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ORIGINAL ARTICLE

Omentin Polymorphism and its Relations to Bone Mineral Density in Women

Dariusz Boron,[a] Boguslaw Czerny,[b,c] Joanna Bartkowiak-Wieczorek,[d,e] Dominik Sieron,[f] and Hubert Wolski[g]

[a]*Department of Histology and Embriology, Medical University of Silesia, Zabrze, Poland*
[b]*Department of General Pharmacology and Pharmacoeconomics, Pomeranian Medical University, Szczecin, Poland*
[c]*Department of Stem Cells and Regenerative Medicine, Institute of Natural Fibres and Medicinal Plants, Poznan, Poland*
[d]*Laboratory of Experimental Pharmacogenetics, Department of Clinical Pharmacy and Biopharmacy, University of Medical Sciences, Poznan, Poland*
[e]*Department of Pharmacology and Phytochemistry, Institute of Natural Fibres and Medicinal Plants, Poznan, Poland*
[f]*Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland*
[g]*Division of Obstetrics and Gynecology, Podhalanski Multidisciplinary Hospital Nowy Targ, Nowy Targ, Poland*

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Background and Aims. Recognition of different genetic variants underlying development of osteoporosis would make it possible to administer individual symptomatic treatment as well as early prophylactics of osteoporosis. The aim of the study was to evaluate frequency of polymorphism 326A/T of gene *ITLN-1* and assessment of its relations with the clinical parameters of osseous turnover and degree of postmenopausal osteoporosis.

Methods. The study included 800 women at the postmenopausal (505) and reproductive (295) age throughout Wielkopolska region in Poland. The postmenopausal group included women with osteoporosis and osteopenia and the healthy ones. Women at the reproductive age were healthy. Frequency of the tested gene polymorphism was evaluated in the group where BMD was marked and in the control group.

Results. The analysis of the polymorphism A326T of gene ITLN-1 showed that in healthy postmenopausal female with genotype AA birth weight, BMD L2–L4 YA (%) and BMD L2–L4 AM (%) were significantly higher (BMD–*bone mineral density*; L2–L4 – *lumbar vertebrae no 2, 4*; YA–*peak adult bone mass*; AM–*age-matched bone mass*). In women with osteopenia BMD L2–L4 YA (%) and BMD L2–L4 AM (%) were significantly higher in women with genotype AA, but BMD L2–L4 was significantly higher in women with genotype TT. In women with osteoporosis with genotype AA T-score was significantly higher, but BMD L2–L4 and BMD L2–L4 YA (%) were significantly lower in this group. BMD L2–L4 AM (%) was significantly higher in women with AA genotype.

Conclusion. In women with osteoporosis and osteopenia homozygous AA genotype may predispose to lower BMD in the lumbar spine.

Key Words: Polymorphism, Gene *ITLN-1* — Intelectin-1 (intestinal lectin omentin), Osteoporosis, Women, Age.

Introduction

The gene of omentin (*ITLN-1*) comprises 8 exons. The gene product contains 16-amino acid signal peptides (1,2). Distinguished in the protein structure may be also a fibrinogen-like domain (amino acids in positions 38–82) and a lectin like one (positions 37–313). In its negative form it appears as a glycolized trimer of ~120 kDa molecular weight. The omentin (*ITLN*-1) gene is localized on chromosome 1q22–q23.

Omentin (*ITLN-1*), also referred to as intelectin, is a poorly recognized compound. Nevertheless, it is known to be composed of 313 amino acids and to have a molecular

Address reprint requests to: Dariusz Boron, Medical University of Silesia, Department of Histology and Embriology, Jordana 19, Zabrze, 41-808, Poland; Phone: +48 32 2722842; FAX: +48 32 2722867; E-mail: metabolizm.db@gmail.com

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weight of ~33 kDa. In humans, synthesis is most intense in the visceral fatty tissue, although it is also produced in the small intestine, lungs and heart. On the other hand, it has not been proven to occur in the muscles or in the kidneys. Yang et al. (1) showed that it is a secretory factor, enhancing the effect of insulin in glucose metabolism. As the effect of local regulation within the fatty tissue, omentin (*ITLN*-1) is likely to perform as an endocrine as well as autocrine and paracrine factor.

The function of omentin (*ITLN*-1) is most probably to increase insulin sensitivity with the effect observed both locally and systemically. Performing through the paracrine effect, omentin is supposed to enhance insulin sensitivity and to stimulate glucose metabolism, affecting in this way distribution of the fatty tissue. Its effect upon the muscular cells, hepatocytes or cells of the subcutaneous fatty tissue is similar (1−3).

