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THE TREATMENT OF SENILE AND POSTMENOPAUSAL OSTEOPOROSIS AS ONE OF THE MAJOR WAYS OF FRACTURE PREVENTION IN ELDERLY PATIENTS

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Summary. *The treatment of fractures in elderly patients is a big orthopaeadic and socio-economic problem. The number of fractures, especially hip fractures, increases year after year. Approximately 250 hip fracture patients per year are hospitalized in the Orthopaedic-Traumatology Clinic in Niš, which makes nearly 20% of all hospitalized patients. Enormous funds are spent for their treatment, especially the surgical one, which demands expensive implants for fracture fixation or total hip replacement. The main cause of fracture in the elderly is osteoporosis. Orthopaedic surgeons are daily occupied with radius fractures, fractures of the proximal part of the humerus, hip fractures, thoracolumbar vertebral body compression fractures, ankle fractures, etc. The low energy trauma is the cause of more than 90% fractures. That is why the proper understanding, diagnosis and treatment of osteoporosis are of great importance for prevention of fractures in the elderly.*

Key words: *Senile and postmenopausal osteoporosis, treatment, fracture prevention in the elderly*

Introduction

Osteoporosis is a huge and growing medical problem all around the world. Due to the increasing population of elderly people, improvement of the quality of life and reduced life activity, the number of patients with osteoporosis is continuously growing. Having in mind a huge interest in the problem of osteoporosis, the continuous effort of scientists in finding the ideal medicine in treatment of this metabolic disease is completely understandable (Fig. 1). Postmenopausal and senile osteoporosis causes a great number of fractures in elderly patients. Clinical signs of osteoporosis become evident after the fracture itself, the fracture being a consequence of the disease which came into being years before the diagnosis has been established (1). Until the fracture, the bone loss is very slow and asymptomatic. The clinical significance of osteoporosis is related to the fractures of the spine, wrist, and hip (fractures of the femoral neck, transtrochanteric and subtrochanteric fractures) (2) (Fig. 2, Fig. 3). The socio-economic significance of osteoporosis patients calls for a doctor's greater informative knowledge concerning this area, aimed at early recognition and treatment of the disease. The progressive growth of osteoporosis goes along with the increase of fractures in elderly people. Osteoporosis is the cause of more than a million fractures annually. The characteristic of all these fractures is that they become evident after a banal trauma. In USA, 340,000 hip fractures are treated every year. It has been estimated that by the year 2050 there will have been 650,000 fractures per year. Twelve point six million dollars are spent for the treatment of the total number of hip fractures, which is 37,000 dollars per each fracture. More than 90% of these fractures occur in people older than 65. Around 250 patients with a hip fracture are treated at the Orthopedic-Traumatology Clinic in Niš every year. These fractures present a direct life threat, and if they are not adequately treated, the quality of life becomes considerably disturbed. A trauma always becomes acute and worsens the already existing diseases, which in turn results in a great percentage of death cases (15-35%). Considering the great significance of the problem (both orthopedic and socio-economic), efforts have been made around the world of how to best prevent and treat fractures. Prevention presupposes the treatment of postmenopausal and senile osteoporosis, as well as wearing devices aimed at hip fracture prevention (hip protector system). Postmenopausal osteoporosis occurs a few years after the menstrual cycle is over, indicating their mutual connection. Women over 50 are twice as more susceptible to fractures than men of the same age. Senile osteoporosis occurs in both sexes, but more in women around 65 due to reduced physical activity, nutrition, etc. (3, 4, 5).

