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Review Article

A REVIEW ARTICLE ON OSTEOPOROSIS

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Abstract:

Osteoporosis is defined as low bone mineral density caused by altered bone microstructure ultimately predisposing patient to low impact, fragility fractures. Osteoporotic fractures leads to a significant decrease in quality of life with an increased morbidity, mortality, and disability. Osteoporosis- related fractures can increase pain, disability nursing home placements, total health care costs. Approximately 10 million men and women in the US have osteoporosis. Over 50% postmenopausal Caucasian women will have an osteoporotic related fracture. Only 30% of senior women who have a hip fracture will be able to return to independence. In Caucasian men, the risk of an osteoporotic fracture is 20%. But the one year mortality in men who have a hip fracture is twice that of women. Black males and females have less osteoporosis than their Caucasian counterparts, but those diagnosed with osteoporosis have similar fracture risk. The aging of the American population expected to triple the number of osteoporotic fractures. Osteoporosisrelated to various factors including menopause and aging is the most common chronic metabolic bone disease. It is seen in all age groups, genders and races but it is more common in Caucasians [white race], older peoples and women Osteoporosis is increasingly becoming a global epidemic. Currently it has been estimated that more than 200 million peoples are suffering from osteoporosis. According to recent statistics from the international osteoporosis foundation, worldwide 1 in 3 women and 1 in 5 men will experience osteoporotic fractures in their life time. The diagnosis of osteoporosis is determined by measuring bone mineral density [BMD] using noninvasive dual-energy X-ray absorptiometry. Osteoporosis medication include bisphosphonates, receptor activator of nuclear factor kappa-B ligand inhibitor, estrogen agonist /antagonist, parathyroid hormone analogues and calcitonin. Key words: Bone mineral density fracture risk, Osteoporosis management, menopause, bone density, bone fracture,

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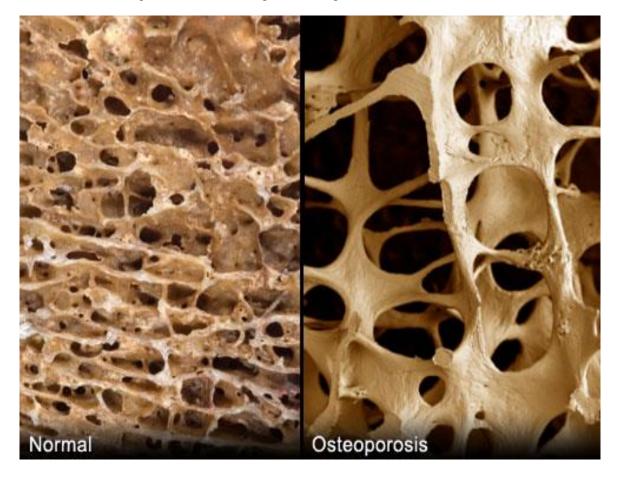
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INTRODUCTION:

Osteoporosis is a bone disease that develops when bone mineral density and bone mass decreases or when the quality or structure of bone changes. This can leads to decrease in bone strength that can increase the risk of bone broken. Parathyroid hormone [PTH] and vitamin D has a significant effect on bone metabolism, triggering both bone resorption and bone formation, depending on which cell- type are activated and the temporal pattern of activation. Osteoporosis starts from about age 25 to age 50. As we get older, we begins to lose more bone then we build. The tiny holes within bones get bigger, and the solid outer layer becomes thinner. In other words, our bones get less dense. Hard bones turn spongy and spongy bones turns spongier. People with osteoporosis are more likely to break bones, most often in the hip, forearm, wrist, and spine while most broken bones are caused by falls, osteoporosis can weaken bones to the point that a break can occur more easily, or example by coughing or bumping into something. There is no cure or osteoporosis, but treatment can help to slow or stop the loss of bone density and reduce the risk of fractures. This may involve medications, diet changes, exercise, and steps to prevent fracturing a bone. Osteoporosis means 'porous bone.' Viewed under a microscope. Healthy bone looks like a honeycomb.

Osteoporosis is not usually painful until a bone is broken. But broken bones in the spine are a common cause of long term pain. Although a broken bone is often the first sign of osteoporosis, some older people develop the characteristic stooped (bent forward) posture.



Classification

Osteoporosis can be classified into four main groups by considering the factors affecting bone metabolism.

