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Different Patterns of Growth Hormone Secretion in Osteoporotic Women

Różny charakter wydzielania hormonu wzrostu u kobiet chorych na osteoporozę

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Abstract

Background. Growth hormone (GH) and its peripheral mediator IGF-1 play an important role in bone remodeling. GH secretion is gradually decreased with aging, which is associated with bone loss and osteoporosis.
Objectives. The aim of the study was to assess the GH secretory patterns in different groups of women with osteoporosis.
Material and Methods. The study was carried out in: I – 20 women with postmenopausal osteoporosis, early (1–2 years) after menopause, without HRT; II – 20 women with postmenopausal osteoporosis, at least 6 months on HRT; III – 20 women with postmenopausal osteoporosis, 10 years after menopause, without HRT at any time; IV – 20 postmenopausal women sufferring from steroid-induced osteoporosis. They were compared to 10 premenopausal healthy controls – group V. All of subjects were analyzed basal serum GH and insulin hypoglycaemia stimulated GH secretion. Serum IGF-1 concentration was analyzed simultaneously.
Results. The patterns of GH secretion were various among the groups of patients. The most significant differences were observed between groups of early menopausal patients on HRT and late menopausal ones never receiving HRT. No differences in IGF-1 among groups of patients were shown.
Conclusions. Postmenopausal osteoporosis is characterized by impaired GH secretion which can be partially reversed by HRT. Steroid-induced osteoporosis is characterized by a low GH secretory reserve (**Adv Clin Exp Med 2004, 13, 6, 927–931**).

Key words: growth hormone, insulin-like growth factor-1, postmenopausal osteoporosis, steroid-induced osteoporosis.

Streszczenie

Wprowadzenie. Hormon wzrostu (GH) i jego obwodowy mediator IGF-1 odgrywają istotną rolę w przebudowie kości. Wydzielanie GH stopniowo zmniejsza się z wiekiem, co wiąże się z ubytkiem tkanki kostnej i osteoporozą.
Cel pracy. Określenie charakteru wydzielania GH u kobiet chorych na osteoporozę.
Materiał i metody. Badanie przeprowadzono w następujących grupach: I – 20 kobiet chorych na osteoporozę pomenopauzalną, 1–2 lata po menopauzie, bez HTZ; II – 20 kobiet chorych na osteoporozę pomenopauzalną, leczonych HTZ co najmniej 6 miesięcy; III – 20 kobiet chorych na osteoporozę pomenopauzalną, 10 lat po menopauzie, nigdy nieleczonych HTZ; IV – 20 kobiet po okresie menopauzy z osteoporozą posteroidową. Grupą kontrolną było 10 zdrowych kobiet w wieku rozrodczym – V. U wszystkich kobiet badano podstawowe i pobudzane insuliną wydzielanie GH, oraz IGF-1.
Wyniki. Charakter wydzielania GH różnił się w poszczególnych grupach badanych kobiet. Największe różnice obserwowano między grupą kobiet we wczesnej menopauzie stosujących HTZ a grupą starszych kobiet po okresie menopauzy nigdy nieleczonych HTZ. Nie stwierdzono różnic w wydzielaniu IGF-1 między grupami badanych.
Wnioski. Objawem osteoporozy pomenopauzalnej jest zaburzone wydzielanie GH, które jest częściowo odwracalne po zastosowaniu HTZ. Osteoporoza posteroidowa charakteryzuje się małą rezerwą wydzielniczą hormonu wzrostu (**Adv Clin Exp Med 2004, 13, 6, 927–931**).

Słowa kluczowe: hormon wzrostu, insulinopodobny czynnik wzrostu 1, osteoporoza pomenopauzalna, osteoporoza posteroidowa.

Growth hormone (GH) and its peripheral mediator insulin-like growth factor-1 (IGF-1) play an important, stimulatory role in a normal bone metabolism. GH exerts strong antiresorptive action, but its secretion decreases with age [1]. GH deficiency in adults may be a cause of decreased bone mass, but its chronical excess in acromegaly increases bone turnover and influences equivocally bone mineral density (BMD) [2–4]. There were several attempts of GH therapeutic application in postmenopausal osteoporosis but they did not succeed [5, 6].

