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WORLD WIDE PREVALANCE OF OSTEOPOROSIS AND ITS MANAGEMENT - A REVIEW

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ABSTRACT

Osteoporosis is a progressive disorder of bone tissue characterized by insidious loss of bone mineral density and microarchitecture leading to impaired skeletal strength and increased susceptibility to fractures. Although it is seen in all age groups mostly in age greater than 50 years, female gender, asian, caucasian, black and hispanic races. However in ageing population, fractures are developed in a faster rate due to late recognition of disease process. The pathological change during osteoporosis is supported by the recent understandings of bone physiology that focuses on the mismatch communication between osteoblasts and osteoclasts. Dual X-Ray Absorpitometry is referred as a standard device for diagnosis of osteoporosis along with osteoporotic fractures. Moreover osteoporosis results in decreased quality of life and disability. Early diagnosis by assessing bone mineral density and providing effective treatment can prevent the osteoporosis. It is important to create the awareness among health care professionals as well as every individual in early recognition of symptoms will be effective in prevention of disease process.

KEYWORDS: Osteoporosis, Bone Mineral Density, Fractures, Osteonecrosis of Jaw and Vitamin D.

INTRODUCTION

Osteoporosis is a progressive disorder of skeletal system[1] characterized by gradual loss of bone mineral density and microarchitecture[2] that leads to impaired skeletal strength and

increases susceptibility of fragility fractures[3] resulting from no identifiable injury or from minimal trauma to fracture of normal bone.[4] It is a silent disease evident until the first fracture occurs.[5] About 20 crore population among worldwide were diagnosed with osteoporosis leading to morbidity and mortality. It is diagnosed by signs and symptoms such as back pain, height loss (> 4cm), kyphosis[6] and tests such as DXA.[7] Treatment pattern include Anti-resorptive therapy, Anabolic therapy and Investigational therapies.[8]

Osteoporosis is highly vulnerable in Post-menopausal women[9], men over age of 50 years[10], long term use of corticosteroids.[11] Late diagnosis may lead to severe non-traumatic fractures that may complicate to altered thoracic anatomy, altered abdominal anatomy, disability and depression.[6]

Epidemology

It is reported that a population of 20 crores in the world are suffering with osteoporosis as per International Osteoporosis Foundation (2015). In India it is 3.6 crore patients (2013)[11], 1 crore patients in U.S.A (2015)[14], 63 lakh patients in Germany (2015)[14], 30 lakh patients in U.K. (2001)[15], 15 lakh patients in Japan (2015)[14] and 140,822 in Australia (2012).[16]

Hip (per 1,00,000) fractures

North America: Fracture rate of United States of America was 195 (2010).[18]

South America: Fracture rate of Colombia has been reported to be 104 (2011).[18]

Europe: Fracture rate of various countries in this continent were 304 (2008-10) in Ireland and 216 in Lithuania (2010).[18] It includes male and female count as 352 and 763.6 (2010) in Norway, 302.7 and 709.5 in Sweden (2010) & 143.6 and 418.2 in England.[19]

Africa: 0.5 osteoporosis related fractures were reported in South Africa (2010)[20] and it is 43.7 in men and 52.1 in women in Cameroon (2010).[19] More scientific studies are required in this continent.

Asia: It is reported that the fracture rate in male and female were 87 and 97 in China (2010), 193 and 484.3 in Hong Kong (2010), 99.6 and 368 in Japan (2010), 216.6 and 316 in Kuwait (2010), 127.3 and 164.6 in Iran (2010) & 152 and 402 in Singapore (2010) respectively. In India it is 135 (2009).[19]

Australia: The fracture rate in male and female were 187.8 and 504.2 in Australia (2010) and it is 197 and 516 in New Zealand (2010).[19]

Vertebral (per 1,00,000) Fractures

It is reported that, vertebral fractures were 707 in males and 1083 in females in U.S.A. (2009-11).[21]

Risk Factors

The 3 types of risk factors that predispose the osteoporotic disorder and its fractures are (1) Non-modifiable risk factors, (2) Medical risk factors and (3) Drugs.