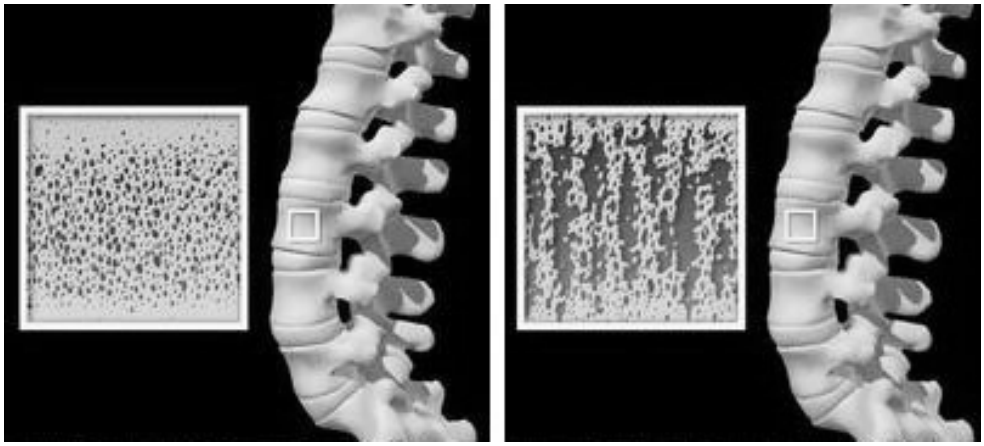

Fig. 1. Normal bone (left) and osteoporosis bone (right)

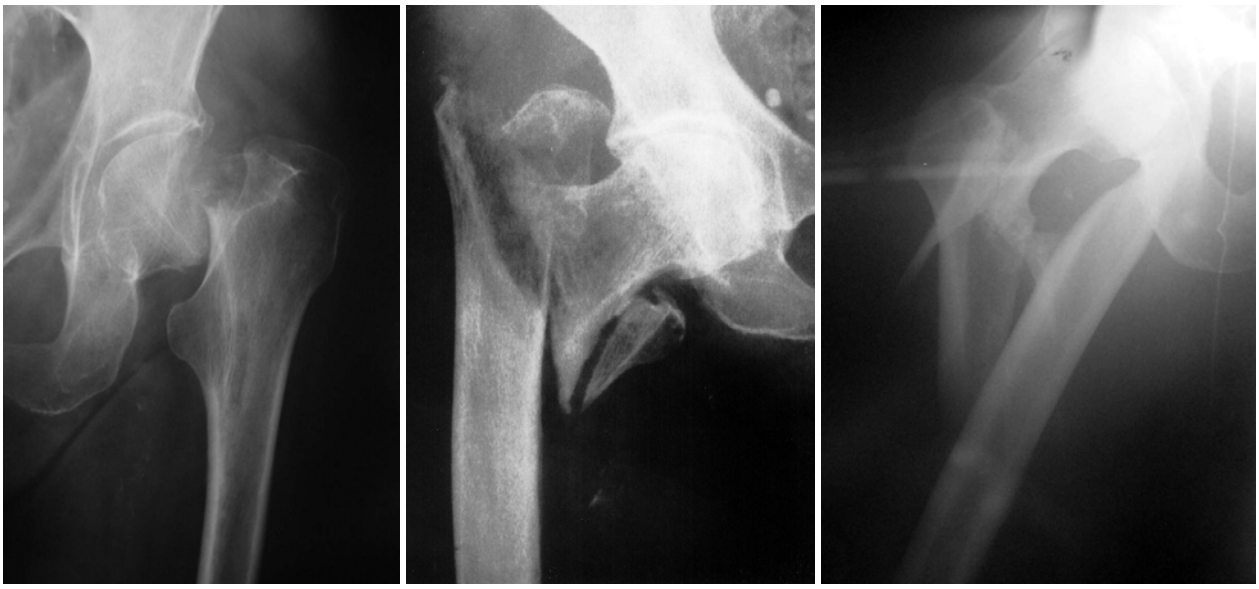

Fig. 2. Hip fracture in the elderly occurs after a banal trauma (fracture of the femoral neck, transtrochanteric and subtrochanteric fracture)