Both oral and transdermal estrogen influences GH and IGF-1 concentrations in postmenopausal women suggesting GH/IGF-1 axis involvement in the pathogenesis of postmenopausal osteoporosis. It has been assumed that oral estrogen increased GH levels but transdermal one did not [7–9]. These different effects may be caused by the first pass liver metabolism of oral estrogen. However, one study revealed similar stimulatory influence of oral and transdermal estrogen on GH secretion [10].

Estrogen, when given orally suppressed plasma IGF-1 levels [9, 11], transdermal estrogen administration had no effect [8], was able either to increase [7] or to decrease IGF-1 [10] in various studies, but intranasal estrogen has been found to have no influence on serum IGF-1 concentration [12].

Corticosteroid-induced osteoporosis shows an increased bone resorption together with decreased bone formation, but the levels of GH and IGF-1 remain normal [13, 14].

The aim of present study was to assess GH secretory patterns in different groups of postmenopausal women with osteoporosis and in a group of women with corticosteroid-induced osteoporosis.

Material and Methods

Subjects

The study was carried out in following groups:

I – 20 women with postmenopausal osteoporosis (51.1 ± 3.2 years), early (1–2 years) after menopause, without HRT;

II – 20 women with postmenopausal osteoporosis (55.2 ± 3.9 years), at least 6 months on HRT;

III – 20 women with postmenopausal osteoporosis (59.8 ± 2.7 years), late (at least 10 years) after menopause, without HRT at any time;

IV – 20 women with steroid-induced osteoporosis (54.0 ± 3.2 years). They were given steroids for at least 5 years in the treatment of bronchial asthma;

V – 10 healthy women at reproductive age (35.1 ± 2.1 years), with normal bone mass, regular menstrual cycles, served as controls.

The subjects were recruited from the patients of Department of Endocrinology and out-patients Clinic. Menopause was defined as complete cessation of menses for at least 6 months associated by elevated serum FSH levels (> 40 mIU/ml). Patients were healthy according to their general medical history, physical examination, and they did not take other medication (except for steroids in group IV). Osteoporosis was diagnosed according to WHO criteria.

The data of subjects are given in Table 1.

Methods

In all of the subjects: basal serum GH concentration and insulin hypoglycemia stimulated GH secretion (secretory reserve) were studied. Insulin Actrapid (Novo Nordisk, Denmark) was injected intravenously at a dose of 0.1 IU per kg of body weight. Blood samples were taken before and after 20, 30, 60 and 90 min following insulin application. GH secretory reserve was assessed by the maximal stimulatory increment and area under the GH curve (AUC) after insulin administration. AUCs were estimated using the trapezoidal method.

During the test serum IGF-1 concentration was analyzed simultaneously. Serum GH and IGF-1 concentrations were studied using RIA commercial kits. Osteoporosis was diagnosed on the basis of BMD measurement (T-score more than 2.5 SD below reference value) by DPX in the lumbar spine, and/or incidence of osteoporotic fracture(s). The patients on HRT (group II) were administered transdermally 17-β estradiol/norethisterone acetate (Estracomb TTS, Novartis) for at least 6 months.

Statistical analysis between groups studied was done using Student's *t*-test.

Results

The results revealed various patterns of GH secretion in subjects studied. In all groups of osteoporotic women basal serum GH concentration was lower than in young healthy controls. Among the patients, the lowest basal GH level was observed in postmenopausal women late after menopause (group III), and the highest one in postmenopausal women on HRT (group II). The difference was statistically significant ($p = 0.03$) between groups III and V (young controls) only (Tab. 1, Fig. 1 and 2).