1. Non-modifiable risk factors: The risk of osteoporosis increases proportionally with the age due to the conditions such as secondary hyper parathyroidism, gonadal sex steroid deficiency, increased bone marrow fat (Neumann's law), physical inactivity, leptin resistance or deficiency, low serotonin levels and cathepsin deficiency.[22]

Increased risk of osteoporosis is seen in age group >50 years, asian and Caucasian (89%), blacks & Hispanics (4%) and other women (3%) (2007).[23] It is reported that osteoporosis and fragility fractures may have positive correlation with familial history.[5][24] The women falling under post-menopausal status are at high risk of getting osteoporotic disorder compared with premenopausal women.[25][26] Patients who had suffered from recent Hip fractures are at high risk of getting osteoporosis related fractures. Polymorphims of VDR gene may lead to the osteoporosis.[14]

2. Medical factors (Secondary Osteoporosis): These following are the disease conditions lead to the development of Osteoporosis. They are:

Gastro-Intestinal related diseases: Patients suffering from malabsorption syndrome, celiac disease, IBD[14], CLD[1][26] and persons who had undergone Gastrectomy are at high risk of developing osteoporosis.

Hematological related diseases: Thalassemia, Pernicious anemia[27], Leukemias, Lymphomas, Sickle Cell Anemia, Multiple myeloma, Hemophilia, Monoclonal gammopathies and Mastocytosis[6][30] may lead to osteoporosis.

Hypogonadal Status: Conditions such as amenorrhea[27], androgen deprivation are leading causes of osteoporosis.

Endocrine disorders: It is reported that the effect of Type 2 Diabetes mellitus is prevalent in osteoporosis related fractures, especially in spine (39.6%) and hip (20%).[28] Recent study reveals that patients with Type 2 Diabetes mellitus has low incidence of osteoporosis.[27]

A recent study had revealed that 4.5% patients with hyperthyroidism diagnosed with increased risk of osteoporosis related fractures, 3.7% of patients with hypothyroidism also diagnosed with increased risk of osteoporosis related fractures (in 2008-13). In the hypothyroid patients, the site of fracture is highest in the Femur (42.9%) followed by Humerous (15.2%), forearm (12.8%), lumbar spine (11.2%), Tibialpilon (10.4%), Dorsal spine (5.6%), Tarsals and metatarsals (1.5%) and lowest in Sacral spine (0.4%), similarly in hyperthyroid patients, the fracture site was highly proned in Femur (55.9%), Humerous (13.6%), Forearm (10.1%), Lumbar spine (9.5%), Tibial palm (5.3%), Dorsal spine (4.9%), Tarsals and metatarsals (0.5%) and lowest in sacral spine (0.2%).[29] Primary and secondary hyper parathyroidism also increases the risk of Osteoporosis.[1]

Pulmonary Diseases: Conditions such as COPD[26] and Chronic Lung Diseases[14] may prone to the osteoporotic risk.

Renal Disorders: Renal Insufficiency and End Stage Renal Disease may increase risk of osteoporosis.[6]

Skeletal disorders: Osteogenesis imperfecta[1], Rheumatoid arthritis[26] and Ankylosing Spondylitis[6] will lead to the osteoporosis.

Neuronal and Muscular disorders: Multiple sclerosis, Parkinsonian disorder, Spinal cord injury, Epilepsy, Stroke, Muscular dystrophy and proximal myopathy may lead to osteoporotic disorder.[6]

Immune system disorders: It is evident that organ transplantation may cause osteoporosis.[31]

Oncological Disorders: Multiple myeloma may cause osteoporosis.[14]

3. Drug-induced Osteoporosis

Anti convulsants: They cause osteoporosis by enhancement of Vitamin D metabolism.[33]

Cancer chemotherapeutic agents: GnRH antagonists cause osteoporosis by raising PTH levels leading to osteoclast activation.[33] In a recent study, the marked changes are observed within 6 months after the initiation of hormonal therapy in men with prostate cancer[34], mean while the biomarkers of osteoclasts and osteoblasts are released into the blood stream.[33] Cyclophosphamide induces negative feedback on gonadal tissues.[32]

Glucocorticoids: 5 mg of Prednisone OD PO for 3-6 months is sufficient to initiate osteoporosis.[11] They reduce the recruitment of osteoblast precursors leading to decrease osteoblast differentiation, function and apoptosis. The symptoms are evident before the BMD is reduced.[32]

Immuno suppressants: The mechanism involved is they cause inhibition of osteoclastogenesis and osteoblast inactivation.[32]