- Primary osteoporosis
- Secondary osteoporosis
- ✤ Osteogenesis imperfecta
- ✤ Idiopathic osteoporosis

Primary osteoporosis

Primary osteoporosis is an age – related disorder characterized by decreased bone mass and increased susceptibility to fracture in the absence of other recognizable causes of bone loss primary osteoporosis can also be divided into two sub groups.

- Post menopausal osteoporosis (type-1)
- -Senile- osteoporosis (type-2)

1) Post – menopausal osteoporosis (type-1)

Post - menopausal osteoporosis is osteoporosis that results from decreased estrogen levels. There are usually no obvious symptoms, and people typically only realize that they have the condition once they have broken a bone, a doctor may use a bone density scan to help diagnose a person with post - menopausal osteoporosis.

2) Senile – osteoporosis (type-2)

Senile- osteoporosis is a bone loss that results from aging. It may cause no symptoms at first, but it can lead to fractures and difficulty moving. Senileosteoporosis cause bone loss and it develops as an adult grows older it can weaken bones and increase the risk of fracture and other injury.

Secondary osteoporosis

Secondary osteoporosis refers to osteoporosis caused by certain medical conditions or medications that can cause bone loss, increase fracture risk, directly or indirectly affect bone remodeling or interfere with the attainment of peak bone mass in younger individuals.

For example: Glucocorticoid – induced osteoporosis The most common form of secondary osteoporosis is that induced by exogenous glucocorticoids, crushing's syndrome, caused by an excess of endogenous glucocorticoids.

Osteogenesis imperfecta (OI)

Osteogenesis imperfecta is a group of genetic disorders that mainly affect the bones, the term "osteogenesis imperfecta" means imperfect bone formation. People with this condition have bones that break easily, often rom mild trauma or with no apparent cause.

Types

Type-1: This is mildest and most common form of 01. Leads to broken bone (bone fractures) or muscle weakness

Type-2: Babies born with type-2 often can't breathe and die young.

Type-3: Babies often have broken bones at birth.

Type-4: Bones may break easily.

Idiopathic osteoporosis

Idiopathic osteoporosis refers to the development of osteopenia and fracture with minimal or no trauma in otherwise young, healthy individuals who are not postmenopausal or have other, identifiable secondary causes of osteoporosis.

Stages

There are four different stages of osteoporosis. Each stage is measured by your actual bone density, which is an indicator of this disease. The four stages of osteoporosis include:

Stage 1:

The first stage in osteoporosis occurs when your bone loss and bone formation occur at the same rate, meaning you no longer make more bone than you're losing. At this stage, there are no symptoms, and your bone density scores are above -1.

Stage 2:

In stage two, you've entered the time when your bone loss is happening faster than your new bone can form. You still won't have any symptoms, and your bone density scores may be lower, possibly indicating osteopenia, a precursor to osteoporosis, and your bone density is anywhere from -1 to -2.5. Stage 3:

Stage three is when you're considered to have osteoporosis. In this stage, your bone loss far exceeds your bone growth, putting you at a higher risk for fractures. Unless you experience a fracture, you likely won't have any other symptoms in this stage, except for a bone density of -2.5 or lower if you're tested. Stage 4:

In this stage, your osteoporosis is very severe. Your risk of fractures is higher than in stage three, and you may actually have symptoms. The severe bone loss in stage 4 leads to changes in your spine, such as a stooped posture and loss of height. You'll likely have one or more fractures when you've entered stage four

Primary Osteoporosis

Primary osteoporosis is often associated with age and sex hormone deficiency. Age-related osteoporosis results from the continuous deterioration of the trabeculae in bone. In addition, the reduction of estrogen production in post-menopausal women causes a significant increase in bone loss. In men, sexhormone–binding globulin inactivates testosterone and estrogen as aging occurs, which may contribute to the decrease in BMD with time.

Secondary Osteoporosis

Secondary osteoporosis is caused by several comorbid diseases and/or medications. Diseases implicated in osteoporosis often involve mechanisms related to the imbalance of calcium, vitamin D, and sex hormones. For example, Cushing's syndrome has been found to accelerate bone loss through excess glucocorticoid production. In addition, manv inflammatory diseases, such as rheumatoid arthritis, may require the patient to be on long-term glucocorticoid therapy and have been associated with secondary osteoporosis. Notably, glucocorticoids are considered the most common medications linked to drug-induced osteoporosis. BMD has been found to decline rapidly within three to six months of initiation of glucocorticoid therapy. The American College of Rheumatology (ACR) has detailed recommendations to aid in guiding therapy selection for the prevention and treatment of glucocorticoid-induced osteoporosis (GIO).

