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# Preventive and Curative Aspects of Reducing the Intensity of Osteoporosis

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#### ABSTRACT

The article examines the preventive and therapeutic aspects of reducing the intensity of osteoporosis. Osteoporosis is a skeletal disease characterized by low bone mass or bone mineral density (BMD), deterioration of bone microarchitectonics and an increased risk of fractures. The rapid growth of an aging population worldwide affects many aspects of human health, and among them osteoporosis is one of the main public health problems for the elderly, especially for those over 50 years old. Exercise or physical training can improve bone mass and strength and therefore promote bone formation, which can effectively treat and prevent osteoporosis without side effects, unlike treatment methods that are overly dependent on pharmacological intervention using anti-osteoporosis drugs.

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## INTRODUCTION

Osteoporosis and related fractures are the most common chronic metabolic bone diseases and represent a serious global health problem. Due to the aging of the population, osteoporosis has become a serious threat to the health of middle-aged and elderly people, especially middle-aged and older women, the prevalence of osteoporosis in women is three times higher than in men. WHO experts say that the number of patients with osteoporosis will grow to 533.3 million in 2050. The theme of the World Menopause Day in 2021 there was a «Bone Health», the decision on which was made by the Board of the International Menopause Society (IMS).

Osteoporosis and related fractures are important factors for increasing mortality and prevalence among postmenopausal women. The remaining life expectancy of menopausal women with more severe fractures is shorter than that of breast cancer survivors. Bone mass decreases rapidly after menopause, for example, in early postmenopause, the distal forearm decreases by an average of about 3% per year, the spine and femoral neck decrease by an average of 2% and 3% per year for 3 years after menopause, and in women with early menopause (up to 45 years) bone mineral density bone tissue (BMDT) decreases at a faster rate, with an average annual decrease in bone mineral density from 3% to 4%[1]. Therefore, the issue of prevention and treatment of osteoporosis in perimenopausal and postmenopausal women is quite important.

## MATERIALS AND METHODS

In the process of writing the work, special literature was examined within the framework of the research topic, the material was processed using comparative and comparative research methods.

# RESULTS

WHO experts have determined that menopause can be divided into four stages:

- 1) Premenopause (the life process before menstruation stops);
- 2) Menopause (complete decrease in ovarian function, cessation of menstruation, biological changes associated with menopause;
- 3) Perimenopausal period (menopausal trend from clinical signs, endocrinology and biology to one year after menopause);
- 4) Postmenopausal period, coming after the menopausal life process.<sup>2</sup>

Acceleration of bone loss in postmenopause is associated with estrogen deficiency. There are no obvious symptoms of osteoporosis in perimenopausal and postmenopausal women. With the progression of the

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Postmenopausal osteoporosis is the main cause of back and leg pain in postmenopausal women, which can cause spinal deformity and compression fracture of the vertebrae, also known as type II osteoporosis, mainly caused by a decrease in estrogen synthesis in the postmenopausal ovary.<sup>3</sup>.

The diagnosis of osteoporosis is mainly based on the results of dual-energy X-ray absorptiometry (DXA) and/or fractures in fractures that must meet one of the following three conditions:

- 1) Fracture of the hip or vertebral body;
- 2) The BMD of the axial bone measured using DXA, or the value of t BMD of the distal radius (t  $\leq$  -2.5);
- 3) BMD measurement corresponded to low bone mass (-2.5 < t < -1.0) and a fragile fracture of the proximal humerus, pelvis or distal forearm. At the same time, secondary osteoporosis was excluded and can be diagnosed as osteoporosis.<sup>4</sup>

Secondary osteoporosis, which must be excluded, includes endocrine and immune diseases affecting bone metabolism, digestive and kidney diseases affecting the absorption and metabolism of calcium and vitamin D, neuromuscular diseases and multiple myeloma, congenital and acquired disorders of bone metabolism, long-term use of corticosteroids or other drugs affecting bone metabolism.

