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MARTA MISIUK-HOJŁO¹, ANNA BRZECKA², MARIA EJMA³, AGNIESZKA KOBIERZYCKA¹

Abnormal Visual Evoked Potentials as a Sign of Lesions in the Optic Tract in Patients with Obstructive Sleep Apnoea Syndrome

Nieprawidłowe wzrokowe potencjały wywołane jako objaw uszkodzenia drogi wzrokowej u chorych z zespołem obturacyjnego bezdechu śródsennego

¹ Department of Eye Diseases, Wrocław Medical University, Poland

² Department of Lung Diseases, Wrocław Medical University, Poland

³ Department of Neurology, Wrocław Medical University, Poland

Abstract

Background. Obstructive sleep apnoea (OSA) syndrome with repetitive nocturnal sleep hypoxemia may be considered as a risk factor of optic nerve damage.

Objectives. The aim of the study was to detect the lesions in optic tract that might occur in the patients with severe OSA syndrome.

Material and Methods. In 16 men with severe OSA syndrome (apnoea index > 35, mean 60 ± 12) the detailed ophthalmologic studies, including automatic perimetry, and the studies of the latency and amplitude of visual evoked potentials (VEPs) have been performed.

Results. In patients with severe OSA syndrome the mean latency of VEPs was 119 ± 7.6 ms. In 81% of patients the latency of VEPs was prolonged and exceeded 118 ms. In four patients the deficits in visual field have been found and in three of them there was prolongation of the latencies of VEPs. In patients with perimetric abnormalities there were extremely severe respiratory disturbances during sleep: mean apnoea index was 67 ± 5 , mean SaO_2 at the end of the apnoeas was $79 \pm 5\%$ (*Adv Clin Exp Med* 2004, 13, 4, 561–565).

Conclusions. Abnormal VEPs might be an early marker of optic tract lesions in OSA patients.

Key words: visual evoked potentials, sleep apnoea syndrome, optic tract.

Streszczenie

Wprowadzenie. Występujące u chorych z zespołem obturacyjnego bezdechu śródsennego wielokrotne epizody niedotlenienia krwi tętniczej w czasie snu mogą stanowić czynnik ryzyka uszkodzenia nerwu wzrokowego.

Cel pracy. Celem pracy było wykrycie uszkodzeń drogi wzrokowej u chorych z ciężką postacią zespołu obturacyjnego bezdechu śródsennego.

Materiał i metody. U 16 mężczyzn z ciężką postacią zespołu obturacyjnego bezdechu śródsennego (wskaźnik bezdechu > 35, średnio 60 ± 12) przeprowadzono szczegółowe badania okulistyczne, obejmujące m.in. automatyczne badanie perymetryczne, oraz badania latencji i amplitudy wzrokowych potencjałów wywołanych (WPW).

Wyniki. U chorych z ciężką postacią zespołu obturacyjnego bezdechu śródsennego latencja WPW wynosiła średnio $119 \pm 7,6$ ms. U 81% chorych stwierdzono wydłużenie (> 118 ms) latencji WPW. U czterech chorych, w tym u trzech z wydłużoną latencją WPW, stwierdzono ubytki w polu widzenia. U chorych ze stwierdzonymi zaburzeniami perymetrycznymi występowały znacznie nasilone zaburzenia oddechowe w czasie snu: wskaźnik bezdechu wynosił średnio 67 ± 5 , SaO_2 w czasie bezdechów śródsennych wynosiło średnio $79 \pm 5\%$.

Wnioski. Nieprawidłowe WPW mogą stanowić wczesny wskaźnik uszkodzenia drogi wzrokowej u chorych z ciężką postacią zespołu obturacyjnego bezdechu śródsennego (*Adv Clin Exp Med* 2004, 13, 4, 561–565).

Słowa kluczowe: wzrokowe potencjały wywołane, zespół bezdechu śródsennego, droga wzrokowa.

Obstructive sleep apnea (OSA) syndrome is a sleep disorder that is characterised by repetitive cessation of respiration during sleep, caused by partial or complete upper airway collapse. It is a common disorder affecting mainly middle-aged or elderly men and postmenopausal women [1]. The main risk factor of OSA is obesity. Typical symptoms suggestive of OSA syndrome are loud, persistent and irregular snoring, witnessed gasping or choking during sleep, excessive daytime sleepiness and non-restorative sleep. The consequences of OSA develop as a result of repetitive arousals, that are generally needed to stop the events [2], and as a result of hemodynamic responses to obstructive apnoeas with the concomitant activation of sympathetic nervous system [3]. Acute consequences of sleep apnoeas are the episodes of arterial oxygen desaturation; the range of sleep hypoxemia may vary from mild to severe, depending of baseline arterial oxygen saturation (SaO_2), apnoea duration, degree of obesity and lung function [4].

