is usually only accessible if the reviewer agrees). Reviewers are often busy and do not have to review a paper. Indeed, reviewers may be close to making a final decision on the whole paper after having read the abstract alone. Therefore, it is fundamental that your title, and abstract, are well written to even be considered for publication.

Search Engines. Gone are the days when students and researchers searched through library journals to find papers, photocopying, and then continuing their search for more related articles. As a student, it always felt very rewarding to find a long sought-after paper. Nowadays, once a manuscript has been accepted by a journal it is uploaded to various electronic libraries, and all searching can be done with the click of a button. However, in most cases only the title, and abstract, are visible to internet search engines. The main text often remains inaccessible behind paywalls. As such, your published abstract will be readily available on the internet, and the choice of keywords you use influences how easily your abstract can be found.

The structure of an abstract

Early journals often published reports as chapters or letters where the writing style was usually descriptive and often chronological, e.g., "first I did [...] then I did [...]". Key points of a paper, such as motivations, assumptions, results, and methodologies, were often buried in the text. As techniques became more advanced and the need for research reproducibility grew, the importance of clear scientific writing became a prominent issue. In the 1950s, Sir Austin Bradford Hill, a British epidemiologist and statistician who was increasingly frustrated with the lack of uniformity in scientific writing, stated that there were four central questions:

1. "Why did you start?" – Introduction
2. "What did you do?" – Methods
3. "What answer did you get?" – Results
4. "What does it mean?" – Discussion

These are usually formulated into the IMRAD (Introduction, Methods, Results, and Discussion) format of papers that has been adopted by most journals. In parallel, the IMRAD format is the most widely used approach for writing an abstract. This is known as a structured abstract with the Introduction, Methods, Results, and Discussion forming subheadings within the abstract. Abstracts often follow a wineglass structure with the opening and closing sentences very general and the detailed content in the methods and results sections. Typically, a structured abstract has 1-2 sentences for the Introduction, 1-2 for Methods, 3-4 for Results, and 1-2 for Discussion.

Not all journals have adopted the IMRAD approach, even many high-profile traditional journals, such as *Nature* and *Science*. However, the parallel structure can still be clearly seen despite the lack of subheading. Often in these cases, a series of related studies have been carried out to address a common problem, and therefore combining methods with results is a clear way to express these findings. Below you can find two examples published from high-impact journals, i.e., *Nature* and *Neuron*. In both, the abstracts open and close with broadly understood concepts understandable to non-specialists. The main section provides sufficient detail for specialists to grasp the novelty and sufficient details of the work.

Activation of microglia and inflammation-mediated neurotoxicity are suggested to play a decisive role in the pathogenesis of several neurodegenerative disorders. Activated microglia release pro-inflammatory factors that may be neurotoxic. Here we show that the orderly activation of caspase-8 and caspase-3/7, known executioners of apoptotic cell death, regulate microglia activation through a protein kinase C (PKC)-δ-dependent pathway. We find that stimulation of microglia with various inflammogens activates caspase-8 and caspase-3/7 in microglia without triggering cell death in vitro and in vivo. Knockdown or chemical inhibition of each of these caspases hindered microglia activation and consequently reduced neurotoxicity. We observe that these caspases are activated in microglia in the ventral mesencephalon of Parkinson's disease (PD) and the frontal cortex of individuals with Alzheimer's disease (AD). Taken together, we show that caspase-8 and caspase-3/7 are involved in regulating microglia activation. We conclude that inhibition of these caspases could be neuroprotective by targeting the microglia rather than the neurons themselves. (Burguillos et al., 2011)

The olfactory bulbs (OBs) are the first site of odor representation in the mammalian brain, and their unique ultrastructure is considered a necessary substrate for spatiotemporal coding of smell. Given this, we were struck by the serendipitous observation at MRI of two otherwise healthy young left-handed women, yet with no apparent OBs. Standardized tests revealed normal odor awareness, detection, discrimination, identification, and representation. Functional MRI of these women's brains revealed that odorant-induced activity in piriform cortex, the primary OB target, was similar in its extent to that of intact controls. Finally, review of a public brain-MRI database with 1,113 participants (606 women) also tested for olfactory performance, uncovered olfaction without anatomically defined OBs in ~0.6% of women and ~4.25% of left-handed women. Thus, humans can perform the basic facets of olfaction without canonical OBs, implying extreme plasticity in the functional neuroanatomy of this sensory system. (Weiss et al., 2020)

