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OSTEOPOROSIS: AN REVIEW ON MANAGEMENT

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Abstract

The elderly population is frequently affected by osteoporosis. It is typically diagnosed only after a person has experienced a fracture. Reduced bone strength in osteoporosis raises the chance of breaking a bone. It is the most frequent cause of fractures in the elderly. The hip, forearm, and back bones are among the bones that break most frequently. Usually, there are no symptoms until a broken bone happens. Bones can deteriorate to the point where they can break spontaneously or under light stress. After a broken bone, there may be chronic pain and a diminished capacity to perform daily tasks. A decline in bone mass and density, which can raise the risk of fracture, is the hallmark of osteoporosis, a progressive bone disease. The amount and variety of proteins in bone are changed, bone microarchitecture deteriorates, and bone mineral density (BMD) decreases in osteoporosis.

Keywords: Osteoporosis, Screening, Therapeutic strategies, Pharmacological treatments, Bone mineral density.

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Introduction

Porous bones with reduced Bone Mineral Density (BMD), disturbed bone microarchitecture, and changed protein arrangements in the bone are all signs of osteoporosis. Osteoporosis, according to the World Health Organization (WHO), is a systemic skeletal disease that is characterized by low bone mass and microarchitectural deterioration of bone tissue, which increases bone fragility and fracture susceptibility [1]. Because it develops without any noticeable symptoms until fractures happen, osteoporosis is regarded as a silent threat. Osteocytes are typically packed closely together inside the bone, resembling a honeycomb. Bone density is a key factor in determining fracture risk because osteoporosis causes the distance between bone cells to widen and the honeycomb walls to thin, weakening the bone and making it more vulnerable to fractures from minor fragility fractures. A t-score is computed according to BMD classification. A statistical test that calculates the Standard Deviation (SD) from the mean is called a t-score. Young adults (those aged 30 and sex-matched) typically have a t-score of one SD, which is considered a normal score. For BMD, the WHO has a t-score. Osteopenia, or low bone mass, is defined as a t-score between -1 and -2.5, while osteoporosis is defined as a score below -2.5 [2]. In Italy, approximately 3.5 million people are affected by osteoporosis, with over 90,000 fractures occurring annually among those aged 50 and older. The risk of osteoporosis increases with age, affecting around 15% of white individuals in their 50s and 70% of those over 80. more prevalent in females than males. In developed nations, the incidence ranges from 2% to 8% in men and 9% to 38% in women, depending on diagnostic methods. Less is known about the prevalence in developing nations. In 2010, the European Union had approximately 22 million women and 5.5 million men with osteoporosis. In the United States, the figures were about eight million women and one to two million men in the same year. White and Asian individuals are at a higher risk, while people of African descent have a lower likelihood of fractures, though they face the highest risk of death following an osteoporotic fracture.

The term "osteoporosis" derives from Greek words meaning "porous bones." It is estimated that around 200 million people worldwide are affected by the condition. Every year, 8.9 million fractures occur globally due to osteoporosis. Approximately one in five men and one in three women over 50 will suffer an osteoporotic fracture. In the United States, data indicates a decline in the prevalence of osteoporosis, particularly among white women, from 18% in 1994 to 10% in 2006. Latitude also plays a role in fracture risk, with higher-latitude areas

such as Northern Europe receiving less sunlight and, therefore, less Vitamin D. As a result, these regions experience higher fracture rates than those closer to the equator. For example, by age 50, Swedish men and women face a 13% and 28.5% risk of hip fractures, respectively, compared to just 1.9% and 2.4% in Chinese men and women. Diet, particularly intake of Vitamin D, calcium, magnesium, and folate, is also thought to influence bone health.

The economic burden of osteoporosis is significant. In 2010, the European Union spent an estimated 37 billion euros annually on osteoporosis-related healthcare, while the United States incurred about 19 billion USD in related costs. Mortality rates following osteoporotic fractures range from 15% to 30%, which is comparable to the mortality rates for breast cancer and stroke. Furthermore, 50% of women who experience osteoporotic hip fractures will develop disabilities, affecting their ability to live independently and often leading to institutionalization. Primary osteoporosis has several identified risk factors, while secondary osteoporosis may result from conditions such as endocrine disorders (e.g., hypogonadism, hypercortisolism), metabolic disorders, rheumatoid arthritis, gastrointestinal malabsorption, renal failure, and certain medications, including corticosteroids, SSRIs, anticoagulants, and antidiabetic drugs [3].