First of all, the above reasons should be excluded by collecting an anamnesis, and then an auxiliary examination can be used to assist in identification. Mandatory tests are serum calcium, phosphorus, alkaline phosphatase and bone radiographs. In patients with primary osteoporosis, serum calcium, phosphorus and alkaline phosphatase are normal, and serum alkaline phosphatase levels may be slightly elevated in patients with fractures. If the above laboratory test does not correspond to the norm, it is necessary to additionally assess the rate of erythrocyte sedimentation, gonadal hormone, 25-hydroxyvitamin D [25 (OH)D], parathyroid hormone and thyroid function.<sup>5</sup>

Perimenopausal and postmenopausal women are recommended to have an annual X-ray examination of the thoracolumbar spine. Small fractures of the vertebrae can be detected as early as possible. Fracture risk assessment should be performed in patients with osteoporosis without osteoporotic fractures.

The Fracture Risk Assessment Tool (FRAX) recommended by WHO can predict the risk of osteoporotic fractures. The FRAX tool is based on some clinical risk factors, and hip neck BMD models have been created to assess the likelihood of hip fractures and major osteoporotic fractures (vertebrae, forearm, hip or shoulder) in the next 10 years.

Clinical risk factors include age, gender, body weight, height, previous history of fractures, history of hip fractures in parents, smoking, taking glucocorticoids, rheumatoid arthritis, secondary osteoporosis, excessive alcohol consumption, etc. According to the recommendations for the diagnosis and treatment of primary osteoporosis, when the probability of hip fracture predicted by FRAX is  $\geq 3\%$  or the probability of

any major osteoporotic fracture  $\geq$  20%, this is a high risk of osteoporotic fracture.<sup>6</sup>

# DISCUSSION

The choice of prevention and treatment of osteoporosis in perimenopausal and postmenopausal women should be based on a balance of effectiveness, risk and cost, as well as take various measures and methods of prevention and treatment in accordance with the characteristics of perimenopausal and postmenopausal women. To maintain bone health at the beginning of the perimenopausal period, measures should be taken, including a healthy lifestyle, sufficient intake of calcium and vitamin D, as well as menopausal hormone therapy (MHT). In addition, women are at high risk of fractures. Including those diagnosed with osteoporosis, and those with low bone mass (-2.5 < t < -1.0), and those with a probability of hip fracture  $\ge$  3% or the probability of any major osteoporotic fracture  $\ge$  20%, calculated using the FRAX tool over the next ten years, you can also treat with other anti-osteoporotic drugs.

Perimenopausal and postmenopausal women should pay attention to a balanced diet and regular exercise. The recommended diet usually includes fresh fruits and vegetables, whole-grain fiber, fish twice a week, low fat intake (for example, olive oil), sugar control ( $\leq 50$  g /day), low oil content (25-30 g /day), salt restriction ( $\leq 6$  g / day), refusal of smoking, restriction of alcohol consumption ( $\leq 20$  g / day).

A weight loss of 5% to 10% is sufficient to improve abnormalities associated with insulin resistance. The body mass index (BMI) of 18.5-23.9 kg/m2 is normal. Being overweight increases the risk of cardiovascular disease, and being underweight increases the risk of osteoporosis. It is necessary to perform regular exercises with weights and exercises to strengthen muscles. Such exercises can reduce the incidence of cardiovascular diseases and overall mortality. The best way to train is to do 150 minutes of moderate intensity exercises per week, and additional weight training twice a week may be better. When recommending the intensity of aerobic exercises, the comfort of aerobic breathing in the elderly should be taken into account.<sup>7</sup>

It should also be said that calcium supplements can increase BMD and reduce the risk of fractures. The recommended dose of calcium for women over 50 years of age and postmenopausal is 1000 mg / day, and the maximum allowable dose is 2000 mg / day. The nutrition study shows that the average intake of calcium with food by households is 366.1 mg/day, of which urban residents (412.4 mg/day) are higher than rural residents (321.4 mg/day). Therefore, it is necessary to add additional calcium 600 mg/ day.<sup>8</sup>

If it is difficult to get enough calcium from the daily diet (for example, with lactose intolerance or the absence of foods with a high calcium content), calcium supplements are recommended to be used to achieve the recommended daily dose. To increase the rate of absorption and total absorption of calcium, it is recommended to take the same amount of calcium in a small amount and repeatedly.

In order to avoid an increased risk of cardiovascular diseases caused by excessive calcium intake, the US National Academy of Medicine has determined that calcium intake with food and supplements should not exceed 2,000-2,500 mg/day. In order to reduce the possible risk of kidney stones, it is recommended that people with a history of such diseases assess the causes, lose weight, drink more water to increase diuresis, control sodium intake and increase calcium intake with food.

