WFL Publisher
Science and Technology
Meri-Rastilantie 3 B, FI-00980
Helsinki, Finland
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Journal of Food, Agriculture & Environment Vol.11 (1): 244-245. 2013 *www.world-food.net*

The evaluation of the leptin implication in postmenopausal osteoporosis

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Received 8 October 2012, accepted 22 January 2013.

Abstract

Postmenopausal osteoporosis represents one of the major diseases of modern times and it can be considered an important source of morbidity, mortality and social service spread worldwide. The objectives of this study were the identification of the risk factors involved in postmenopausal osteoporosis, the evaluation of the bone mineral metabolism in postmenopausal women not suffering from osteoporosis and in patients suffering from postmenopausal osteoporosis, as well as the evaluation of the leptin (protein hormone produced by adipocytes) implication in postmenopausal osteoporosis. The study included a control group with 32 postmenopausal women, with bone mass values within normal limits (group 1) and a group of 107 postmenopausal women with osteoporosis (validated by dual energy X-ray absorptiometry DEXA method), without other pathological conditions (group 2). An individual sheet was drawn up for each patient. Each sheet included a general questionnaire (the bone mass index (BMI) was calculated on the basis of the body weight and height), a questionnaire regarding the life style (smoking habits or alcohol consumption), a questionnaire evaluating the daily calcium intake, a questionnaire assessing the physical effort rate, the use of medicines, the evaluation of the estrogenic status). The level of the intact serum parathormone iPTH, 25-hydroxyvitamin D and serum leptin levels were analysed with the ELISA technique. Calcemia and phosphatemia were evaluated with standard methods. We found significant statistical differences between the control group and the group with osteoporosis patients regarding the menopause age ($p<0.05$), the menarche age ($p = 0.006$), the number of births ($p<0.001$) as well as the height and weight ($p = 0.03$ and $p<0.05$, respectively). We didn't find statistically significant differences regarding the serum i-PTH and 25-hydroxyvitamin D. Moreover, we found a statistically significant positive correlation between the BMD and leptin for both groups (group 1 $p = 0.01$; group 2 $p = 0.05$). Postmenopausal osteoporosis is a multifactorial disease, the bone loss rate being influenced by several factors (among which the estrogen deficiency plays an important role). Our results suggest that leptin is involved in the regulation of bone mass and bone turnover, having a protective effect against the bone mass loss.

Key words: Osteoporosis, postmenopause, leptin, bone mineral density, bone mass index.

Introduction

Due to the significant impact, not only to the bone health, but also to the vital functions of the entire body, due to the dreadful complications - fragility fractures, as well as to the major social economic impact on the person affected and the health systems, osteoporosis becomes a public health issue of large interest. Osteoporosis, the main chronic metabolic bone disease, also called the "silent epidemic" has been declared by WHO the third most important public health issue after cardiovascular diseases and cancer [1, 2].

The actions of estrogens on bone are not yet fully known. Leptin is thought to be involved in the postmenopausal osteoporosis pathophysiology, and the studies conducted so far on this aspect are extremely controversial.

The purpose of this study was to clear up new aspects regarding postmenopausal osteoporosis, with their clinical and pathophysiological implications. This study has the following objectives: the identification of the risk factors involved in postmenopausal osteoporosis, the evaluation of the bone mineral metabolism in postmenopausal women not suffering from osteoporosis and in patients suffering from postmenopausal osteoporosis, as well as the evaluation of the leptin (protein hormone produced by adipocytes) implication in postmenopausal osteoporosis.

Materials and Methods

A total of 139 postmenopausal women have been investigated in order to achieve the objectives of the study herein. They have been divided into two study groups: group 1 (control group), made up of 32 postmenopausal women, with bone mass values within normal limits and group 2, made up of 107 postmenopausal women with osteoporosis (validated by dual energy X-ray absorptiometry DEXA method), without other pathological conditions. An individual sheet was drawn up for each patient(each sheet included: a general questionnaire (the BMI - bone mass index - wascalculated on the basis of the body weight and height), a questionnaire regarding the life style (smoking habits or alcohol consumption), a questionnaire evaluating the daily calcium intake, a questionnaire assessing the physical effort rate, the use of medicines, the evaluation of the estrogenic status). The evaluation of the patients consisted of anamnesis, general clinical examination, bone densitometry investigations (by dual energy X-ray absorptiometry: the result is expressed as bone mineral

density (BMD) in g/cm^2 and in T score), biological investigations (the determination of calcemia, phosphatemia, intact serum parathormone iPTH, 25-hydroxyvitamin D and serum leptin). The level of the intact serum parathormone iPTH, 25-hydroxyvitamin D and serum leptin levels were analysed with the ELISA technique. Calcemia and phosphatemia were evaluated with standard methods.

