EFFECTIVENESS OF BIPHOSPHONATED THERAPY AND PERSONALIZED DIET UPON A GROUP OF FEMALE PATIENTS WITH OSTEOPOROSIS FROM TÂRGU-MUREŞ, ROMANIA

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Abstract: *Osteoporosis, the most common systemic bone disease, is a real public health problem, and it is a major cause of fragility, disability, morbidity and mortality, especially in the elderly. Methods: We monitored data collected from the archives of Endocrinology Ambulatory in Târgu-Mureş city, for a group of 100 female patients with newly diagnosed postmenopausal osteoporosis. Results: The present study confirms the increase of bone density both at 1 year and 2 years of anti-resorption therapy, their efficacy and placement in osteoporosis management. There is a close correlation between age of patients and bone mass density decreasing, the older they are, the lower the T score is also the younger they are, the faster they recover, with negative correlations although. We have good results with a personalized diet and a proper treatment. Conclusions: Alendronate and Ibandronate have proven effective in both DMO recovery and fracture risk prevention*

INTRODUCTION

Osteoporosis, the most common systemic bone disease, is a real public health problem, and it is a major cause of fragility, disability, morbidity and mortality, especially among the elderly. Low bone strength involves diminished bone density and bone quality alteration. Relative fracture risk increases as bone mineral density (BMD) decreases.(1) Osteoporosis has probably existed throughout human history but only recently became a major clinical problem as human lifespan increased.(2)

The clinical significance of osteoporosis is fractures that occur.(3) Hip fractures are associated with the highest morbidity and mortality rates in people over 75 years of age, leading to highest direct health care costs.(4) Low bone strength involves diminished bone density and bone quality alteration.(5) Relative fracture risk increases as bone mineral density (BMD) decreases.(6,7) In 2008, WHO introduced a fracture risk estimation tool (FRAX), which estimates the likelihood of hip fracture at 10 years and of major osteoporotic fracture (hip, spine, proximal or forearm humerus) in untreated patients between 40 and 90 years, using clinical risk factors for fracture and BMD in the femoral neck.(8) Country-specific FRAX prediction algorithms are available for many online countries.(9) Worldwide, osteoporosis causes 8.9 million fractures every year, which means that every 3 seconds there is a new osteoporotic fracture. Hip fractures are a major burden on public health, both by the social cost and by affecting the health status of older people, being one of main causes of morbidity and mortality in women and men.(10)

Osteoporosis and pre-osteoporosis occur in approximately 53 million men and women in United States, accounting for 55% of the population aged 50 or over. There are approximately two million fragility fractures in United States each year: 547,000 vertebral fractures, 297,000 hip fractures, 397,000 wrist fractures, and 675,000 other skeletal sites. It was estimated that 75 million people in Europe, the US and Japan are affected by osteoporosis.(11) At European Union level, in 2010, approximately 22 million women and 5.5 million men aged 50 to 84 were estimated to have osteoporosis. Due to population demographic changes, the number of women and men with osteoporosis will increase in the EU from 27.5 million in 2010 to 33.9 million in 2025, recording a 23% increase.(12) The prevalence of osteoporosis in Romania, in women and men over 50 years, is 20.5% and 6.2%, so that about one million women and men over 50 years of age suffer from osteoporosis (4:1 report in favour of women). In Romania there are about 100,000 fragility fractures annually, of which 15,000 are at hip level. However, less than 1/3 of patients who have already had a fracture are evaluated and treated for osteoporosis.(13)

Osteoporosis is caused by the cumulative effect of excessive bone resorption and poor bone formation. Bisphosphonates inhibit bone resorption with fewer side effects, which are widely used for the prevention and treatment of osteoporosis. In postmenopausal osteoporosis, they are considered to be first-line therapy due to their efficacy, favourable cost and long-term safety data.(14,15)

AIM

The present study aims to analyze the improvement in bone mineral density (BMD), measured by dual energy X-ray absorptiometry (DXA) expressed as the T-score calculated in standard deviations (DS), under bisphosphonate anti-resorption therapy at 1 year and 2 years of therapy, on a group of patients with osteoporosis in the Târgu-Mureş area.

MATERIALS AND METHODS

Data from the Archives of the Endocrinology Ambulatory in Târgu-Mureş was retrospectively processed, from 2015-2016. We studied 100 female subjects with newly diagnosed postmenopausal osteoporosis, who received anti-osteoporotic treatment of Alendronate or Ibandronate. Study

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samples have been divided into three: diagnostic sample (baseline), 1-year bisphosphonate sample, and 2-year bisphosphonate therapy dissociated on the type of bisphosphonate used: alendronate or Ibandronate.

Inclusion criteria: newly diagnosed patients with primary osteoporosis; the T-score measured by dual energy X-ray absorptiometry (DXA) in the femoral neck and / or the backbone with a value less than or equal to - 2.5 DS; normal level of corrected serum calcium; the anti-resorption therapy used is alendronate bisphosphonates (70 mg/week) or Ibandronate (150 mg/month); the absence of other endocrine or metabolic disorders considered to be causes of secondary osteoporosis.