Vitamin D plays an important role in calcium absorption and bone health, improving muscle activity, improving balance, reducing the risk of falls, increasing BMD and preventing osteoporotic fractures. The recommended intake of vitamin D is 400 IU/day for adults in China and 600 IU/day for people over 65 years of age. When using vitamin D for the prevention and treatment of osteoporosis, the dose can be 800-1200 IU/day.<sup>9</sup>

The state of vitamin D in the body is assessed by measuring the level of 25(OH)D in serum. Level 25(OH) ResearchD in serum helps to identify the needs of different people. Guidelines for the diagnosis and treatment of primary osteoporosis to reduce the risk of falls and fractures (2017) recommend that the level of 25 (OH)Serum D in postmenopausal women was  $\geq$  75 nmol/l.

The main sources of vitamin D in the body are exposure to sunlight on the skin and diet. If necessary, you can add exogenous vitamin D. Vitamin D supplements can be divided into regular vitamin D and active vitamin D. Regular vitamin D is the main supplement for bone health. Active vitamin D is a medicine that can effectively treat osteoporosis. Currently, there are two types of active vitamin D, and its analogues can be used in China for the treatment of osteoporosis:  $1-\alpha$ -hydroxyvitamin D3 (alfacalcidol) and 1,25-dihydroxyvitamin D3 (calcitriol). In the treatment of osteoporotic drugs. When using it, one should pay attention to individual differences and safety and regularly monitor the concentration of calcium in the blood and urine.<sup>10</sup>

The 2016 IMS Recommendations on the Health of Middle-aged Women and Hormone Therapy during Menopause indicated that the benefits of primary prevention of osteoporotic fractures were available for women who started HT before and after menopause. In 2019, the clinical practice guide «Pharmacological Treatment of osteoporosis in postmenopausal women», issued by the Endocrinological Society, recommended that women younger than 60 years old, with menopause for more than ten years, low risk of venous thrombosis, symptoms associated with menopause, without a history of HT, after evaluation, menopausal HT could be treated. improve the negative balance of bone remodeling.

Additional benefits of HT indicated by the studies included the following:

1) The effect of HT on cartilage. Although there is no clear link between estrogen exposure and osteoarthritis, systemic muscle and joint pain is one of the most common symptoms in postmenopausal women. Thinning of the lumbar intervertebral disc after menopause, compared with men, the frequency and prevalence of osteoarthritis in women is higher. In addition, female arthritis is more prone to progression and development of symptoms. Estrogen receptors (ER)  $\alpha$  and  $\beta$  have been identified in chondrocytes.

Recent studies have confirmed that ER exists in synovial cells and have shown slow degradation of cartilage in women treated with selective estrogen receptor modulators and HT. At the same time, it was found that the use of HT in women reduces the number of surgical interventions on the joints by 45%.

- 2) The effect of HT on the skin. ER has been found in various skin structures, so estrogen deficiency in postmenopausal women can affect skin health. Studies have shown that postmenopausal skin becomes thinner and inelastic, and the use of estrogen can improve the texture of the skin surface, the ability to retain water, collagen content and elasticity of the dermis.
- 3) The effect of HT on ligaments and tendons. Although the mechanism of the effect of estrogen on the function of ligaments and tendons has not been fully elucidated, women with HT demonstrated low tendon hardness, high fiber density and high collagen metabolism.<sup>11</sup>

HT is the main measure of prevention of osteoporosis in perimenopausal and postmenopausal women. Menopausal HT can prevent bone loss in perimenopausal and early postmenopausal women, as well as increase or maintain BMD in women. It has been reported that  $17\beta$ -estradiol in combination with progesterone increases the BMD of the lumbar vertebrae and femoral neck. There was no significant difference between 1 mg of  $17\beta$ -estradiol and 2 mg of  $17\beta$ -estradiol in combination with progesterone, it was significantly higher than in the placebo group. At the same time, other estrogens can increase BMD.

Although HT can prevent fractures at any age after menopause, the age at which HT is started is very important:

- 1) For patients aged 50 to 60 years or during menopause for less than ten years, HT can be used as first-line therapy;
- For patients aged 60 to 70 years, the benefits and risks of HT should be assessed individually, in addition, drugs with other effects and minimum effective doses should be taken into account;
- 3) HT is not recommended for patients over 70 years of age.

