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Original Article

The Relevance of Osteoclastic and Osteoblastic Activity Markers Follow-Up in Patients on Antiresorptive Osteoporosis Treatment

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Abstract

In general, markers of bone formation and markers of bone resorption are changing synergistically, so the monitoring of any osteoclastic and any osteoblastic marker should reflect the rate of bone transformation. The aim of the study is to monitor the bone metabolism markers in postmenopausal women with osteoporosis and osteopenia along with the variations caused by the effects of bisphosphonate therapy. The study involved 55 women of average age of 57.95 years, with osteopenia or osteoporosis. The patients with osteoporosis were treated with bisphosphonates (75 mg once a week); the laboratory tests were performed before the treatment and 6 months later. Patients with osteopenia were evaluated at the first assessment and 6 months later. The tests included bone densitometry, dual-energy X-ray absorptiometry, osteocalcin, alkaline phosphatase, collagen 1 N-terminal pro-peptide (P1NP), and beta C telopeptide of type I collagen (CTX). The mean T-score was -2.80 ± 0.63 before therapy and -2.64 ± 0.45 6 months later ($p < 0.001$). Women with osteoporosis had elevated levels of osteocalcin and P1NP at the first assessment, whereas the alkaline phosphatase level did not change with the treatment. After the introduction of antiresorptive therapy, the levels of osteocalcin and P1NP significantly decreased ($p < 0.001$). In the group with osteopenia, the biochemical markers activity were increased in both assessments. In patients with osteoporosis, Beta-CTX was increased in the first evaluation, and decreased after treatment ($p = 0.001$). The results indicate that the assessment of biochemical markers of bone metabolism show excellent results in the assessment of prognosis, monitoring the course and the response to various treatment regimens of osteoporosis and evince strong correlation with standard densitometry and dual-energy X-ray absorptiometry procedures. P1NP and CTX show better diagnostic applicability compared with osteocalcin and alkaline phosphatase. The analysis of the activity of biochemical markers may obtain early information on the therapeutic response, before definitive assessment by bone density measurements.

Key Words: CTX; osteopenia; osteoporosis; P1NP; T-score; Z-score.

Background

Osteoporosis is a generalized, progressive, and irreversible process of losing bone mass with impaired bone microarchitecture beds *(1)*. The fractures may develop at the vertebrae, hip, lower part of the forearm, pelvis, and upper arm, but may also occur elsewhere *(2)*. Osteoporosis is a global public health problem, currently affecting more than 200 million people worldwide *(3)*.

About 50% of women and 20% of men over 50 experience at least 1 osteoporotic fracture *(4)*. Women have a higher incidence of osteoporosis *(5,6)*.

The basic pathologic mechanism leading to osteoporosis may be (1) inadequate achievement of the optimal bone mass, (2) excessive bone resorption, and (3) the lack of bone formation after increased degradation *(6)*.

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According to the osteoporosis diagnostic and treatment guidelines, densitometry and dual-energy X-ray absorptiometry (DXA) are considered the "gold diagnostic standard"; these methods are also the keystones for planning and monitoring of treatment effectiveness *(1,2,7)*. According to the World Health Organization (1994), osteoporosis in women was defined as bone mineral density (BMD) at least 2.5 standard deviations (SD) below the mean value for young healthy women (T-score ≤ –2.5). A T-score between +1 and –1 is considered normal, a T-score between –1 and –2.5 indicates low bone mass (osteopenia), and a T-score of –2.5 or lower indicates osteoporosis; severe osteoporosis is consistent with a T-score of more than –2.5 SD along with 1 or more pathologic fractures. An alternative to T-score is Z-score, defined as the ratio of the expected (age-adjusted) and the obtained values of the BMD. When considering the fracture risk, each deviation of –1 SD in Z-score is proportional to –2.5 SD in T-score *(1,2,8)*.

Bone remodeling involves 2 sequential processes—bone formation and bone resorption; they can be evaluated by measuring the osteoblastic and osteoclastic enzyme activity. Assessment of bone metabolism markers may be used in monitoring of prevention and treatment efficiency. The levels of these markers can identify patients with an intensive bone loss. In general, the markers of bone formation and the markers of bone resorption are changing synergistically, so the monitoring of any osteoclastic and any osteoblastic marker should reflect the rate of bone transformation. The treatment of osteoporosis rely on 2 types of drugs: antiresorptive and anabolic *(9–12)*. Antiresorptive drugs include bisphosphonates (first-choice medications), selective estrogen receptor modulators, hormone replacement therapy, and calcitonin. Teriparatide, a parathyroid hormone analog, is osteoanabolic drug. Strontium ranelate combines both of the mechanisms of action.

Aim

The aim of the study is assessment and monitoring of the levels of bone metabolism markers in postmenopausal women with osteoporosis and osteopenia along with their variations caused by the effects of bisphosphonate therapy.

Methodology

Study Design

This prospective study was conducted after permission of the Ethics Committee of the Medical Faculty in Pristina, Kosovska Mitrovica, and with a written consent of the subjects. The survey was conducted, respecting ethical principles for human clinical trials by the Declaration of Helsinki of 1983 *(13)*. The study included patients who were clinically tested and treated in the Ambulance for rheumatic diseases of the Health Center Medicus "Universalis in Krusevac" in the period January 2013 to April 2014.

The criteria for inclusion in the study were lack of menstrual cycle for at least 1 year or a confirmed menopause, or fulfilled criteria for the diagnosis of osteopenia or osteoporosis. Criteria for exclusion from the study were secondary osteoporosis, a high risk of fracture, the use of drugs with effects on bone density (diuretics, anticonvulsants, heparin, corticosteroids), severe infections, cancer, and other conditions, which make the patient unsuitable for inclusion in the study.

The study involved 55 women of average age of 57.95, which fulfilled the criteria for the diagnosis of osteopenia or osteoporosis *(1,2,8)*. The patients were divided into 2 groups—patients with osteoporosis (25) and patients with osteopenia (30). The medical history, family history of osteoporosis, smoking status, and data on current diseases were registered. Alcohol intake was evaluated by the questionnaire (The CAGE questionnaire) *(14)*. The level of physical activity was assessed using the translated version of a standardized International Physical Activity Questionnaire-short form *(15)*.

Anthropometric, Clinical, and Biochemical Measurements

The patients with osteoporosis were treated with bisphosphonates (75 mg once a week); the laboratory tests were performed before the treatment and 6 months later. The laboratory tests included standard biochemical analyses, the detection of specific bone markers of bone formation—osteocalcin (OC) and alkaline phosphatase (ALP), collagen 1 N-terminal pro-peptide (P1NP), and markers of bone degradation—beta C telopeptide of type I collagen (beta CTX), or beta CrossLaps collagen degradation product. Venous blood samples were taken in the morning (between 8 and 9 AM) after a night fasting. Biochemical parameters were analyzed on the ELEKSUS device by hemiluminescent method, using Roche reagents. All patients were examined on Lunar DXA instrument. The BMD was measured at the lumbar spine and hip. The bone density has been calculated in the form of T-score *(1,2,8)*. Each individual patient's body height and body weight were registered, and individual body mass index was calculated *(16)*.

Statistical Methods

The data were analyzed using SPSS Statistics 19.0. The data with normal distribution were tested by Student *t* test for the small independent samples and analysis of variance test; for the data with the non-normal distribution, Kruskal-Wallis, chi-square, and Mann-Whitney *U* test were used. The correlations were calculated using Pearson linear correlation analysis.

Results

The study involved a total of 55 subjects, 25 of which met the criteria for the diagnosis of osteoporosis. The latter