As a result of repetitive nocturnal hypoxemia caused by sleep apnoeas the optic nerve damage may result [5]. Recently, there is an increasing number of reports showing that OSA syndrome may be considered as a risk factor of optic nerve damage presenting as normal-tension glaucoma [6–8]. However, in most of the patients with OSA the clinical ophthalmologic examination results are normal [9].

Visual evoked potentials (VEPs) are the neuroelectrophysiological response to the external visual stimuli and reflect the function of the both optic nerve and the other structures of optic tract [10]. The study of VEPs is the most sensitive method of the detection of the subclinical damage of the optic tract, including optic nerves [10]. Thus the authors performed VEPs studies and detailed ophthalmologic examinations in OSA patients exposed to frequent (> 35 per hour of sleep) episodes of nocturnal hypoxemia due to obstructive sleep apnoeas in order to detect the lesions in the optic tract that might occur in the patients with severe OSA syndrome.

Material and Methods

Material of the study consisted of 16 men with severe OSA syndrome, i.e. with apnoea exceeding 35. The diagnosis of OSA syndrome was based on the results of the nocturnal studies of respiration. The authors used a portable unit (POLYMESAM) and during sleep – between 11.00 p.m. and 6.00 a.m. – continuously measured: thoracic and abdominal respiratory movements, respiratory oronasal air-

flow and arterial oxygen saturation (SaO_2) to detect the obstructive apnoeas and hypopnoeas. The software automatically calculated the apnoea index (mean number of obstructive apnoeas and hypopnoeas per hour of sleep), mean apnoea duration and the average low SaO_2 at the end of apnoeas.

VEPs were investigated with the use of averaging system Nicolet CA-1000. The eyes were stimulated subsequently with the reversal checkerboard pattern of high contrast (over 90%), emitted with black-and-white TV screen. Size of the whole screen was $18^\circ \times 22^\circ$, and angular size of individual squares was 1.1° . Surface recipient electrodes were placed in occipital region (OZ – international 10–20 system), with reference electrode in frontal region (Fz). The authors evaluated latency of positive wave P100, amplitude of P100/N120 complex and the difference of latency of wave P100 registered during the stimulation of left and right eye (interocular latency). VEPs studies were performed after the sleep studies during the daytime in awake patients. The range of normal VEPs's latencies and amplitudes has been established on the basis of examination of 50 healthy people.

The ophthalmological examinations included: visual acuity, eye fundus, intraocular pressure, and slit-lamp examinations; all the patients have been also studied during at least one visit with the Octopus automated perimeter and in case when the abnormalities in the visual field have been found the perimetry was repeated.

Results

The results of anthropometric studies, daytime arterial blood gases analysis, and the studies of respiratory function during sleep in the patients with OSA syndrome are presented in the Table 1. All the patients were obese with body mass index (BMI) exceeding 30 (four patients were extremely obese with $\text{BMI} > 40$). Daytime arterial blood gases analysis revealed mild with $\text{PaO}_2 < 9.3$ kPa in 9 patients and the signs of chronic alveolar hypoventilation ($\text{PaCO}_2 > 5.99$ kPa) in 5 patients. The range of apnoea index was from 36 to 89. The range of mean SaO_2 at the end of the apnoeas was from 62 to 89%. The range of the mean apnoea duration was from 20 to 40s.

The prolongation of VEPs latencies was found in 13 (81%) of patients. In three patients the latency of the wave P100 was prolonged unilaterally (> 118 ms) and in 10 patients the latency of the wave P100 was prolonged bilaterally, exceeding 120 ms in each eye. The results of neuroelectrophysiologic VEPs studies in OSA patients and in

the control group are shown in Table 2. The mean absolute latency of the wave P100 was longer in OSA patients than in the control group.