Maximal stimulatory GH increment was low in postmenopausal patients on HRT (group II), significant in early postmenopausal patients without HRT (group I) and in patients with steroid-induced

Table 1. Clinical and hormonal characteristics of patients

Tabela 1. Charakterystyka kliniczna i hormonalna badanych osób

Group (Grupa)	Number (Liczba)	Age – years (Wiek – lata)	Menopause duration – years (Czas trwania menopauzy – lata)	BMI kg/m^2	Basal GH (Podstawowe wydzielanie GH) µIU/ml	Max GH increment (Maksymalnie zwiększone wydzielanie GH) %	Basal IGF-1 (Podstawowe wydzielanie IGF-1) ng/ml
I	20	51.1 ± 3.2	1.1 ± 0.4	25.8 ± 3.4	5.3 ± 4.2	207	210.6 ± 63.0
II	20	55.2 ± 3.9	6.0 ± 0.8	26.1 ± 4.1	6.7 ± 6.2	10	177.5 ± 56.2
III	20	59.8 ± 2.7	12.4 ± 4.2	26.5 ± 2.9	3.6 ± 0.9	588	179.9 ± 98.5
IV	20	54.0 ± 3.2	5.6 ± 2.5	27.2 ± 3.8	4.9 ± 3.9	173	184.6 ± 86.7
V	10	35.1 ± 2.1	–	24.8 ± 3.1	8.0 ± 5.6	388	345.5 ± 45.7

osteoporosis (group IV), but the highest one in late postmenopausal patients (group III) (Tab. 1, Fig. 1 and 2). Some differences were statistically significant: group I vs. group II, p = 0.031; group I vs. group III, p = 0.026; group II vs. group III, p = = 0.003; group II vs. group V, p = 0.008; group III vs. group V, p = 0.01.

The peak of insulin-stimulated GH secretion was reached in all groups of menopausal patients later than in young controls, showing almost flat course in women on HRT (group II) and biphasic one in steroid-induced osteoporosis (group IV) (Fig. 1).

Stimulated GH secretion assessed by AUC is low in postmenopausal women on HRT (group II), higher in early postmenopausal women without HRT (group I) and the highest one in late postmenopausal patients (group III) (Fig. 3).

The most evident differences in all parameters studied were shown between groups II and III (Fig. 1, 2 and 3, Tab. 1).

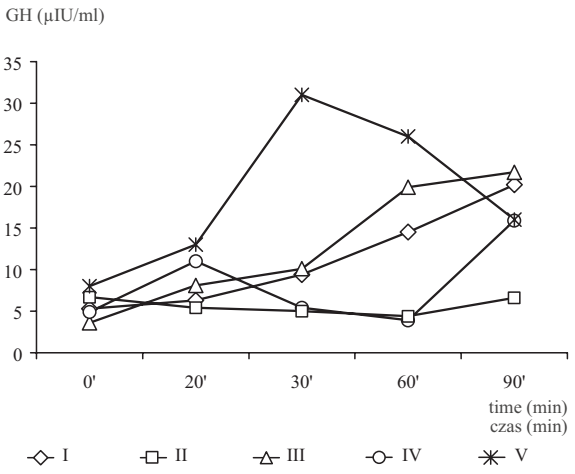

Fig. 1. Serum growth hormone (GH) responses during insulin-stimulation in osteoporotic patients (groups I–IV) and control group (V)

Ryc. 1. Odpowiedź wydzielnicza hormonu wzrostu (GH) w surowicy po insulinie u chorych na osteoporozę (grupy I–IV) i w grupie kontrolnej (V)

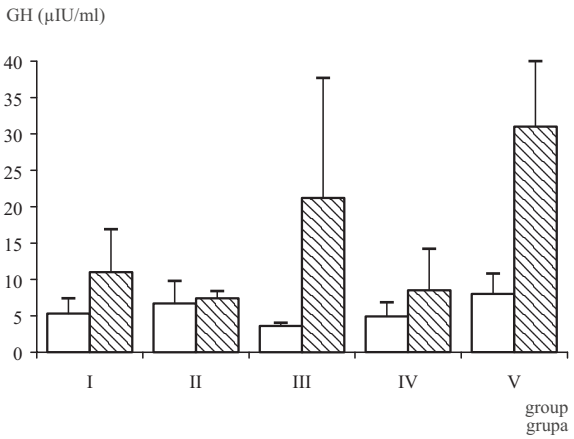

Fig. 2. Basal and maximal stimulated serum growth hormone (GH) secretion in patients with osteoporosis (groups I–IV) and control group (V) (mean ± SD): ☐ basal, ▨ maximal insulin-stimulated