Anti-coagulants: Heparin induces osteoclast differentiation by inhibiting OPG and favouring RANK-L on osteoclasts, thereby causing increased bone resorption, osteoblast inhibition and decrease bone formation.[32] Warfarin also induces the osteoporosis by decreasing bone mineralization.[32]

Sex Hormones: Medroxy progesterone potentiates bone resorption by reducing plasma estrogen levels.[32]

Aromatase inhibitors: They reduce the plasma estrogen levels, there by leading to increased bone resorption.[32]

Estrogen Agonists/antagonists: Tamoxifen therapy is associated with significant loss of BMD in premenopausal women and prevention of bone loss in post-menopausal women.[35]

Total Parenteral Nutrition: TPN causes Vitamin-D deficiency and hypercalciuria. On long-term administration and hence osteoporosis is induced.[36]

Proton Pump Inhibitors: Pantoprazole suppresses the acid secretion decreases intestinal absorption of calcium, leading to bone resorption and osteoporosis.[32]

Thiazolidinediones: Rosiglitazone impairs the differentiation of osteoblast precursors by altering bone remodeling (increasing adiposity of bone marrow, decreasing aromatase

activity and promoting osteoclast differentiation) leading to increased bone resorption, thereby preventing bone formation leading to osteoporosis.[32]

Anti-depressants: Lithium induces osteoporosis by causing hyperparathyroidism.[37]

4. Miscellaneous factors

Vitamin D deficiency: Deficiency of Vitamin D leads to osteoporosis. It is mostly seen in women with age group of 60-70 years.[38]

Malnutrition: Deficiency of Inorganic minerals (e.g., calcium, magnesium, phosphorus, sodium, potassium, and various trace elements), vitamins (A, D, E, K, C, and some B complex vitamins), macronutrients (protein and fatty acids) may affect that bone health and that can lead to osteoporotic risk.[39]

Alcohol: Excessive alcohol consumption may lead to inhibition of osteoblastic function, reducing bone formation leading to osteoporosis.[40]

Calcium: Negative calcium balance such as dietary deficiency and hypercalcinuria may increases risk of osteoporosis.[40]

Smoking: It is reported in a recent study that increased risk of osteoporosis related fractures were seen in smoking population.[41]

Pathogenesis

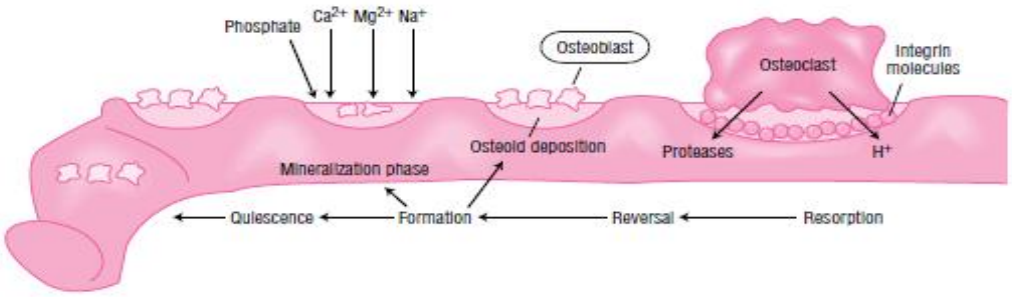

Figure 1: Steps in bone remodeling: resorption, reversal, formation, and quiescence.[8]

The Mechanisms involved in the pathogenesis of osteoporosis are:

- Failure to produce a skeleton of optimal mass and strength during growth.
- Excessive bone resorption resulting in decreased bone mass and microarchitectural detoriation of skeleton.

- Inadequate bone formation in response to increased resorption during bone remodeling.[43]

Hormonal changes during ageing: These changes were responsible for the bone loss, particular due to decrease in sex steroid and relative increase in cortisol may influence bone remodeling negatively. The decreased sex-steroid concentration with age is proportional to bone density and increased fracture risk in men. Lower biovailable estradiol more than lower free testosterone appears to be cause of bone loss in old men.[30]

Central role of Estrogen: The concept of estrogen deficiency leads to pathogenesis was based on fact that post-menopausal women (whose estrogen levels decline) are proned to highest risk of suffering from osteoporosis.