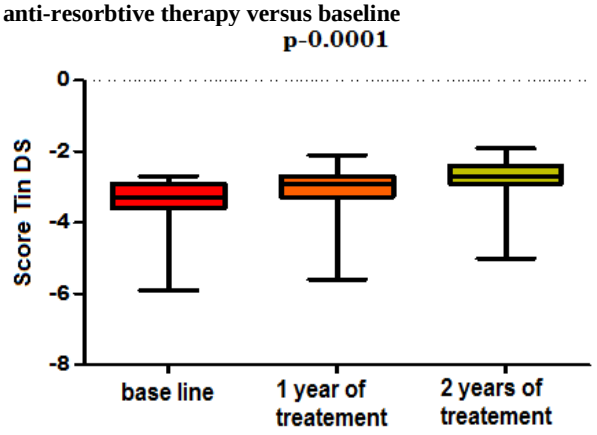
Exclusion criteria: male subjects; T score greater than -2.5 Ds obtained by DXA technique; T score less than or equal to -2.5 DS measured by calcanean ultrasonography; patients with severe osteoporosis who at the time of diagnosis have documented fragility fracture; creatinine clearance <35 ml/min; patients diagnosed with secondary endocrine causes of osteoporosis (disorders of hormones involved in phosphocalcic metabolism, glucocorticoid treatment, Cushing's syndrome, thyrotoxicosis or hyperthyroidism, diabetes, growth hormone deficiency); patients diagnosed with other conditions that may cause secondary osteoporosis (haematopoietic diseases, connective tissue diseases, gastrointestinal and nutritional disorders, kidney disease); patients being under chronic treatment with one or more of the following medicine: heparin, methotrexate, cyclosporine, aluminum-containing antacids, proton pump blockers; long-term immobilized patients for various conditions (rheumatoid arthritis, arthrosis, ankylosing spondylitis, neurological disorders); patients known to be non-compliant to treatments and / or periodical re-evaluations.

RESULTS

Between 2015 and 2016, 100 cases were processed, aged between 50 and 81 years. All subjects studied were female, diagnosed for the first time with primary osteoporosis.

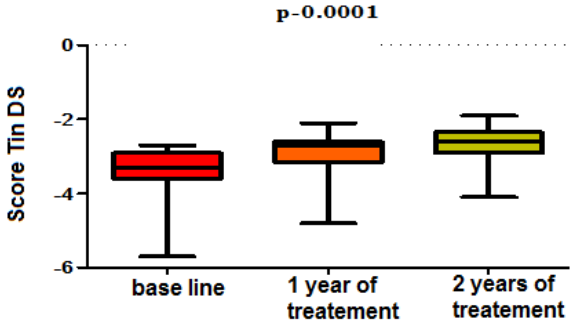
Of the total number of cases, the proportion of patients treated with Alendronic acid with anti-resorption medication was significantly the same as that used with Ibandronic acid (figure no. 1).

Figure no. 1. T-score distribution at 1 year and 2 years of anti-resorbtive therapy versus baseline



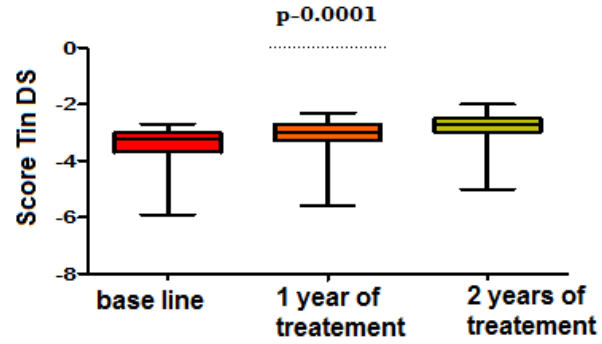
There is a statistically significant difference ($p < 0.05$) in the mean of the studied samples in the T-score improvement, both at 1 year and 2 years of anti-resorption therapy, thus proving their efficacy and place in osteoporosis management. Also, on both forms of bisphosphonate, there is a statistically significant difference in the mean of both the Acidum Alendronicum and the Ibandronicum from the baseline.

Figure no. 2. T-score distribution at 1 year or 2 years of alendronic acid treatment versus baseline



In the studied sample, it was a correlation between age of patients and in bone mineral density decreasing, the older they are, the lower the T score (figure no. 3).

Figure no. 3. T-score distribution at 1 year and 2 years of Ibandronicum acid therapy versus baseline



The age of the patients correlates inversely with the increase in bone mineral density in patients receiving bisphosphonate anti-resorption therapy, the younger they are, the faster they recover, and the negative correlations are there (figure no. 4).