It has been proven that omentin 1 (*ITLN*-1) stimulates proliferation of human osteoblasts. It has also been shown that PI3K/Akt signalling pathway is the key mediator of such performance. The fatty tissue produces different adipokines (e.g., adiponectin, leptin, resistin, vaspin and visfatin). Such adipokines control, among other processes, sensitivity to insulin and bone metabolism (4,5). Omentin 1 (*ITLN*-1) is expressed mainly in the visceral fatty tissue and in plasma (1). It has been shown that both mRNA for omentin 1 and its plasma level are reversely correlated to obesity, BMI and insulin resistance (6). Moreover, omentin 1 has a critical role in hampering differentiation of osteoblasts from smooth muscle cells (7). Some adipokines induce proliferation of osteoblasts (8,9), which points, among others, to a close relations between omentin 1 and osteoblasts. Clinical investigations have shown that serum omentin 1 is reversely correlated with BMD in females with mental anorexia (10) and in Iranian postmenopausal females (11). Xie et al. (5,12) also noted that omentin 1 compensates for bone loss in mice deficient in ovaries and $OPG^{-/-}$mice, stimulates proliferation and hampers differentiation of osteoblasts in mice.

Omentin (*ITLN*-1) expression was shown in human fatty tissue in 2005. It is secreted by the fatty tissue stromal cells, not by adipocytes (13). On the other hand, no mRNA presence was noted for omentin in preadipocytes (2). Omentin expression had been noted earlier also in other tissues such as myocardium, small and large intestine cells or in thyroid cells (14−16).

Omentin expression is reduced in obesity, insulin resistance and type 2 diabetes. Recent studies showed that omentin is also positively related with adiponectin, high-density lipoprotein levels and negatively related with body mass index, waist circumference, insulin resistance, triglyceride and leptin levels (17).

The association between cigarette smoking and bone mass has been extensively described in the scientific and epidemiologic literature. It has been concluded that smokers had significantly reduced bone mass compared with nonsmokers at all bone sites. Smokers had greater rates of bone loss over time compared with nonsmokers (18).

Although the biological function of omentin 1 (*ITLN*-1) remains mostly unknown, some recent reports point, among other, to promotion of glucose transport in adipocytes (19) or induction of blood vessel angiectasia (20,21). Recently it has been proven that omentin 1 hampers differentiation of osteoblasts from calcifying smooth muscle cells *in vitro* (22). Omentin 1 (*ITLN*-1) is probably involved in resorption of the osseous tissue. It was proven that omentin 1 levels correlated reversely with BMD in the lumbar vertebrae of postmenopausal Iranian women (11). Thorough recognition of such mechanisms might allow for introduction of some new therapeutic methods. The need for better understanding of the role of omentin 1 in bone mineral metabolism justifies further studies focused on BMD and osteoporous fractures.

The aim of the study was to evaluate frequency of polymorphism 326A/T of gene *ITLN-1* and assessment of its relations with the clinical parameters of osseous turnover and degree of postmenopausal osteoporosis in order to search the relationship between polymorphic variants and risk of osteoporosis.

Materials and Methods

Test Group

The study comprised a group of unrelated Caucasian women inhabiting the region of Wielkopolska. Investigations included 800 women (505 postmenopausal age) and 295 of reproductive ages. The postmenopausal group included 314 women with osteoporosis, 110 with osteopenia and 81 healthy individuals. The majority of the studied population lived in urban areas (55.0%), whereas 45.0% lived in rural areas. Demographic and clinical data of the studied population are presented in Table 1.

Densometric measurements were performed to define the bone mineral density (BMD) as well as T-score, Z-score, mean bone mineral density index as compared to the mean value for young adult women (YA−*young adults*) and mean bone mineral density as compared to the mean value for a given age (AM−*age matched*). Additionally, body weight and height were measured to calculate body mass index (BMI).

Detailed history of each patient was taken to gain information on the diseases developed, medication prescribed, age of first and last menstruation, number of deliveries, birth weight and smoking habits. Women participating in the study were not patients of the hospital. They only participated in the research prepared by the Hospital Clinic.

Qualified for genetic tests were healthy women of reproductive age and women after menopause in whom menopause occurred at least 1 year earlier and who did not receive therapies possibly influencing bone mass, including