There is an imbalance between bone creation and resorption in all cases of osteoporosis, regardless of the cause: while osteoclast resorption is elevated, bone synthesis is frequently occurring at a normal pace 4. It is still unclear what exactly triggers the osteoclastic activation process, though.

Screening and diagnosis of osteoporosis

Every woman over 65 should have her osteoporosis status determined. 2. The existence of risk factors, such as early menopause (≤ 45 years), anorexia, smoking or alcohol addiction, chronic use of certain medicines, or conditions linked to an elevated risk for osteoporosis, should be checked for in men ≥ 65 years of age or women < 65 years of age. To rule out potential causes of secondary osteoporosis, the first-line evaluation consists of measuring the erythrocyte sedimentation rate, blood cell count, protein electrophoresis, serum calcium, serum phosphorus, serum alkaline phosphatase, serum creatinine, and 24-hour urine calcium excretion. It is not advised to determine bone turnover indicators.

DXA (Dual-Energy X-ray Absorptiometry) is widely regarded as the gold standard imaging method for diagnosing osteoporosis due to its ability to accurately predict fracture risk. DXA can assess bone mineral density (BMD) at various sites, such as the radius, ulna, spine, or proximal femur, providing a reliable estimate of fracture risk. For individuals aged 65 and older, DXA should be conducted on the proximal femur since osteoarthritis in the spine can interfere with the results. Additionally, hip BMD is a stronger predictor of fracture risk than spinal BMD. Typically, the risk of fracture increases by 1.5 to 3 times for every standard deviation decrease in BMD compared to the reference population [3]. A T score between 1 and −1 is considered normal, while a T score of −2.5 or lower confirms osteoporosis. T scores between −1 and −2.5 indicate osteopenia, a condition that carries a low to moderate fracture risk but often progresses to osteoporosis. Correctly identifying and managing individuals with osteopenia is crucial, as approximately 35 million Americans are affected by this condition [5].

BMD determination alone should not be used to estimate the absolute risk of fractures and, consequently, to make therapeutic decisions; rather, a thorough assessment of the patient is necessary, accounting for all known risk factors for osteoporotic fractures. Sensitive instruments have been created in this context and are frequently employed in therapeutic settings. In addition to helping detect osteoporosis, DXA can be used to track how well certain treatments are working. An estimated 0.5 to 2% of bone mass is lost annually, but anti-osteoporosis treatments enable an annual gain of 1 to 6%. It is advised to repeat the DXA no earlier than 1-2 years after the start of treatment because the least meaningful improvement is 2-4 percent [3].

Therapeutic strategies against osteoporosis

Non-pharmacological treatments

Numerous methods exist for preventing osteoporosis and its complications, including vitamin D and calcium supplements (500–1,000 mg daily), physical activity, and multidisciplinary interventions to reduce the risk of falls5. Since the most prevalent cause of non-responsiveness to anti-osteoporotic drugs is a calcium and vitamin D deficit, these principles also serve as the foundation for all specialized pharmacological treatments.

Vitamin D supplementation

1α,25-dihydroxy-colecalciferol [1,25 (OH)2D3], the main active metabolite of vitamin D, is derived from 20% of the food, especially from dairy and blue fish, and 80% from the conversion of 7-dehydrocholesterol by UV radiation. The liposoluble precursor of vitamin D primarily accumulates in adipose tissue. The primary circulatory vitamin D metabolite, 25-hydroxycolecalciferol [25 (OH) D], is produced in the liver from the free quota. Its levels are the most accurate indicator of vitamin D status. A complicated homeostatic process involving parathyroid hormone (PTH) and serum levels of calcium and phosphorus transforms 25 (OH) D into the active metabolite in the kidney. There are vitamin D receptors everywhere, but they are particularly prevalent in muscle cells, hepatocytes, chondrocytes, osteoblasts, and parathyroid cells. 6Via a genetic route, vitamin D stimulates cell division and proliferation. Additionally, vitamin D influences how cells react to different stimuli through a non-genomic method 7-8 In relation to bone homeostasis, vitamin D primarily regulates calcium

metabolism by enhancing intestinal absorption and renal reabsorption and stimulating osteoblasts to produce bone proteins such osteocalcin [9].