Ryc. 2. Podstawowe i maksymalne po stymulacji wydzielanie hormonu wzrostu (GH) u chorych na osteoporozę (grupy I–IV) i w grupie kontrolnej (V) (średnia ± SD): ☐ podstawowe, ▨ maksymalne po stymulacji insuliną

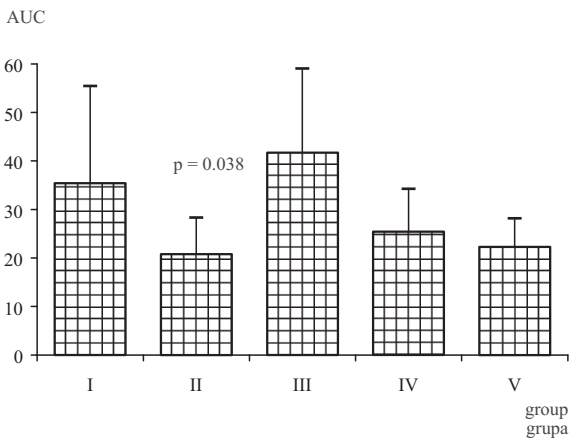

Fig. 3. Area under the curve (AUC) of serum growth hormone (GH) concentration after insulin-stimulation in groups of patients with osteoporosis (I–IV) and control group (V) (mean ± SD)

Ryc. 3. Pole pod krzywą (AUC) stężenia hormonu wzrostu (GH) w surowicy po stymulacji insuliną u chorych na osteoporozę (I–IV) i w grupie kontrolnej (V) (średnia ± SD)

No statistically significant changes in basal serum IGF-1 concentrations were observed among groups of patients, all of them had basal IGF-1 statistically significantly lower than younger group of healthy controls (Tab. 1).

Discussion

The results show relatively higher basal serum GH concentration and low stimulatory reserve in postmenopausal women on HRT in contrast to lower basal GH level accompanied by high stimulatory reserve in postmenopausal women without HRT. The differences in GH secretion tended to be greater within aging of the patients. The results stay in contrast with observation on lack of the effect of transdermal HRT on basal GH secretion in postmenopausal women [7, 8], but they support other study on stimulatory influence on GH secretion by both oral and transdermal estrogen [10]. In the latter, increased GH concentrations were manifested by greater GH pulses amplitude and higher interpulse basal GH levels [10].

The present study was not designed to assess the influence of HRT on GH secretion, but to compare GH stimulatory reserve in various groups of subjects. The authors were interested in GH secretory patterns after insulin hypoglycemia test, known as the golden standard in assessment of GH response. The menopausal patients from groups I–III differred between themselves in terms of age and time after menopause and they were not compared with age matched women without osteoporosis, but with young women with normal estrogen function and normal GH secretion. The authors did not expect the complete normalization of GH secretory patterns in patients on HRT since GH secretion is not restored by attainment of physiological estradiol concentrations after transdermal ERT [7].

The authors observed changes in both spontaneous and stimulated GH secretion according to aging, also. In relatively older untreated postmenopausal women basal GH levels were lower, but insulin-stimulated ones were higher. In one study, peak and integrated GH secretory responses to exogenous GHRH, but not basal GH levels, were decreased both with aging and increasing transdermal ERT dose [15]. A trend to lower values of AUC for GH after GHRH was observed in women on HRT in another study [16]. In both above mentioned studies medroxyprogesterone acetate as an oral progestin was given [15, 16]. Similarly, the findings that neither oral nor transdermal ERT reversed age-related decline in GH secretion in postmenopausal women suggest more pronounced role of aging than estrogen deficiency alone [8].

The authors have shown decreased GH secretory reserve, characterized by a biphasic curve course in corticosteroid-induced osteoporosis, but basal and insulin-stimulated GH secretion did not differ significantly from the healthy controls. The differences in basal IGF-1 concentrations in groups studied reflected the age of subjects, rather than the influence of the treatment.

The authors conclude that postmenopausal osteoporosis is characterized by impaired insulin-stimulated GH secretion, which can be partially reversed by transdermal HRT; and corticosteroid-induced osteoporosis is characterized by a low GH secretory reserve.

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