Causes of secondary osteoporosis may differ between genders. For men, excessive alcohol use glucocorticoid use, and hypogonadism are more commonly associated with osteoporosis. For example, men receiving androgen-deprivation therapy (ADT) for prostate cancer are at increased risk of osteoporosis; Shahinian et al. found that 19.4% of those treated with ADT experienced a fracture compared with 12.6% of those who were not. Tannenbaum et al. found that osteoporosis in 32.4% of women was attributed to secondary causes, most often hyper calciuria. Mal-absorption of calcium, hyperparathyroidism, vitamin D deficiency, hyperthyroidism, Cushing's disease, and hypo calciuric hypercalcemia. Of note, disorders of calcium metabolism and hyperparathyroidism contributed to 78% of the secondary causes.

Epidemiology

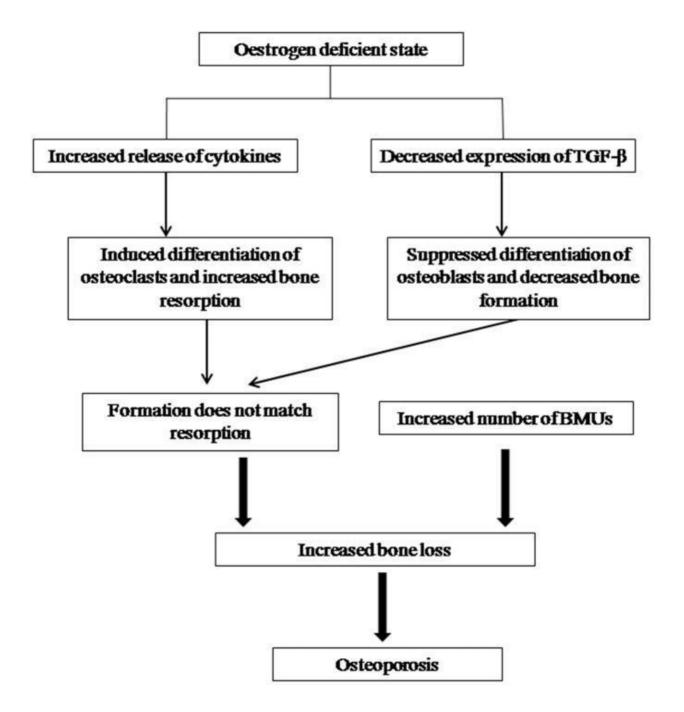
Over 200 million peoples have osteoporosis and the incidence rate increase with age. Over 70% othose over age 80 are affected. It is more common in female than males. In the developed world, 2% to 8% of males and 9% to 38% of females are affected. Worldwide, there are approximately 9 million fractures per year as a result of osteoporosis.

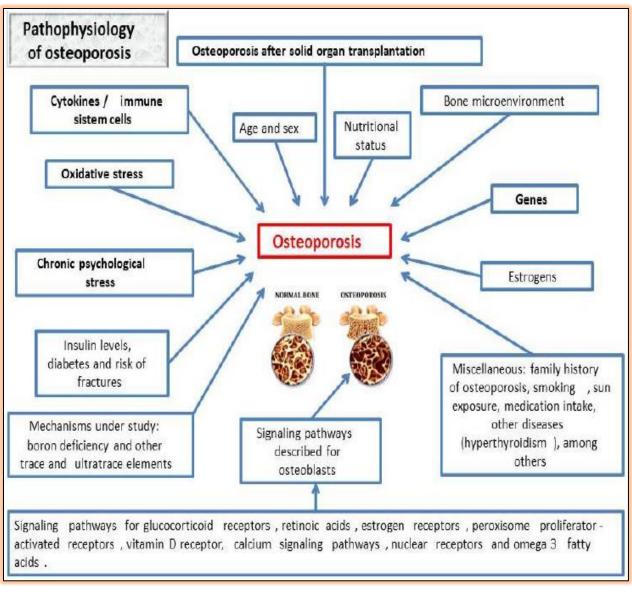
One in 3 females and one in 5 males over the age of 50 will have an osteoporotic fracture. Areas of the world with less vitamin D through sun light compared to regions closer to the equator have higher fracture rates in comparison to people living at lower latitudes.