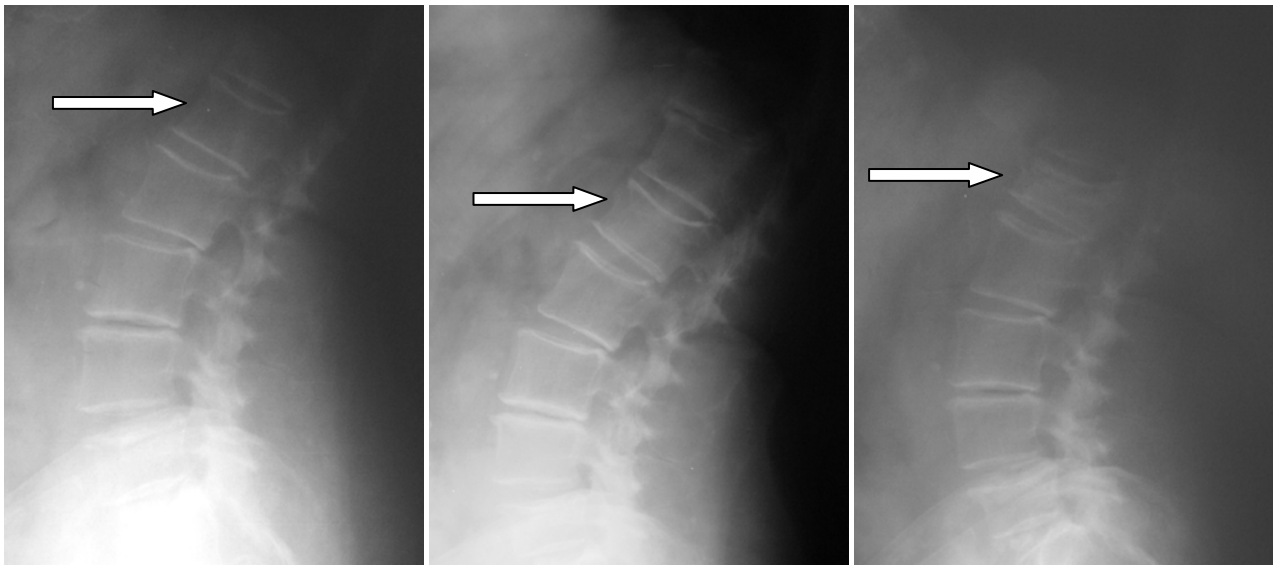

Fig. 3. The compression fracture of the first lumbar vertebral body consequence of banal trauma

Hip protector systems for prevention of hip fractures

Diaphysis of the femur consists of a sponge substance (substantia spongiosa) surrounded by the cuddled bone marrow (substantia compacta). The order of bone tissue depends on mechanical factors affecting the bone. In each bone, lamellar bones are oriented in the direction to render maximal resistance to mechanical factors. Resistance in the defective bone is randomly ordered, set along the lines called trajectories. Depending on the forces affecting the diaphysis of the femur, the bone marrow groups into trajectories, trabeculas occupying the position necessary to fulfill the maximum of the function. In 1838, Ward described the inner trabecular system of the diaphysis of the femur, as well as the order of bone trajectories. It consists of tension and compressive lines of bone trabeculas that board the weakest zones of the femoral neck – Ward's triangle (the zone of weakness). On the spot of the highest pressure, the main compressive group is formed (an arch leading from the inner zone of diaphysis to the upper part of the head). The secondary compressive group starts from the medial zone of the diaphysis cortex and spreads towards the great trochanter. The main tension group passes under the outer side of the great trochanter, goes through the neck and finishes in the lower zone of the head (Fig. 4). Using the trabecular system, in 1970, Singh described Singh's index of osteoporosis consisting of 6 groups (Fig. 5). The break of main tension trabeculas (6) has the crucial role in gradation of osteoporosis levels.