Figure no. 4. Dispersion of the T score at the time of diagnosis based on the age of the patients

DISCUSSIONS

Osteoporosis is a disease whose incidence is steadily rising, affecting predominantly the active age group to the third. The female population is four times more prone to experiencing this disease. It is a silent disease without producing any symptoms until the first fragility fracture occurs. Roughly 9 million osteoporotic or fragility (low-trauma) fractures occur worldwide per year.(16) Hip fracture represents a real burden on public health, both through the social cost and the health of the elderly, which is one of the main causes of morbidity, decreased

quality of life, and female mortality.(17)

Increasing numbers of people who eat low-nutrient diets, associated with aging and sedentary lifestyle, are among the major risk factors for osteoporosis. Until recently, Calcium and Vitamin D have been considered the main nutrients essential to bone health, but there is more and more evidence that whole foods and other micronutrients such as Iron, Copper and Selenium have important roles in primary and secondary potential osteoporosis. Fruits and vegetables are still consumed in insufficient amounts, although they contain micronutrients useful in remodelling the bones and are essential for reducing inflammation and oxidative stress. Dried fruits such as plums offer significant amounts of vitamin K, Bor, Manganese, Magnesium, Copper and Potassium, along with large amounts of anthocyanins, with antioxidant properties. Traditional dry fruit is a convenient snack that could be encouraged as a healthy alternative to many popular snacks, rich in fat, sugar and salt, with the added benefit of positively contributing to bone health.(18) Daily consumption of only 50 grams of dried plums over a minimum of 6 months has been shown to be effective in reducing bone resorption in women with postmenopausal osteoporosis.(19)

Dairy products play an important role in bone health and should not be replaced by carbonated beverages.(9) A personalized diet that contains the groups of foods and nutrients necessary for bone health throughout the lifecycle can help prevent osteoporosis. Greater efforts are required to use prevention strategies that involve changing diets and physical activity, so beneficial in preventing osteoporosis.

Pathogenesis of osteoporosis is multifactorial, involving physiological processes including hormonal status, along with genetic and environmental factors. By adopting appropriate nutrition and moderate physical activity performed periodically, these diseases can be partially prevented. Worldwide, it is estimated that about two billion people have a inadequate micronutrient diet.(20) This, combined with increased life expectancy, leads to a decrease in the quality of the last few years of life through the presence of partially prevented health problems, including osteoporosis.(21) From an economic point of view, the rates of disability due to osteoporosis in Europe are higher than those caused by cancer (with the exception of lung cancer).(22)

Achieving maximum bone mass, the point at which optimal bone mass and resistance is achieved, occurs in the second decade of life. Equally, the transition to menopause leads to increased bone resorption and microarhitectural disruption by lowering estrogen which is a major regulator of bone metabolism. These seem to be the appropriate times to adapt the modifying factors that affect bone density and quality. Previously, there has been a general tendency to focus on individual nutrients or supplements, rather than on an "integral diet" approach.

Data from the United Kingdom National Diet and Nutritional Survey (conducted between 2015 and 2016) revealed that only 8% of children aged between 11 and 18 and 27% of adults aged 19 to 65 have met the recommendation to consume vegetables and fruits 5 times a day. It has also been found that a substantial proportion of adults aged 19 years (especially women) have the proportion of Iron, Potassium and Selenium below the lower limit of the reference range.(23)

The vitamin D deficiency, which is overwhelmingly encountered in Romania, could be corrected by diet programmes and food supplements considered as ways to prevent osteomalacia and rickets. There is a general tendency for vitamin D-rich foods such as fish fat, eggs, and meat to be insufficiently consumed. Additional meta-analytical evidence also indicates that supplementation with vitamin D might be beneficial to institutionalized individuals. In the general population, supplements should not replace a balanced diet that contains a multitude of important functional components that work beyond bone health. Lifelong nutrition improvement is considered to help prevent disability, protect health, and improve economic productivity.(23)

While a personalized diet, with enough vegetables and fruits (24), as well as optimal lactation, are very important throughout life, likewise integrity of skeleton becomes more vulnerable at certain stages of life. For example, when bone loss is accelerated in middle-aged women, the increase of fruit and vegetable and siliceous consumption influences this in a positive way. However, to prevent osteoporosis, a "full" approach is needed. The patient's approach with real empathy is an integral part of a good and lasting therapeutic relationship, with the doctor being responsible for assessing the psychosomatic features of the patients.

CONCLUSIONS

We have noticed in our study that Alendronate and Ibandronate therapy was effective in primary postmenopausal osteoporosis treatment with an increase in bone mineral density, especially in the first and second year of treatment, with both statistically significant correlations between sample sizes. The severity of the T score was found in categories over 70 years.

There was a direct correlation between patient age and bone mineral recovery (the higher the age, the better the T score). The body mass index did not directly influence the T-score under bisphosphonate therapy.

There was no evidence of fragility fracture with bisphosphonate therapy, which proved to be effective in preventing fragility fracture.

Given the increased incidence of osteoporosis among the postmenopausal age population, the negative implications associated with fractures produced by it, as well as low adherence to treatment, it is advisable to improve doctor-to-patient communication and understanding of the importance of compliance with treatment as well as periodic and continuous monitoring of disease progression. A balanced diet not only provides proteins, vitamins, minerals and trace elements at optimal doses necessary for bone health but also phytonutrients and other bioactive components that have been increasingly linked to the integrity of the skeleton.

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