HT can be used for primary prevention of osteoporosis. However, it should be carefully evaluated before use.:

- Patients with suitable indications and intentions to take HT without contraindications can take HT after an individual assessment;
- 2) Patients with contraindications will not take HT;
- Absolute contraindications to HT include estrogendependent tumors (breast cancer, endometrial cancer), thrombotic diseases, severe hepatic-renal insufficiency, unexplained vaginal bleeding, hematoporphyria, otosclerosis, meningioma (progesterone is prohibited);
- HT should be used with caution in uterine leiomyoma, endometriosis, endometrial hyperplasia, thrombosis, benign breast diseases and a family history of breast cancer, gallbladder diseases, etc.<sup>12</sup>

There are many HT schemes that need to be selected in accordance with the specific conditions and wishes of patients.

 The monoestrogen regimen is suitable for women who have undergone hysterectomy, for example, oral estradiol valerate 0.5-2 mg / day, estradiol gel 0.5-2 lines / day or a patch with estradiol hemihydrate (0.5-2 patches per week) is applied to the skin of the hands, thighs and buttocks, avoiding the chest and perineum. 2) Sequential estradiol and progesterone regimens are suitable for perimenopausal or postmenopausal women with an intact uterus and maintaining menstruation. A continuous sequential regimen uses estradiol 1 mg/day for 14 days, followed by estradiol didrogesterone in tablets (containing 1 mg of estradiol and 10 mg of didrogesterone) one tablet per day for 14 days.

In a cyclic sequential mode, estradiol valerate tablets / estradiol ciproterone tablets are used one tablet per day for 21 days, then stopped for seven days, after which another cycle begins.

- A continuous combination of estradiol and progesterone is suitable for postmenopausal women with an intact uterus, but without menstruation. Estradiol / drospirenone tablets can be taken continuously every day.
- 4) Treatment with tibolone can be used continuously at a dose of 1.25-2.5 mg / day[13].

There is no exact time limit for achieving the goal of HT treatment. Although some effect on fracture prevention remains after HT treatment is discontinued, the protective effect on BMD will decrease at an unpredictable rate after HT treatment is discontinued. Therefore, as the sole purpose of continuous use of HT, fracture prevention should take into account the risk of fractures and other possible long-term risks and benefits. At least once a year, conduct a comprehensive assessment of the benefits and risks. If there are no obvious risks, the benefits far exceed the possible risks, and HT can be continued.

Regular follow-up of HT is very important, and it is also necessary to develop individual adaptation programs to encourage suitable patients to adhere to treatment.

Proper use of postmenopausal HT in perimenopausal and postmenopausal women is generally safe. However, a few points should be noted:

- Breast cancer is a contraindication to postmenopausal HT. The increased risk of breast cancer is mainly due to the addition of synthetic progesterone to the HT regimen and the duration of progesterone use. Micronized progesterone and didrogesterone have a lower risk of breast cancer than synthetic progesterone;
- 2) The risk of venous thrombosis increases with age and is positively correlated with obesity. Oral HT increases the risk of venous thrombosis, and oral estrogen therapy is prohibited for women with a history of venous thrombosis. Transdermal estrogen does not increase the risk of venous thrombosis, and transdermal estrogen may be safer for women with a high risk of venous thrombosis (BMI > 30 kg/ m2, smoking, family history of thrombosis) [14].

Thus, HT reduces the frequency of all fractures (fractures of the spine and hip) and acts as a fairly effective way to reduce the frequency of fractures in perimenopausal and postmenopausal women with osteoporosis.

# CONCLUSION

The early stage of osteoporosis is not so easy to attract the attention of perimenopausal and postmenopausal women. Therefore, obstetricians and gynecologists should pay attention

to the condition of bones in perimenopausal and postmenopausal women, carrying out the prevention of osteoporosis. At the same time, these specialists should work with early screening, timely detection of perimenopausal and postmenopausal osteoporosis and risk factors, timely prevention and treatment to avoid the occurrence of osteoporosis and the occurrence of osteoporotic fractures and repeated fractures.

#### Author Contributions

All authors contributed in reviewing the final version of this paper.

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