Level 6 – All trabecular groups are present.
Level 5 – The main tension and compressive groups are emphasized
Level 4 – The main tension trabeculas have been reduced
Level 3 – The main tension trabeculas have been broken opposite the great trochanter. This level marks the definite osteoporosis.
Level 2 – The presence of only main compressive trabeculas.
Level 1 – The main compressive trabeculas have been reduced.

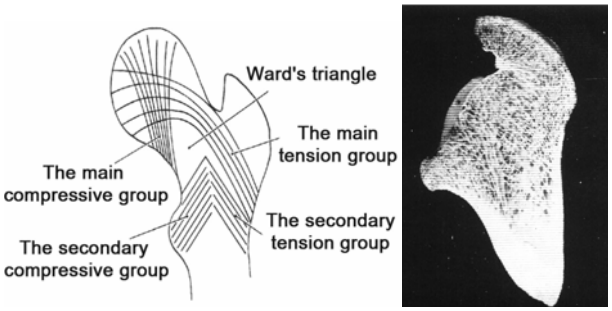

Fig. 4. Trabecular built of proximal dyaphisis of femur

The trohanteral region presents a multidirectional stress transmitter towards the hip joint. The wearing of a system that protects the trohanteral region significantly reduces the risk of fracture occurrence (Fig. 6). Protective systems during a hip fall amortize the fall and absorb the energy, thus lessening the possibility of fracture occurrence. They are recommended to elderly persons with an increasing risk of fall, as well as to all persons with osteoporosis. Moreover, they are recommended for wearing during snowy periods when there is an increasing risk of fall. Along with osteoporosis treatment, hip protector systems present a step forward towards the prevention of hip fracture (7, 8, 9).