Ophthalmologic examination revealed the deficits in visual field in four patients. These were: concentric visual field deficit (in 1 patient), upper nasal left and upper temporal right, quadrantic visual field deficit (in 1 patient), diffused visual field deficits, persisting during the control examination and consistent with normal-tension glaucoma

Table 1. The results of anthropometric studies, daytime arterial blood gases analysis, and the studies of respiratory function during sleep in the patients with OSA syndrome

Tabela 1. Wyniki badań antropometrycznych, gazometrycznych i czynności oddechowej w czasie snu u chorych z zespołem obturacyjnego bezdechu śródsennego

| | |
|----------------------------------------------------------------------------------------------------|-------------|
| Age – years (Wiek – lata) | 47.6 ± 7.7 |
| Height – cm (Wzrost – cm) | 177 ± 8 |
| Weight – kg (Waga – kg) | 114 ± 16 |
| BMI | 36.7 ± 4.6 |
| PaO ₂ (kPa) | 8.78 ± 0.67 |
| PaCO ₂ (kPa) | 5.73 ± 0.67 |
| Apnoea index (Wskaźnik bezdechu) | 60 ± 12 |
| SaO ₂ during sleep apnoeas – % (SaO ₂ w czasie bezdechów śródsennych – %) | 79 ± 7.4 |
| Sleep apnoea duration – s (Czas trwania bezdechów śródsennych – s) | 29 ± 4.61 |

PaO₂ – arterial oxygen partial pressure.

PaCO₂ – arterial carbon dioxide partial pressure.

SaO₂ – arterial oxygen saturation.

PaO₂ – ciśnienie parcjalne tlenu.

PaCO₂ – ciśnienie parcjalne dwutlenku węgla.

SaO₂ – wysycenie krwi tętniczej tlenem.

(in 1 patient), paracentral scotoma with the signs of open-angle glaucoma (in 1 patient). Primary open-angle glaucoma has been diagnosed 8 years ago and since that time was fully controlled with beta-blockers and carbonic anhydrase inhibitors in drops. The results of clinical and neuroelectrophysiological studies in OSA patients with ophthalmologic abnormalities are shown in the Table 3. In the patient with open-angle glaucoma VEPs were normal. In three other patients with the deficits in visual field there was P100 latency prolongation. In the patients with the deficits in visual field the mean apnea index was ≥ 60 (mean 67 ± 5) and the mean SaO₂ at the end of the sleep apnoeas was $\leq 86\%$ (mean $79 \pm 5\%$).

Discussion

The results of the study show that in most of the patients with severe OSA syndrome there are neuroelectrophysiological, subclinical signs of lesions in the optic tract, as shown by prolonged latencies of VEPs and in approximately 1/5th of the patients with severe OSA syndrome and abnormal VEPs the deficits in visual field can be found.

Recently it has been reported that OSA syndrome might be a risk factor of glaucoma, especially of normal-tension glaucoma [6–8, 11–13]. Mojon and Hess [12] found that the prevalence of glaucoma among OSA patients (AHI ≥ 10) was 7.2%, while expected prevalence in the Caucasian population was much lower, i.e. 2% [12]. These authors diagnosed normal-tension glaucoma in 2.9% of OSA patients [12]. In the study glaucoma has been found in 2 patients (12.5% of patients with severe OSA), in one patient it was primary open-angle glaucoma, successfully pharmacologically treated for the last 8 years, and in the other patient – normal-tension glaucoma, diagnosed at

Table 2. The results of VEPs studies in OSA patients and in the control group

Tabela 2. Wyniki badań WPW u chorych z zespołem obturacyjnego bezdechu śródsennego i u osób zdrowych

| | OSA patients (Chorzy z zespołem obturacyjnego bezdechu śródsennego) | Control group (Grupa kontrolna) | p |
|---------------------------------------------------------------------------------|------------------------------------------------------------------------|------------------------------------|---------|
| Absolute latency of the wave P100 – ms (Bezwzględna latencja fali P100 – ms) | 119 ± 7,6 | 104 ± 4.57 | < 0.001 |
| Interocular latency – ms (Względna latencja – ms) | 4.3 ± 3.4 | 2.2 ± 2 | NS |
| Amplitude of the wave P100 – mV (Amplituda fali P100 – mV) | 5.5 ± 2.39 | 7.62 ± 3.04 | NS |

NS – not statistically significant.

NS – nieistotne statystycznie.

Table 3. The results of VEPs studies in patients with severe OSA syndrome and the deficits in visual field