Results and Discussion

Table 1 shows the clinical, bone densitometry and biochemical characteristics for the subjects taking part in the study. Table 2 shows the correlations obtained between the clinical and biological parametres on the two groups.

Table 1. Comparative demographic, densitometry and biochemical characteristics of women in the two groups.

Variable	Postmenopausal control group (n=32)	Postmenopausal study group (n=107)	p (Student's test)
Age (years)	54 ± 8	58 ± 9	p<0.001
Age of menopause (years)	48.9 ± 3.87	47.13 ± 3.01	p<0.05
Age of menarche (years)	12.9 ± 2	13.8 ± 2	p=0.006
Bone mass index (kgm^{-2}) (BMI)	27.04 ± 2.64	23.12 ± 4.05	p<0.001
Births (number)	2 ± 1	1 ± 0.98	p<0.001
BMD (g cm^{-2})	1.169 ± 0.121	0.709 ± 0.101	p<0.001
T score	-0.15 ± 0.89	-2.88 ± 0.73	p<0.001
PTH (pgml^{-1})	33.75 ± 13.67	35.17 ± 16.25	N/A
25-hydroxyvitamin D (ngml^{-1})	18.03 ± 6.63	17.65 ± 9.83	N/A
Leptin (ngml^{-1})	34.79 ± 10.33	23.58 ± 16.05	p<0.001
Calcemia (mgdl^{-1})	9.21 ± 0.69	8.95 ± 1.07	N/A
Phosphatemia (mgdl^{-1})	3.4 ± 0.19	3.32 ± 0.27	N/A

Table 2. Correlations between the clinical and biological parametres on the two groups.

Variables	r value
BMI / BMD	r = 0.394 (p<0.01)
BMD / body weight	r = 0.568 (p<0.001)
BMI / leptin	r = 0.502 (p<0.001)
Body weight / leptin	r = 0.551 (p<0.001)
Leptin / BMD	r = 0.309 (p=0.01) – group 1 r =0.315 (p=0.05) – group 2

Menopause appeared significantly later for the control group, as compared to the osteoporosis patients group, which shows that a later onset of menopause has a protective effect on bone mass loss for postmenopausal women.

As for the onset of menarche, the differences were statistically significant between the women in the two groups, more precisely for those in the control group menarche occurred earlier. This proves the fact that during a longer period between menarche and menopause there are enough estradiol resources to support and maintain bone mineralization.

Our information regarding parity shows that multiparity represents a protective factor against osteoporosis, which confirms other studies [3], as well. This could be due, among others, to the higher calcium intake in women during pregnancy.

We obtained a statistically significant difference between the two groups for the body mass index. A low body mass index determines the reduction of bone mass and increases the fracture risk. Our findings regarding the height and weight of the patients under study prove the fact that a low height and weight increase the risk of osteoporosis and fractures.

The difference between the bone mineral density of the two groups was extremely significant. A low BMD increases the fracture risk.

Between the serum leptin levels of the women in the two groups we found significant differences, more precisely significantly higher levels in the subjects from the control group with bone mass values within normal limits, which shows that leptin has a protective effect for the bone mass.

Leptin is a protein hormone produced by adipocytes with a key role in regulating the body weight. Between the body mass index of the subjects under study and leptin we found an extremely significant positive correlation. Between the body weight of the women under study and the leptin levels we also found an extremely significant positive correlation. An extremely significant positive correlation was found between the bone mineral density and leptin, as well. We thus proved that both leptin and bone mass positively correlate with BMI and body weight, these correlations being supported by other studies [4, 5], as well, this leading to the hypothesis that leptin can be a systemic and/or local regulator of bone mass. Pasco *et al.* [6] proved for the first time the positive correlation between the leptin levels and bone mass in postmenopausal women.

Conclusions

Postmenopausal osteoporosis is a multifactorial disease, the menopause-induced estrogen deficiency playing a key role. An important predictive factor for postmenopausal bone mass is the menarche age. A long fertile period (when there are enough estradiol resources to support bone mineralization) offers protection against postmenopausal osteoporosis. An early age of menopause has a negative impact on bone status, increasing the osteoporosis risk. Nulliparity represents a risk factor for osteoporosis, while multiparity represents a protective factor. Low weight and height determines the increase of osteoporosis and fracture risk. The results support the fact that leptin has a protective role against postmenopausal bone mass loss due to estrogen deficiency. The decrease of leptin levels determines the increase of osteoporosis risk in postmenopausal patients.

Acknowledgements

Special thanks to the entire team. All authors contributed to the manuscript and approved the final version.

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