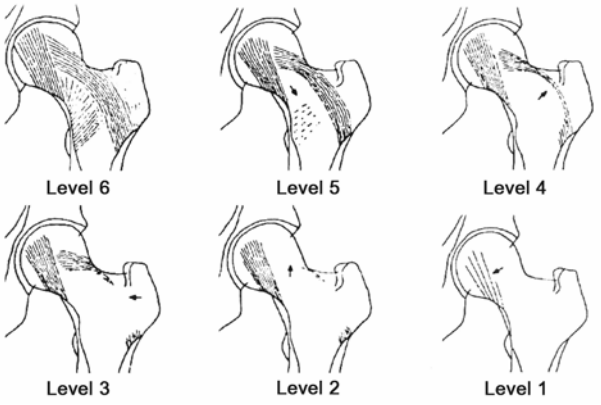

Fig. 5. Singh's index of osteoporosis

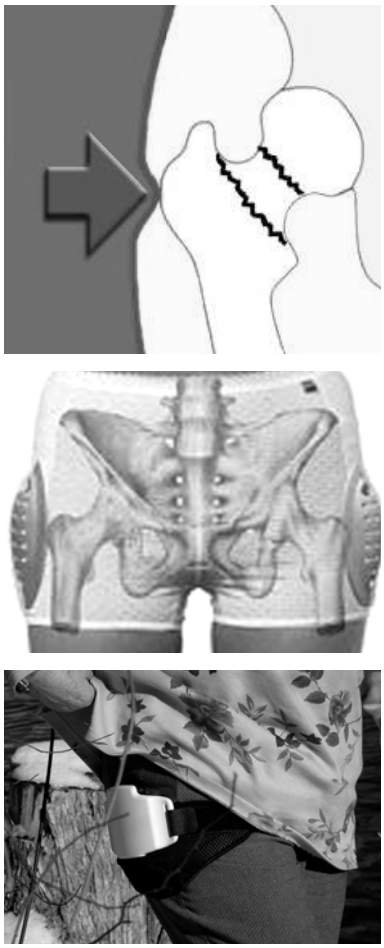

Fig. 6. Hip protector system for hip fracture prevention

Medicament treatment of osteoporosis

The basic mechanism governing bone homeostasis remains unknown; it is probably the result of multi-factor effects such as genetic, harmonic, nutritive, etc. A negative amount of calcium is considered to be the cause of osteoporosis. The cause of negative amount of calcium is tapering not the absorption of calcium but an increased damage to the bone, at least in women with osteoporosis after menopause. It has been noticed that these women have an increased secretion of calcium at night compared to their state before menopause. Estrogens prevent this increased secretion, probably by preventing the effect of parathormones on bone resorption. At the very old age, the absorption of calcium is decreased due to both inadequate nutrition and lack of D-vitamin. In addition, it is impossible not to mention the irritation of the mechanical forces effect on the bone, which is less due to the decreased muscle power and flexibility. Finally, the lowered level of calcitonin was found in the circulation in elderly women with osteoporosis. If the difference between the speed of creation and resorption of bone mass is continuously maintained, no matter how small it is, it will lead to the state in which the loss of bone marrow is so great that the bone can no longer resist the pressure it is being exposed to, and the fracture will occur. Therefore, the treatment of osteoporosis is of great significance for the prevention of all fractures, especially hip ones. For the purpose of easier orientation, osteoporosis therapy is roughly divided into hormone and non-hormone (Table 1). Likewise, physical activity and accurate nutrition are very significant in osteoporosis treatment. Smoking alcohol consummation, as well as consumption of some medicines (corticosteroids, citostatics), have a negative effect on osteoporosis (10).

Table 1. Hormone and non-hormone osteoporosis therapy

Non-hormone	Hormone
Calcium	Vitamin D
Fluorides	Estrogens and progesterons
Bifosphonats	Calcitonin
ADFR	Anabolic steroids
Siliceous, strontium and aluminum	PTH
Tiazids	
Ipriflavone	

Calcium

It should be emphasized that calcium is absolutely necessary in all forms of osteoporosis both in treatment and prevention, mostly as adjuvant therapy. The basic effect mechanism is PTH secretion inhibition. The increased calcium intake cannot stop the process of bone resorption; however, the lessening of calcium quantity below optimal considerably speeds up the process of bone mass loss.

It is necessary to add calcium in the form of pharmaceutical preparations (11) if there is not enough intake of calcium through food as the main source of calcium. Optimal doses: perimenopausal 100 mg/d, postmenopausal 1,500 mg/d, over 70 years of age 1,500 mg/d. The maximal therapeutic effect in calcium therapy is achieved in combination with fluorides, which enables the avoiding of defects in mineralization, in combination with biphosphonates, which considerably alleviates the mineralization process, as well as in combination with calcitonin, which alleviates the positive bone balance, suffocating the PTH response.

If calcium is solely applied, it has a considerably weaker effect, although there are studies in favor of the fact that after 4 years of calcium therapy application along with a physical treatment the hold up of bone resorption occurs.

However, while applying this therapy it is necessary to have in mind persons with nephrolithiasis, heart patients on digitalis therapy and persons suffering from sarcoidosis.

Fluorides

Among all flour salts, sodium fluoride and monofluorophosphate (MFP) are the most used nowadays. It is the only medicine leading to the increase in the number of osteoblasts and thus to the increase of bone mass (12). They are efficient in osteoporosis of trabecular bone. A newly formed mass, after a therapy with fluorides, differs from a normal bone; nevertheless, considerable bone strength is achieved. Research carried out up to the present day has shown that an ideal dose would be 50 mg NaF/d (20-25mg of elementary fluor) with a maximal duration of 3 to 5 years. One of the hindrances is that 25-45% of women do not respond to this therapy ("non-responders"). It is important to mention that fluorides in therapy have to be combined with calcium so as to avoid mineralization defects and the appearance of osteomalice, which is manifested in the fracture of cortical bones. In 30-50% of the cases the appearance of side effects can be noticed as a gastric irritation (in that case it is better to apply MFP), periarticular pain of lower extremities (which is explained by multiple trabecular stress fractures) or toxicity, and it is even thought that they have a potentially malign effect since they stimulate mitogenicities of osteoblasts. Fluorides should not be used in kidney insufficiency, osteomalicia, and cortical osteoporosis.