Morphologic studies and measurements of certain biochemical markers were indicated that bone remodeling is accelerated. In menopause both the markers of resorption and formation has increased. Albright hypothesis explains that increased bone resorption but not impaired bone formation appears to be driving force for bone loss in setting of estrogen deficiency. However increased bone formation occurs normally in response to mechanical loading which is diminished in estrogen deficiency, suggesting that estrogen is both anti-catabolic and anabolic. Moreover, recent studies in humans had shown that level of estrogen required in maintaining normal bone remodeling in older post-menopausal women are lower than that required to stimulate classic target tissues such as wrist and uterus. Estrogen acts through 2 receptors named as ER-α and ER-β. ER-α is a primary mediator of estrogen actions on the skeleton. Osteoblasts donot express ER-β but the actions of ER-β on bone are less clear. Single Nucleotide polymorphism of ER-α may affect bone fragility. Other studies have suggested that SNPs of ER-α can affect BMD, rates of bone turnover and fracture risk in both men and women. SHBP affects entry of estrogen into cells.[30]

Role of Calcium or Vitamin-D or PTH: Low calcium intake, decreased calcium absorption or Vitamin-D deficiency leads to secondary hyperparathyroidism.

VDR Polymorphisms results in varied effect produced by the Calcitriol therapy. Calcium sensing receptor polymorphism regulates Calcium secretion by suppression of PTH translation and secretion.[43]

Receptor activation of NFKB, its ligand and OPG: Osteoblasts produce RANKL ligand that interact with the RANK receptor of hemopoietic cells which in turn causes the activation of NFKB leading differentiation of Osteoclasts. OPG inhibits the interaction of RANKL-RANK system. Polymorphisms in OPG causes Osteoporosis related fractures and alterations of BMD.[43]

Local and systemic Growth factors: Specific defects in production or activity of local and systemic growth factors contribute to impaired bone formation.

- Cytokines, Prostaglandins, NO and Leukotrienes: PGE_2 is reported to raise BMD and reduce fracture risk. NO plays an important role in inhibition of bone resorption and production of OPG. Leukotrienes potentiates the bone resorption and inhibits the bone formation.
- Collagen abnormalities: Polymorphism of first intron of gene encoding Type-I collagen α1 chain is reported to raise homocysteine levels and increase fracture risk (independent of BMD).
- Leptin and Neural Pathways: Leptin deficiency or resistance is reported to increase BMD.[43]

Clinical Presentation

General: Many patients are unaware of osteoporosis and only present after fracture. Fractures can occur after performing physical activity.[8]

Signs and symptoms: Common sites of fractures include vertebrae (spine), proximal femur (hip), distal forearm (wrist) and shoulder.

Hip fracture: Decreased quality of life, social isolation, depression and loss of self-esteem due to long term nursing home care and are associated with 15-20% increased mortality rate within 1 year.[6]

Vertebral fracture: Acute or chronic back pain, kyphosis, height loss (> 3cm).[26] Vertebral thoracic fractures further provoke restrictive lung disease and cardiac abnormalities.[6]

In lumbar fractures, decreased volume between the ribs to the pelvis, alter abdominal anatomy are seen which may complicate to gastrointestinal problems such as premature satiety, reduced appetite, abdominal pain, constipation.[6]

Others fractures include distal radius (wrist), arm (humerous), pelvis, ribs.[6] Other physical findings, such nodular thyroid, hepatic enlargement jaundice or cushingoid features, may reveal secondary causes of osteoporosis.[27]

Investigations of Osteoporosis

- Routine tests to detect secondary osteoporosis include, complete blood count, ESR or C-reactive protein.[26] Serum and urine markers of bone turnover, serum PTH, Vitamin D deficiency, 24 hour urinary calcium examination also aid in final diagnosis.[25]
- Evaluating TSH, free T_4 levels, 24 hour urinary free cortisol or fasting serum cortisol levels can exclude secondary causes.[26] Serum testosterone, SHBG, FSH, LH. Serum prolactin levels to rule out hormonal causes of osteoporosis.[26]

Other diagnostic tests

- Spine and hip BMD measurement using DXA.[27]
- Bone marrow examination.[25]

Measurement of BMD

International Society for Clinical Densitometry has developed official positions for diagnosis of osteoporosis by using DXA. These positions are lumbar spine, hip, and forearm.[45]

Measurement of BMD using DXA can estimate the fracture risk and responsiveness towards treatment.[7]