For healthy adults, the daily allowance for vitamin D is 1,500 IU; for elderly people with inadequate calcium intake, it is 2,300 IU. Individuals who do not receive enough sun exposure should receive 1,200–2,000 IU of vitamin D daily, as the normal Mediterranean diet only supplies about 300 IU [10-12].

In Italy, around 50% of healthy young individuals experience vitamin D insufficiency (serum 25(OH)D levels between 20–30 ng/mL) during the winter months. The prevalence of vitamin D deficiency (serum 25(OH)D levels below 20 ng/mL) increases with age, affecting nearly all elderly individuals who do not take supplements [14]. Consequently, people aged 70 and older should be considered vitamin D insufficient unless they have significant sun exposure. It is recommended that older adults receive a daily dose of 800 IU of vitamin D as a preventive measure. If deficiency is diagnosed, a cumulative dose of 300,000 to 1,000,000 IU over 1 to 4 weeks is advised, followed by a maintenance dose of 800 to 2,000 IU per day (or the equivalent weekly or monthly). The appropriate dosage should depend on age, sun exposure, and baseline 25(OH)D levels. For individuals at ongoing risk of deficiency, vitamin D levels should be checked 3 to 6 months after starting supplementation. Additionally, supplementation should be closely monitored in patients at risk of vitamin D toxicity (such as those with granulomatosis) or primary hyperparathyroidism [15].

Physical activity

Engaging in physical activity can significantly reduce the loss of bone mass that comes with aging [17]. Because of its beneficial effects on bone mass and the danger of falling, it is therefore advised to engage in at least some activity each day, such as a 30-minute walk [18].

Comprehensive interventions on the risk of falls

Gait training and muscle strengthening exercises have been demonstrated to lower the incidence of falls and associated injuries in older participants.18 Antipsychotics, antidepressants, and benzodiazepines are examples of psychotropic medications that should be taken very carefully or avoided at all costs. Finally, proper precautions should be taken to prevent falls at home, such as installing handrails on stairs and handholds in the restroom.

Pharmacological treatments

Treatment threshold

DXA-estimated BMD is insufficient to initiate anti-osteoporotic therapy. As stated before, a thorough evaluation is required to determine the risk of long-term fractures.18 Actually, people who are already osteoporotic and hence at danger of osteoporotic fractures or refractures are the target of pharmaceutical therapy. Several tools for estimating the 10-year fracture risk are discussed in the literature. The "Derived Fracture Risk Assessment," or "DeFRA," is one of the most widely used. It contains several risk variables, including a family history of hip fractures, smoking, immunosuppressive medication usage, hyperthyroidism, alcoholism, prior vertebral or femoral fractures, rheumatoid arthritis, or other autoimmune illnesses [19]. Regardless of BMD values, people who are at high risk for fractures as determined by DeFRA or other comparable algorithms are candidates for treatment.

Drugs

Pharmacological treatments for osteoporosis can directly promote increases in bone mass or reduce bone resorption to result in secondary gains in bone mass.20In the following subsections, the primary medications now used to treat osteoporosis are briefly reviewed.

Bisphosphonates

Synthetic substances with anti-resorption properties are called bisphosphonates. By attaching themselves to hydroxyapatite and preventing osteoclast activation, they affect bone. Bisphosphonates have minimal impact on other organ systems and a strong affinity for bone. Bisphosphonates' generally good tolerability is explained by their pharmacokinetics. After oral treatment, bisphosphonates have low plasma levels due to their limited intestinal absorption. In contrast to the half-life of bisphosphonate depots in the bone, which is likely up to ten years or longer, the plasma half-life is very brief because circulating levels of bisphosphonates rapidly decline due to fast adherence to the bone surface [21].

Alendronate, clodronate, etidronate, ibandronate, risedronate, and zoledronate are among the bisphosphonates that are presently approved in Europe for the treatment of osteoporosis. Bisphosphonates come in a variety of forms for the treatment of osteoporosis, including oral and intravenous forms with weekly, monthly, and yearly dosage schedules. Convenient dosing is essential to the long-term care of chronic illnesses. According to studies evaluating adherence to once-monthly, once-weekly, or once-daily dosing, adherence to weekly or monthly dosing is noticeably superior to that of once-daily formulations [22].