Osteoporosis is a major non-communicable disease and the most common bone disease, affecting one in three women and one in five men over the age of 50 worldwide. The clinical consequence of osteoporosis is fragility fractures. It has been shown that an initial fracture is a major risk factor for a new fracture. With the rapid ageing of the population worldwide and the changes in lifestyle habits, the incidence of osteoporosis and related fractures has significantly increased and will continue to increase markedly in the future. Due to its prevalence worldwide, osteoporosis is considered a serious public health conce It is estimated that 75 million people in Europe, USA and Japan are affected by osteoporosis. In Asia, osteoporosis is greatly under-diagnosed and undertreated, even in the most high-risk patients who have already fractured. The problem is particularly acute in rural areas. In the most populous countries like China and India, the majority of the population lives in rural areas (60% in China), where hip fractures are often treated conservatively at home instead of by surgical treatment in hospitals.

Pathophysiology

Osteoporosis is a classic example of a multifactorial disease with a complex interplay of genetic, intrinsic, exogenous, and lifestyle factors contributing to an individual's risk of the. Disease. Osteoporosis is caused by an imbalance of bone resorption and bone remodeling leading to decreased skeletal mask. In most individuals, bone mass peaks in the third decade, after which bone resorption exceeds bone formation. Failure to reach a normal peak bone mass or acceleration of bone loss can lead to osteoporosis.





Symptoms

Osteoporosis doesn't have symptoms the way lots of other health condition do. That's why health care providers sometimes call it a silent disease. You won't feel or notice anything that signals you might have osteoporosis. You won't have a head ache, fever or stomachache that lets you know something in your body is wrong. The most common symptom is suddenly breaking a bone, especially after a small fall or minor accident that usually wouldn't hurt you. These warning signs of osteoporosis can include:

- Losing an inch or more of your height.
- Changes in your natural posture (stooping or bending forward more).
- Shortness of breath (if disks in your spine are compressed enough to reduce your lungs capacity).
- Lower back pain (pain in your lumbar spine).



• Neck and Legs pain.



Causes of osteoporosis

Osteoporosis happen as you get older and your bones lose their ability to regrow and reform themselves. Your bones are living tissue like any other of your body. It might not seem like it, but they are constantly replacing their own cells and tissue through your life. Up until above age 30, your body naturally builds more bone than you lose. After age 35, bone breakdown happens faster than your body can replace it, which causes gradual loss of bone mass if you have osteoporosis, you lose bone mass at grater rate. People in post menopause lose bone mass even faster.



Risk factors

Risk factors you can change

- Low body weight
- Smoking
- Drinking too much alcohol
- Slips, trip, and falls
- Risk factors you can't change
 - Your gene
 - Aging
 - Being a women

A history of bone broken

- Medications that increases risk
 - Glucocorticoid tablets
 - Anti- epileptic medication
 - Breast cancer treatments
 - Prostate cancer treatments
 - Gender confirmation
 - Proton pump inhibitors
 - Diabetic medication
 - Tricyclic antidepressant
 - Selective serotonin reuptake inhibitor

Medical condition that increase risk

- Rheumatoid arthritis
- Hyperthyroidism
- Parathyroid
- Crohn's
- Coeliac disease
- Diabetes
- HIV
- Liver disease
- Parkinson's disease
- Dementia
- Cystic fibrosis

Evaluation of osteoporosis

Osteoporosis affects women as well as men and it can often go undiagnosed until a patient visits the clinic due to a fracture. Unless proved otherwise, the diagnosis of osteoporosis is always considered secondary.

History and Physical Examination

A good history of the patient including a history of past medical conditions, long-term drug exposure, dietary history, history of fragility fractures to parents, especially the mother may provide adequate information about the cause of osteoporosis.

Fractures may cause chronic pain, reduced mobility, disability, increasing degree of dependence, and even death. Physical signs such as loss of height (caused by vertebral compression due to fractures), dorsal kyphosis (though not diagnostic criteria for osteoporosis), chest deformity, protuberant abdomen, rib-pelvic overlap suggest evidence of vertebral fractures.

Lumbar compression fractures are also responsible for crowding of internal organs causing gastrointestinal complaints such as reduced appetite, early satiety, constipation, abdominal pain. Persistent back pain and positional restrictions are additional complaints. Findings such as impaired ambulation, muscle weakness, impaired balance, reduced vision, orthostatic hypotension are risk factors for falls leading to fractures.