Introduction | Methods and Results | Discussion

Example of a badly structured abstract

Introduction: Huntington's (HD) disease is an autosomal dominant neurodegenerative disease with no known cure. It is caused by progressive nerve cell death primarily affecting the dorsal striatum and leads to motor and cognitive symptoms. The mean age of onset is 35 to 44 years and the median survival time is 15 to 18 years after onset and was first identified by George Huntington in 1872. The HTT mutation that causes Huntington disease involves a DNA segment known as a CAG trinucleotide repeat. Here, we investigated whether creatine treatment would slow the progressive functional decline in HD.

Methods: We conducted a randomized, double-blind, placebo-controlled study of up to 40 g daily of creatine monohydrate in participants with stage I and II HD treated for up to 3 years. Functional decline was assessed using the Unified Huntington's Disease Rating Scale. The study was carried out at the Department of Neurology, Jupiter Hospital, Jupiter Road, Leeds, England. All data were originally collected with appropriate preapproval of human ethics committees and written informed consent at each site in each respective study. Eligible participants were in stage I or II of HD (TFC ≥7), were over 18 years old and had a confirmatory family history. Study personnel, participants, caregivers, steering committee members, and NIH program staff were blinded to treatment assignment until study conclusion.

Results: We analyzed all four domains – motor function, cognitive function, behavioral abnormalities, and functional capacity. Next, we examined if the changes in each domain were correlated with each other. Adverse events, mainly gastrointestinal, were significantly more common in participants on creatine. Subgroup analysis suggested that men and women may respond differently to creatine treatment.

Discussion: Comparison between the findings reported here and in other studies are discussed. This study's primary limitation was that the data were gathered only from a small number of patients and therefore, further research is needed to confirm the generalizability of the study's results.

Critique

These are common problems which can be found in abstract.

Introduction. This is much too long. The only really important sentences are the first and the last one. The sentences in between are all superfluous information for this type of abstract.

Methods. This is also much too long. The only essential sentences are the first two sentences. The rest belong in the Methods section of the paper. It is not necessary to state specifically, with the full address, where the study was carried out. Ethics approval statements and details of methodology do not belong here either. Abbreviations, e.g., TFC, should not be used unless spelled out in full. Numbers of patients are also not stated.

Results. The important results are not presented at all, just statements that these data can be found in the main text! This is a surprisingly common mistake, and it puts your abstract at an immediate disadvantage when the reader does not see clearly what your results are. The only concrete result is that there were drug side effects. It's perfectly correct to include this information, as it might be an important finding, and negative data as well as positive data do need to be reported.

Discussion. Another common issue is that the authors do not draw out a single message from their paper. Was creatine potentially beneficial or not? Does the data support the use of this drug in the treatment of HD or not? A simple sentence is all that is needed. Limitations, unless specifically requested by an editor, are very rarely included in the main abstract. This belongs in the Discussion section of the main paper.

Linguistic and stylistic correctness in a good abstract

An abstract is very short, typically 200-300 words. So, it can be hard to encapsulate the full manuscript, which is typically 4,000-6,000 words into such a short piece of text. Since the main language used in international publication is English, this can put authors whose first language is not English at a disadvantage but not severely so, since scientists are writing scientific, rather than literary, works. Researchers whose second language is not English might consider that scientific language should be complicated, using multiple clauses, and essentially esoteric and only understood by an enlightened few. Nothing could be further from the truth. Good scientific writing is clear and concise. Use of superfluous words, clauses, and certainly metaphors should be avoided. It is important that the terms used are consistent with those used in the existing canon of scientific language but, aside from terminology, the expression should be as simple as possible (refer to the abstract shown in this article).