Bifosfophonats

They have been used for years in the therapy of various metabolic bone diseases. The main effect mechanism is the inhibition of bone resorption. Clodronat (Bonephos) is used as an additive to oncology therapy in osteolytic processes on bones, occurring as a consequence of metastatic tumors. Alendronat and Risedronat are nowadays widely used in the therapy of senile and postmenopausal osteoporosis. The effect of bisphosphonates lasts long after ceasing its application, within small biodegradability (13, 14, 15, 16, 17, 18).

Coherent therapy – ADFR

This type of osteoporosis treatment belongs to the group of those that can affect the overall process of bone remodeling (1). This therapy consists of four phases:

A – activation of resorption – we give resorption activators,
D – depression of resorption – immediately after giving activators, we give inhibitors,
F – free period, without treatment, in which osteoblasts build a bone (2-3 months)
R – his kind of regime is repeated several times.

The activating substances usually mentioned nowadays are: phosphates, PTH, growth hormone, thyroid hormone, whereas the usual depressing substances are calcitonin, biphosphonates, etc. Clinical application of this osteoporosis therapy is unfamiliar to us, but it can present the therapy of future according to the majority.

Ipriflavone

Out of all flavonides (benzo-gamma-pyronic derivatives) that have various pharmacological characteristics, the most interesting for osteoporosis treatment is ipriflavone, which has been proved to have estrogenic effects on bones. It is of a similar built as estrogens, so that it recognizes estrogenic receptors, stimulates synthesis of bone collagen, influences the inhibition of bone resorption, and directly stimulates osteoblasts. Daily dose is 600mg for 6 months in duration (19).

Thiazides

The diuretic characteristic of thiazides is used in osteoporosis treatment as it is known that they influence a decrease in urine excretion of calcium and thus increase the bone mass.

They are applied to those persons who, apart from osteoporosis, have hypertension as well. So, in hypertension treatment with diuretics we opt for thiazides and by doing so we positively influence osteoporosis (1).

Siliceous, strontium, aluminum

These preparations are used for experimental purposes, in small doses and very carefully as well, considering their well-known toxic characteristics. It has been proved that they stimulate the work of bone cells and that, even to a certain degree, influence the inhibition of resorption (20).

Vitamin D

There are divided opinions concerning the role of vitamin D in osteoporosis therapy. Nevertheless, vitamin D is considered to be necessary in the therapy of senile osteoporosis due to the feeble kidney's function in the elderly, which is inevitable for the creation of active metabolite of vitamin D. Small doses of vitamin D are considered to be the most efficient in a continuous daily therapy: in elderly people during the whole year and in postmenopausal women only in winter months, the recommended doses are 400-800 IJ/d. These doses can be used with no danger of hypervitaminosis and they do not require a frequent control of calcemias. Vitamin D is nowadays recommended both in therapy and in prevention of primary forms of osteoporosis (11).

Estrogens

A widely accepted opinion is that estrogens present a chosen medicine in the therapy of postmenopausal osteoporosis, considering the progesterone mechanism of the development of this osteoporosis. They inhibit bone resorption when they are applied during the menopausal period, that is, they stop further putrefaction of bones at a particular level. They can usually be applied up to 60 years of age, even though there are opinions that they can be used later than this period. It is important to mention that nowadays only preparations of natural estrogen are used, and always in combination with progesterone in order to avoid carcinogenic effect of estrogen on the endometrium and breast. There are several forms of estrogen administration: tablets, gel (percutanic, transcutanic), vaginal tablets, and subcutanic implants. A transdermal way of application (stitches) is considered to be one of the most optimal ways since it enables the avoidance of estrogen metabolism in the liver. It is applied twice a week. Doses of estrogen application would be the following: 1.5-2.0 mg/d for humane estrogen. It is applied from 5 to 10 years. Considering all the risks of such a hormone therapy, gynecologic check-ups are necessary every 3 months, although it is nowadays thought that this kind of estrogen therapy application avoids all serious risks and complications (21, 22).