It has been demonstrated that all licensed bisphosphonates reduce bone turnover in a dose-dependent way. Only a few bisphosphonates are useful in lowering the risk of hip and non-vertebral fractures, even though they all raise BMD and lower the risk of vertebral fractures. Giving the patient instructions on how to take the medication can help prevent some of the typical gastrointestinal adverse effects.21Additionally, weekly or monthly formulations reduce the likelihood that the gastro-esophageal mucosa may experience repeated stressors.23-28 Thirty percent of patients experience acute phase response (APR), a brief flu-like illness that

typically lasts two to three days following the initial intravenous dose of amino-bisphosphonates.29It is linked to a sharp decline in circulating lymphocytes and an increase in C-reactive protein levels in the blood. APR can be prevented or controlled with paracetamol or non-steroidal anti-inflammatory medications.30 Patients on long-term biphosphonate treatment, especially those on glucocorticoids and/or another anti-resorptive drug, have been reported to experience atypical femoral subtrochanteric/diaphyseal fractures [31-35].

Atypical femur fractures can occur on their own or with minor trauma. The processes underlying these fractures and the traits of people at risk for them require further research. A greater risk of atrial fibrillation has been linked to bisphosphonate treatment in certain, but not all, studies36-40 The Food and Drug Administration (FDA) came to the conclusion in 2011 that there were insufficient grounds to believe that using bisphosphonates could cause atrial fibrillation. Furthermore, rheumatoid arthritis patients using bisphosphonates recently showed a decreased risk of myocardial infarction [41].

In patients receiving bisphosphonates, osteonecrosis of the jaw (ONJ) is an uncommon occurrence, and there is little data to predict risk factors.42From a pathogenic perspective, ONJ is characterized by a persistent osteomyelitis brought on by oral flora bacteria, specifically actinomyces.43 On the other hand, the pathophysiology of ONJ remains unclear. Prolonged uses of oral bisphosphonates, corticosteroid therapy, or immunosuppressive medications are the primary risk factors for ONJ. The primary risk factors are tooth extraction and periodontal and dental disorders.44-45 5 ONJ cases have also been reported in individuals who have never received bisphosphonate treatment. 43Seldom documented side effects from bisphosphonates include musculoskeletal pain, which is typically transitory after stopping the medication,47 eye inflammation,48 urticaria,49 or mucositis [50].

Table01: Dose Recommendations for Bisphosphonates [51-53].

Bisphosphonate	CrCl Recommendation	Prophlactic Dose	Treatment Dose
Ibandronate	≥ 30 mL/min	2.5 mg PO once daily or 150 mg PO once monthly	2.5 mg PO once daily or 150 mg PO once monthly or 3 mg IV every 3 months
Risedronate (IR)	≥ 30 mL/min	5 mg PO once daily	5 mg PO once daily or 35 mg once weekly
			or 35 mg PO once weekly or 150 mg PO once monthly
Zoledronic acid	≥ 35 mL/min	5 mg IV every 2 years	5 mg IV once yearly
Alendronate	≥ 35 mL/min	5 mg PO once daily or 35 mg PO once weekly	10 mg PO once daily or 70 mg PO once weekly

Conclusión

A verycommonconditionthatisincreasing as thepopulationages and growsis osteoporosis. It has a highcost, and fractures associatedwithit can drasticallylowerquality of life. Eventhough DEXA isavailable, many cases of osteoporosis goundetecteduntil a fracture occurs. Osteoporosis alsoaffectspeoplepsychologically and financially, and itisfrequentlydiscoveredonlyafter a fragility fracture and itscomplications. A thorough fracture riskassessment, which can be acquiredusingvalidatedalgorithms, shouldserve as thefoundationfortherapeuticdecision-making. Non-pharmacologicalmethodsshould be used in conjunctionwiththeprescription of anti-osteoporoticmedicationsafterthedecision to treat has beenmade.There are many medications available today to treat osteoporosis, and safety and effectiveness factors should be taken into account when selecting a particular compound.

Disclosure Statement

There are no conflicts of interest.

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