Laboratory Investigation

These include complete blood count, serum creatinine, serum calcium, serum phosphorus, and magnesium, alkaline phosphatase, alanine aminotransferase (ALT), aspartate aminotransferase (AST), thyroidstimulating hormone (TSH), serum protein electrophoresis, 25-hydroxy Vitamin D (25-OH-D), total testosterone and gonadotropin in younger men, and biochemical turnover markers (BTMs).

Vitamin D levels should be measured after 3 - 4 months of adequate supplementation and need not be repeated if the level is 30 ng/ml or more is achieved.

More extensive laboratory evaluation may be required in men with osteoporosis, in cases of unexplained fracture or low BMD and inadequate response to osteoporosis treatment, and clinical suspicion of secondary causes in a patient of osteoporosis. It may include iron and ferritin levels, homocysteine, prolactin, urinary histamine, urine protein electrophoresis.

Bone Mineral Density (BMD) Measurement

Bone quality and BMD are the two factors that reflect bone strength. While bone quality cannot be measured, BMD can be easily measurable and is able to establish the diagnosis of osteoporosis. Bone mineral density can be measured by dual X-ray absorptiometry (DXA); it is the actual expression of the bone in absolute terms of grams of mineral (primarily, as g/cm^2 of calcium) per square centimeter of the scanned bone. Hip and spine are the common sites used for BMD measurements to confirm the diagnosis of osteoporosis to predict the risk of future fractures. The difference between the patients BMD and mean BMD of females in the age range of 20 - 29 years (divided by the standard deviation (SD) of the reference population) yields the T-score. The Z-score is calculated by comparing the BMD of a particular age, sex, and ethnicity-matched adult reference population. The preferred sites for BMD measurements are total hip, femoral neck, or total lumbar spine (or a combination of these). If the hip and/or lumbar spine sites cannot be measured or become unusable (e.g., hyperparathyroidism or very obese patients), one-third (33%) of the radius can be used. The WHO definition of osteoporosis based upon the T-scores is applicable only for postmenopausal women and men aged 50 years or more. Z-scoring is used for children,

premenopausal women, and men aged less than 50 years.

The National Osteoporosis Guideline Group (NOGG) recommends the assessment of fracture risk in postmenopausal women and men above the age of 50 years, using the Fracture Risk Assessment Tool (FRAX). It is recommended that in individuals at intermediate risk, the BMD measurement should be performed using DXA and re-estimation of fracture probability to be done using FRAX.

Vertebral Fracture Assessment/Vertebral Imaging

Vertebral fracture assessment (VFA) by DXA is a useful tool for imaging the thoracic and lumbar spine to detect vertebral fracture deformities. This method has the advantage of greater patient convenience, a smaller dose of ionizing irradiation, and lower cost when compared with standard radiographs of the spine.

Indications of vertebral fracture assessment include

- Women aged ≥70 years or men aged ≥80 years
- History of previous vertebral fracture
- Prospective height loss (difference between the current height and a previously documented height measurement) of ≥2 cm
- Long-term glucocorticoid treatment (glucocorticoid therapy equivalent to ≥5 mg of prednisone or equivalent per day for ≥3 months)
- Non-availability of BMD measurements

Biochemical Bone Turnover Markers (BTMs)

Biochemical markers of bone remodeling include resorption and formation markers. The advantages of BTMs are that they are non-invasive, can be repeated many times. They are useful in assessing bone dynamics, monitoring response to therapy, and promoting adherence. In combination with BMD, assessment of BTMs improves fracture risk prediction. However, the disadvantages include potentially high biological and analytical variability, the inability to reflect the process of mineralization. Another major disadvantage is that their levels are influenced by the rate of renal clearance, food intake, diurnal variation, storage conditions.

BTMs play an important role in providing prognostic information on fracture risk that supplements radiographic measures of bone mass, but the utility of BTMs is limited by a large number of pre analytic factors and comorbid clinical conditions that influence BTM levels. Any change in bone physiology causes rapid alterations in BTM levels, therefore, they can be utilized in assessing the patient's response as well as compliance with therapies for osteoporosis. The pre analytic factors include controllable factors such as seasonal or circadian variation and uncontrollable factors such as the age and sex of the patient. The use of BTMs is not currently recommended as a public health tool to identify patients at increased risk of rapid bone loss due to the lack of prospective RCTs to assess the efficacy and cost-effectiveness of this program.