DXA scans are used to calculate T score and Z score.[7]

$$\text{T score} = \frac{\text{Measured BMD} - \text{Young adult BMD}}{\text{Young adult population SD}}$$

$$\text{Z score} = \frac{\text{Measured BMD} - \text{Age matched mean BMD}}{\text{Age matched population SD}}$$

Normal ranges for BMD measurement includes T score: $\geq$ -1.0; Osteopenia: 2.5 < T < -1.0; Osteoporosis: T $\leq$ -2.5; established osteoporosis: T $\leq$ - 2.5 in the presence of one or more fractures.[7]

Assessment of Fracture Risk by Using the Fracture Risk Assessment Tool (FRAX)

In the United States, the National Osteoporosis Foundation recommends using FRAX to calculate fracture risk for patients who have T-scores between 2.10 and 2.25 in the spine,

femoral neck, or total hip region. FRAX tool is available at web page http://www.shef.ac.uk/FRAX.[46]

Pharmacotherapy

Goals of treatment

- The primary goal of osteoporosis management should be prevention.
- Optimizing skeletal development and peak bone mass to reduce the future incidence of osteoporosis.
- In patients who have already suffered osteoporotic fractures, reduce future falls and improve quality of life.[8]

I. Antiresorptive agents

Serm

Raloxifen: It acts as partial agonist on bone skeleton by reducing the rate of bone loss in postmenopausal women.[47] Mostly indicated for spinal osteoporosis in postmenopausal women[49] at a dose of 60 mg PO OD.[49] Deep vein thrombosis, hot flashes[1], fatal stroke[50] are the adverse effects.

Monitoring Parameters: Breast examination and Mammograms.[51]

Biphosphonates: Oral bisphosphonates include Alendronate and Risendronate. Intravenous bisphosphonates include Ibandronate and Zolendronic acid.[47]

They act by inhibiting bone resorption and produce their effect by reducing the recruitment and activity of osteoclasts and increase their apoptosis[47], indicated for postmenopausal osteoporosis osteoporosis and in men[49], a Alendronate-5 mg PO OD or 35 mg PO weekly, Risedronate- 5 mg PO OD or 35 mg weekly PO or 150 mg PO monthly, Ibandronate- 3 mg IV every 3 months and Zoledronic acid- 5 mg IV once yearly are indicated.[50] GI - disturbances, atypical femoral fractures, oesophagitis[26], ONJ is of the major adverse effects of bisphosphonates.[47] They interact with PTH causing reduced calcium sparing effect.[52]

Monitoring parameters: Reassessment of fracture risk using FRAX index and biochemical markers.[51]

Calcium

Table 1: Recommended dietary allowance for Calcium.[49]

Age	Sex	Recommended dietary allowance (mg / day)
0-6 months	M, F	200
6-12 months	M, F	260
1-3 years	M, F	700
4-8 years	M, F	1000
9-18 years	M, F	1300
19-50 years	M, F	1000
51-70 years	M	1000
51-70 years	F	1200
≥ 71 years	M, F	1200

Calcium acts by increasing intracellular calcium which enhances downstream signaling pathways for Runx2 through the Ras—MAPK pathway. Upon activation of Runx2 controls many osteogenic genes through this multicomponent complex, resulting in bone mineralization.[53] Increased cardiovascular risks at low doses[26] and Renal calculi[50] are the common side effects. It interacts with Fluroquinolones, tetracyclines, diuretics.[54]

Monitoring parameters: Monitor serum calcium levels.[55]

Vitamin D: It is indicated for postmenopausal osteoporosis. Increased risk of hypercalcemia and hypercalciuria are the common adverse effects.[47]

Table 2: Recommended dietary allowance for Vitamin D.[54]

Age (years)	Vitamin D (IU / day)
4–8	200
9–13	200
14-18	200
19-30	200
31-50	200
51-70	400
>70	600

Hormonal replacement therapy

Estrogen: It acts by inhibiting bone resorption and inducing osteoclasts apoptosis resulting in reduction of bone resorbing cells.[9] It is indicated for postmenopausal osteoporosis.[9] Conjugated equine estrogen 10 mg OD and Medroxy progesterone 200 mg OD are available.[9]

Venous thromboembolism, coronary event, stroke and breast cancer are major adverse effects.[9]