Calcitonin

In recent years calcitonin has become very important in the treatment of osteoporosis and it has been widely applied. It has been proved that calcitonin of salmon is the most potent out of all calcitonins, so it has been applied most. It is applied in the form of ampoules of nasal spray or suppository. It inhibits bone resorption and it reduces both the activity and the number of osteoblasts. It is applied in doses of 100-200 IJ/d if it in spray or every other day if ampoules are used. It is given intermitentically in the proportion of 1:2 (2:3) treatment: pause, as it quickly creates antibodies. The effect starts 30 minutes after its application. It is important to emphasize that calcitonin has a strong analgesic effect, which is maximal after 3 weeks, particularly if it is applied in the form of spray. The analgesic effect is explained by direct central effect on hypothalamus regulation of pain by stimulating the synthesis of beta-endorphin (23).

Anabolic steroids

This group of medications comprises synthetic derivatives of natural androgens with no androgenic effect, but

they have a strong influence on protein synthesis. The most famous is nandrolon decanoate (Deca-durabolin). They decrease bone resorption, increase intestinal calcium resorption, decrease calcium excretion and directly influence bone formation. Deca-durabolin is used in doses of 50mg a month for a year in duration, and the effect lasts for almost two years. A key indication for this therapy application is senile osteoporosis. Postmenopausal osteoporosis is a contraindication for this therapy application, as well as liver diseases and breast cancer (24).

PTH

Small doses of PTH fragments Teriparatide (1-34 fragment PTH) are applied, thus stimulating creation of bone mass by their mechanism of negative reversal interaction (25, 26).

Conclusion

Fractures in elderly persons are of an epidemic character. As years go by, the number of fractures is increasing, which has a great socio-economic and medical importance. Significant financial resources from poor health funds are used for the prevention of these fractures. Trauma, especially the trauma of the spine and hip, worsens and makes basic diseases in elderly people more acute, the consequence of which is a high percentage of mortality. The main cause of fracture in elderly people is osteoporosis. The number of fractures in elderly people can significantly be reduced by proper treatment of osteoporosis.

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LEČENJE SENILNE I POSTMENOPAUZALNE OSTEOPOROZE - JEDAN OD GLAVNIH PUTEVA PREVENCIJE PRELOMA KOD BOLESNIKA STARIJEG ŽIVOTNOG DOBA

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Kratak sadržaj: *Lečenje preloma bolesnika starije populacije je veliki ortopedski i socio-ekonomski problem. Broj preloma, naročito kuka se povećava iz godine u godinu. Na Ortopedsko-traumatološkoj klinici u Nišu se godišnje hospitalizuje oko 250 bolesnika sa prelomima kuka, što predstavlja blizu 20% od ukupnog broja hospitalizovanih. Za lečenje se troše ogromna materijalna sredstva, pogotovu kada je u pitanju hirurško lečenje koje zahteva skupe implantate za fiksaciju preloma ili aloartroplastiku kuka. Glavni uzrok nastanka preloma bolesnika starije životne dobi je osteoporoza.Ortopedi se svakodnevno susreću sa prelomima žbice na tipičnom mestu, prelomima proksimalnog okrajka ramene kosti, prelomima kuka, pršljenskih tela, distalne potkolenice ili prelomima gležnjeva. U preko 90% slučajeva uzrok preloma je banalna trauma. Zato je pravilno razumevanje, otkrivanje i lečenjem osteoporoze od velike važnosti kako bi učinili da se broj preloma kod bolesnika starije životne dobi značajno smanji.*

Ključne reči: *Senilna i postmenopauzalna osteoporoza, terapija, prevencija preloma kod starijih pacijenata*