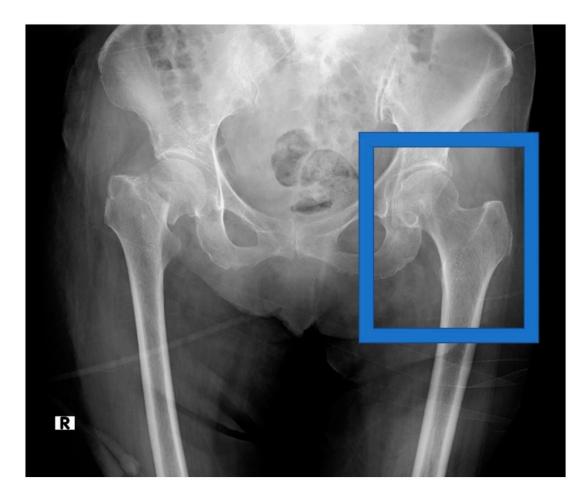
- A hip or vertebral fracture.
- Determination of fractures at the femoral neck, hip, or lumbar spine when the T-score is ≤-2.5.
- Low bone mass with T-score between −1.0 and −2.5 at the femoral neck or lumbar spine, 10-year probability of a hip fracture ≥3, or a 10-year probability of a major osteoporosisrelated fracture ≥20%.

Diagnosis

A doctor will consider family history and any risk factors. If they suspect osteoporosis, they will request a bone mineral density scan (BMD).



Bone density scanning uses a type of X-ray known as dual-energy X-ray absorptiometry (DEXA).



DEXA can indicate the risk of osteoporotic fractures. It can also help monitor a person's response to treatment.

- Two types of devices can carry out a DEXA scan:
 - ✤ A central device:

This is a hospital-based scan that measures hip and spine bone mineral density while the individual lies on a table.

✤ A peripheral device:

This is a mobile machine that tests bone in the wrist, heel, or finger.

DEXA test results

Doctors give the results of the test as a DEXA T score or a Z score.

The T score compares an individual's bone mass with the peak bone mass of a younger person. -1.0 or above shows good bone strength

- From -1.1 to -2.4 suggests mild bone loss (osteopenia)
- 2.5 or below indicates osteoporosis

- The Z score compares the bone mass with that of other people of a similar build and age.
- A doctor will typically repeat the test every 2 years as this allows them to compare results.

Other tests

An ultrasound scan of the heel bone trusted source is another method that doctors use for assessing osteoporosis, and they can carry it out in the primary care setting. It is less common than DEXA, and the doctors cannot compare the measurements against DEXA T scores.

Treatment

Treating osteoporosis involves treating and preventing fractures, and using medicines to strengthen bones.

Although a diagnosis of osteoporosis is based on the results of your bone density scan, the decision about what treatment you need, if any, is based on a number of other factors including your:

- Age
- sex

- risk of breaking a bone
- previous injury history

If you've been diagnosed with osteoporosis because you've had a broken bone, you should still receive treatment to try to reduce your risk of further broken bones.



You may not need or want to take medicine to treat osteoporosis.

However, make sure you're getting enough calcium and vitamin_D.

To achieve this, your healthcare team will ask you about your diet and may recommend that you make changes or take supplements.

Pharmacological treatment for osteoporosis Medicines for osteoporosis

Several different medicines are used to treat osteoporosis (and sometimes osteopenia).

Bisphosphonates

Bisphosphonates slow the rate that bone is broken down in your body. This maintains bone density and reduces your risk of a broken bone.

There are several different bisphosphonates, including:

- Alendronic acid
- Risedronate
- Zolendronic acid

They are given as a tablet, a liquid that you swallow, or an injection.

Always take bisphosphonates on an empty stomach with a full glass of water. Stand or sit upright for 30 minutes after taking them. You'll also need to wait between 30 minutes and 2 hours before eating food or drinking any other fluids.

Bisphosphonates usually take 6 to 12 months to work, and you may need to take them for 5 years or longer.

You may also be prescribed calcium and vitamin D supplements to take at a different time to the bisphosphonate.