Tabela 3. Wyniki badań WPW u chorych z ciężką postacią zespołu obturacyjnego bezdechu śródseennego i ubytkami w polu widzenia

| VEPs (WPW) | Diagnosis (Rozpoznanie) | | | |
|---------------------------------------------------------------|--------------------------------------------------------|-------------------------------------------------------------------------------------|------------------------------------------------------------------|-------------------------------------------------------------|
| | open-angle glaucoma (jaskra otwar- tego kąta) | concentric defects in visual field (koncentryczne ubytki pola widzenia) | normal-tension glaucoma (jaskra normal- nego ciśnienia) | quadrantic defects (kwadrantowe ubytki pola widzenia) |
| P100 latency, right – ms (Latencja P100 po prawej – ms) | 106 | 132 | 120 | 120 |
| P100 latency, left – ms (Latencja P100 po lewej – ms) | 104 | 120 | 128 | 120 |
| Interocular latency – ms (Latencja względna – ms) | 2 | 12 | 8 | 0 |
| P100 amplitude, right – mV (Amplituda p100 po prawej – ms) | 2.8 | 4 | 6.5 | |
| P100 amplitude, left – mV (Amplituda P100 po lewej – mV) | 2.75 | 2.4 | 5.1 | 5.85 |

Table 4. The results of arterial blood gases analysis and the studies of respiration during sleep in patients with OSA syndrome and the deficits in visual field

Tabela 4. Wyniki badań gazometrycznych i czynności oddechowej w czasie snu u chorych zespołem obturacyjnego bezdechu śródseennego i ubytkami w polu widzenia

| | Diagnosis (Rozpoznanie) | | | |
|--------------------------------------------------------------------------------------------------|------------------------------------------------------|---------------------------------------------------------------------------------------|------------------------------------------------------------------|-------------------------------------------------------------|
| | open-angle glaucoma (jaskra otwartego kąta) | concentric defects in visual field (koncentryczne ubytki pola wi- dzenia) | normal-tension glaucoma (jaskra normalne- go ciśnienia) | quadrantic defects (kwadrantowe ubytki pola widzenia) |
| PaO ₂ (kPa) | 9.33 | 8.8 | 8.26 | 7.06 |
| PaCO ₂ (kPa) | 4.8 | 5.07 | 6.93 | 6.53 |
| Apnoea index (Wskaźnik bezdechu) | 69 | 70 | 60 | 70 |
| SaO ₂ during apnoeas – % (SaO ₂ w czasie bezdechów śródseennych – %) | 86 | 73 | 78 | 80 |

the time of this study. In the other 2 patients the deficits in visual field have been found that might indicate the functional lesions of optic tract (quadrantic homonymous deficits and concentric deficits).

Sleep-disturbed breathing may play a significant role in the pathogenesis of the optic neuropathy [6, 9]. The optic nerve damage in the patients with OSA syndrome may result from repetitive nocturnal hypoxia [5]. In one of author's patients the ophthalmologic study revealed the signs of normal-tension glaucoma (diffused deficits in visual field in two consecutive studies). In this patient the apnoea index was very high (60), SaO₂ during sleep apnoeas was very low (78%), and additional-

ly he had the signs of chronic alveolar hypoventilation with daytime hypoxemia and hypercapnia. This observation confirms the possible relation between hypoxemia and the development of normal-tension glaucoma in OSA patients [5].

The causal relationship between recurrent sleep apnoeas and optic nerve damage has been confirmed by the previous observations that the deficits in the visual field might be reversible after the successful treatment of OSA patients with continuous positive airway pressure during sleep [7, 9, 11].

In the patient with the diffuse deficits in the visual field the latency of VEPs was prolonged and this observation confirms the presence of a lesion in optic tract in the case of normal-tension glauco-

ma in the course of severe OSA syndrome. In the other two patients with the deficits in visual field (concentric and quadrantic homonymous) the prolongation of VEPs latency (in the range of 120–132 ms) indicated the possible functional lesions in the optic tract; in these patients apnoea index was also very high, i.e. was at least 60 per hour of sleep and the mean SaO₂ during apnoeas was low, i.e. it was 80% or lower. Moreover, in these patients there was daytime hypoxemia (with chronic alveolar hypoventilation in the patient with quadrantic deficits in visual field). Chronic daytime hypoxemia with repetitive profound arterial oxygen desaturation during sleep might have influenced the function of optic tract in these patients.

The examination of VEPs has been used in various clinical situations, including early detection of optic nerve damage in the course of neurological diseases or developing as a result of pharmacological treatment [14, 15]. In the study the analysis of VEPs has shown that there was very high percentage of patients (81%) with severe OSA syndrome who had abnormally prolonged latencies of VEPs. Additionally, there was high percentage of patients (23%) with prolonged latencies of VEPs and the deficits in the visual field.

The measurement of the latencies of VEPs may serve as a marker of increased risk of optic tract lesion in the patients with severe OSA syndrome.

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Address for correspondence:

Marta Misiuk-Hojło
Department of Eye Diseases Wrocław Medical University
T. Chalubińskiego 2
50-367 Wrocław
misiuk@linux.okulist.am.wroc.pl

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