The language of the abstract should be adjusted to the scientific indicators. Thus, the authors should avoid using any colloquial expressions and those which may be not understood – or even misunderstood. The scientific character of the paper has two sides – one concerns the message, and therefore the essence of the text, and the other, by contrast, is related to the meticulous and appropriate selection of specialist terminology. This is particularly important when the papers are written by non-native speakers of English – as it is the lead language used in international journal publications. It is essential to take care in finding the proper equivalents and to avoid any ambiguous wording that may cause readers' – but firstly, reviewers' and editors' – doubts. Another crucial matter is the aesthetics of the manuscript. Almost every editorial board provides the formal

and editorial requirements that have to be applied in scientific papers. They mainly concern editing the paper according to the common patterns, i.e., font style, its size, line spacing, paragraphs, and highlights. Although these elements do not significantly affect the reception, they play an important part in the manner it is read. Editorial requirements, however, do not only refer to the described elements. There are also those that determine the proper reception of the text and its adequacy, i.e., the length of the abstract, the way thoughts are organized, placement of figures and other secondary elements, as well as creation of bibliographic descriptions.

Phrases to use in an abstract (and main text)

Below we present some expressions that authors may find useful in the different sections of a structured abstract.

Introduction

- "[...] is a neurodegenerative disease with no known cure."
- "However, it remains unclear how [...]"
- "We have shown recently that [...]"
- "The objective/purpose of this study was [...]"
- "We hypothesized that [...]"

Methods

- "A cohort/total of [...] patients were examined."
- "We recorded from [...]"
- "We conducted an [...]"
- "[...] was used to assess [...]"
- "We compared/measured/modeled [...] using [...]"
- "We carried out a systematic review of [...]"

Results

- "We found/showed that [...]"
- "[...] analysis revealed that [...]"
- "Using a set of [...] tests we found."
- "We further identified [...]"
- "Consistently [...]"

Conclusions

- "Taken together, our findings indicate that [...]"
- "These findings demonstrate/suggest that [...]"
- "Our findings provide compelling evidence that [...]"
- "We speculate/propose that [...]"
- "This study confirms that [...]/does not confirm that [...]"

References

1. Burguillos MA, Deierborg T, Kavanagh E, Persson A, Hajji N, Garcia-Quintanilla A, et al. Caspase signalling controls microglia activation and neurotoxicity. Nature 2011 Apr 21; 472(7343): 319–324.
2. Andrade C. How to write a good abstract for a scientific paper or conference presentation. Indian J Psychiatry 2011 Apr-Jun; 53(2): 172–175.
3. Hunt MJ, Ochmańska M, Cilulko-Dołęga J. Scientific writing for the biomedical sciences. MSP 2018; 12(1): 29–33.
4. Sollaci LB, Pereira MG. The introduction, methods, results, and discussion (IMRAD) structure: a fifty-year survey. J Med Libr Assoc 2004 Jul; 92(3): 364–367.
5. Weiss T, Soroka T, Gorodisky L, Shushan S, Snitz K, Weissgross R, et al. Human olfaction without apparent olfactory bulbs. Neuron 2020 Jan 8; 105(1): 35–45.e5.

Word count: 2318 • Tables: – • Figures: – • References: 5

Sources of funding:
The research was funded by the authors.

Conflicts of interests:
The authors report that there were no conflicts of interest.

Cite this article as:
Hunt MJ, Raflik K, Wesołowski D, Sibilska-Woźniacka A, Sakowska-Hunt DE.
How to write a good abstract for a biomedical paper.
MSP 2020; 14, 1: 57–60. Published online: 30 Mar 2020.

Correspondence address:
Mark Jeremy Hunt
eCORR ECTOR Ltd, Mill Lane, Sawston,
CB22 3HY Cambridge, United Kingdom
E-mail: mhunt@ecorrector.com
Phone: (+48) 22 122 80 71

Received: 2.03.2020
Reviewed: 11.03.2020
Accepted: 12.03.2020