The main side effects associated with bisphosphonates include:

- irritation to the food pipe
- swallowing problems
- stomach pain

Osteonecrosis of the jaw is a rare side effect linked with the use of bisphosphonates, although most frequently with high-dose intravenous bisphosphonate treatment for cancer and not for osteoporosis.

In osteonecrosis, the cells in the jaw bone die, which can lead to problems with healing. If you have a history of dental problems, you may need a check-up before you start treatment with bisphosphonates. Speak to your doctor if you have any concerns. Selective estrogen receptor modulators (SERMs)

SERMs are medicines that have a similar effect on bone as the hormone estrogen. They help to maintain bone density and reduce the risk of fracture, particularly of the spine.

Raloxifene is the only type of SERM available for treating osteoporosis. It's only recommended for women, after the menopause. It's taken as a daily tablet.

Side effects associated with raloxifene include:

- Hot flushes
- Leg cramps
- A potential increased risk of blood clots
- Parathyroid hormone
- Parathyroid hormone is produced naturally in the body. It regulates the amount of calcium in bone.
- Parathyroid hormone treatment are used to stimulate cells that create new bone. You take them as an injection once a day.

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- While other medicines can only slow down the rate of bone thinning, parathyroid hormone can increase bone density. However, it's only used in a small number of people whose bone density is very low and when other treatments are not working.
- Nausea, headaches and dizziness are common side effects of the treatment.

Biological medicines

Biological medicines are made from proteins or other substances produced by the body.

Biological medicines that can be used to treat osteoporosis include denosumab and roomsozumab. They may be recommended if you cannot take other medicines such as bisphosphonates, or if you have severe osteoporosis.

They work by slowing down the rate at which your bones are broken down and speeding up the rate at which your cells build bone. They're given by injection every month or every few months.

Common side effects include muscle or joint pain, rashes, constipation and cold-like symptoms.

Calcium and vitamin D supplements

Calcium is the main mineral found in bone, and having enough calcium as part of a healthy, balanced diet is important for maintaining health_bones.

For most healthy adults, the recommended amount of calcium is 700 milligrams (mg) of calcium a day, which most people should be able to get from a varied diet that contains good sources of calcium.

However, if you have osteoporosis, you may need more calcium, usually as supplements. Ask your GP for advice about taking calcium supplement.

Non-Pharmacological treatment for osteoporosis Lifestyle modifications

- Exercise
- No excess drinking
- Bone density test
- Calcium intake
- No smoking

Prognosis

The outlook for those with osteoporosis is generally a positive one⁴. Particularly if the condition is detected during the initial stages of the disease and treated effectively. Bone density, even if osteoporosis is severe, can generally be improved or stabilized.

Through detection and treatment, the risk of bone fractures is significantly reduced.

If one suffers from mild osteoporosis then a significantly positive outlook is expected if effective treatment commences and is adhered to. If a fracture occurs, bones will generally heal effectively and the pain associated with the fracture will typically resolve within a few weeks.

In some people with osteoporosis, the cause of the condition is not always known, this makes their prognosis difficult to determine. The outlook is often better if the cause can be correctly identified and treated.

People living with osteoporosis experience a reduced quality of life and lower life expectancy rates. The length of time a person can live with osteoporosis depends on their treatment and the age when they were diagnosed.²

What Is the Average Life Expectancy for People with Osteoporosis?

When looking at the average, research has shown that males who begin treatment before 60 and women who begin treatment before 75 can expect to live 15

The Importance of Early Detection

Because osteoporosis is progressive, detecting it early is vital. In addition, the treatments in place for the condition can both slow bone loss and help rebuild new bone, so if a person is diagnosed early and follows a treatment plan, they can better avoid disease complications, such as bone_fractures.

CONCLUSION:

Osteoporosis is a common entity that is occurring with increased frequency due to the aging of the production, and affects women more than man, though both sexes are at risk Osteoporosis is a worldwide concern, causing more than 8.9 million fractures per year. The expected increase in medical visits, hospitalizations, and nursing home placements related to osteoporotic fractures will contribute to a substantial economic burden on health care systems. Thus, screening is important based on age, gender, and other risk factors. Bisphosphonates remain the first-line and most costeffective treatment option for osteoporosis, but there is increasing concern about their long-term safety. Medications with novel mechanisms to treat osteoporosis can be expected in the near future. Al though appropriate BMD screening and treatment with medication is important, osteoporosis is preventable with proper management of diet, lifestyle, and fall prevention interventions.

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