Testosterone: It acts as a protective agent of bone resulting inactivating proosteoblasts.[57] Transdermal patch should be 5 mg applied to arm, back or thigh every evening and gel 5 mg gel is applied to shoulder, upper arm, or abdomen every morning, Cypionate 200-300 mg administered through IM every 2-3 weeks or methyl testosterone- 1.25 - 2.5 mg with esterified estrogen is indicated.[8]

Monitoring parameters: Evaluation of BMD for 1-2 months of initiation and then 3-6 months thereafter.[8]

Calcitonin: It acts by inhibiting osteoclastic bone resorption and resulting in apoptosis of osteoclastic cells.[50] It is approved by the USFDA for treatment of postmenopausal osteoporosis.[49] 200 IU should be administered intra-nasally OD.[8] Adverse effects include increased risk of liver cancer.[57]

II. Anabolic Therapies

Teriparatide: It is a recombinant N-terminal PTH, acts by increasing bone formation.[8] It is approved for postmenopausal osteoporosis, glucocorticoid induced osteoporosis.[49] Prefilled pen delivery device is used to administer 20µg Teriparatide SC OD.[8] Transient hypercalcemia is the major adverse effect noted.[50]

III. Investigational therapies

RANKL Inhibitor

Denosumab: It binds to RANKL present on osteoblast cell resulting in inhibition of osteoclast and osteoblast interactions.[58] It is approved by the USFDA for treatment of postmenopausal women at high risk of fracture.[49] 60 mg SC q6m is administered OD.[58] ONJ is the major adverse effect.[58]

Cathepsin K inhibitors

Odanacatib: It inhibits the cathepsin K, which is a key lysosomal enzyme of activated mature osteoclasts resulting in inhibiting of osteoclastic function. During the phase 1 clinical trial of odanacatib the doses administered are 50 mg and 100 mg. Headache, influenza like symptoms, odynophagia, eating disorders are the common adverse effects reported.[58]

Src kinase inhibitors

Saracatinib: It inhibits the Src kinase and the ABL kinase implied in the cell proliferation, differentiation and response to oxidative stress resulting in osteoclastic bone resorption. It is administered at a dose of 250 mg OD. Papular eruption is the major side-effect.[58]

Antagonists of the WNT signaling

(a) Inhibitors of dickkopf (DKK) 1: The LRP5 can form a complex with DKK 1 resulting in activation and depletion of LRP5 leading to inhibition of WNT signaling pathway. The inhibition of DKK1 prevents formation of osteoclastic lesions.[58]

(b) Anti-sclerostin monoclonal antibodies: (e.g., Romosozumab, Blosozumab)

Mechanism of action: sclerostin is a product of the SOST gene that inhibits osteoblastogenesis. Anti-sclerostin monoclonal antibodies acts by improving WNT signaling resulting in increased bone mass.[58]

8. Guidelines

Table 3: Drugs approved by the USFDA for prevention and treatment of Osteoporosis.[49]

Drug	Post-menopausal Osteoporosis		Gluco-corticoid induced osteoporosis		Male Osteoporosis
	Prevention	Management	Prevention	Management	
Estrogen (multiple formulations)	Multiple regimens	-	-	-	-
Calcitonin	-	200 IU intranasally once daily / 100 IU qod SC	-	-	-
Denosumab	-	60 mg SC every 6 months	-	-	-
Raloxifene	60 mg PO OD	60 mg PO OD	-	-	-
Ibandronate	2.5mg PO OD / 150 mg PO monthly	2.5 mg PO OD / 150 mg PO monthly / 3 mg IV every 3 months	-	-	-
Alendronate	5 mg PO OD / 35 mg PO weekly	10 mg PO OD / 70 mg PO weekly / 70 mg + Vit. D	-	5 mg PO OD / 10 mg PO OD	10 mg PO OD / 70 mg PO weekly
Risedronate	5 mg PO OD / 35 mg PO weekly / 150 mg PO monthly	5 mg PO OD / 35 mg PO weekly / 150 mg PO monthly	5 mg PO OD	5 mg PO OD	35 mg PO weekly / 150 mg PO once monthly
Zoledronic acid	5 mg IV every 2nd year	5 mg IV once yearly	5 mg IV once yearly	5 mg IV once yearly	5 mg IV once yearly
Teriparatide	-	20µg SC OD	-	20µg SC OD	20µg SC OD

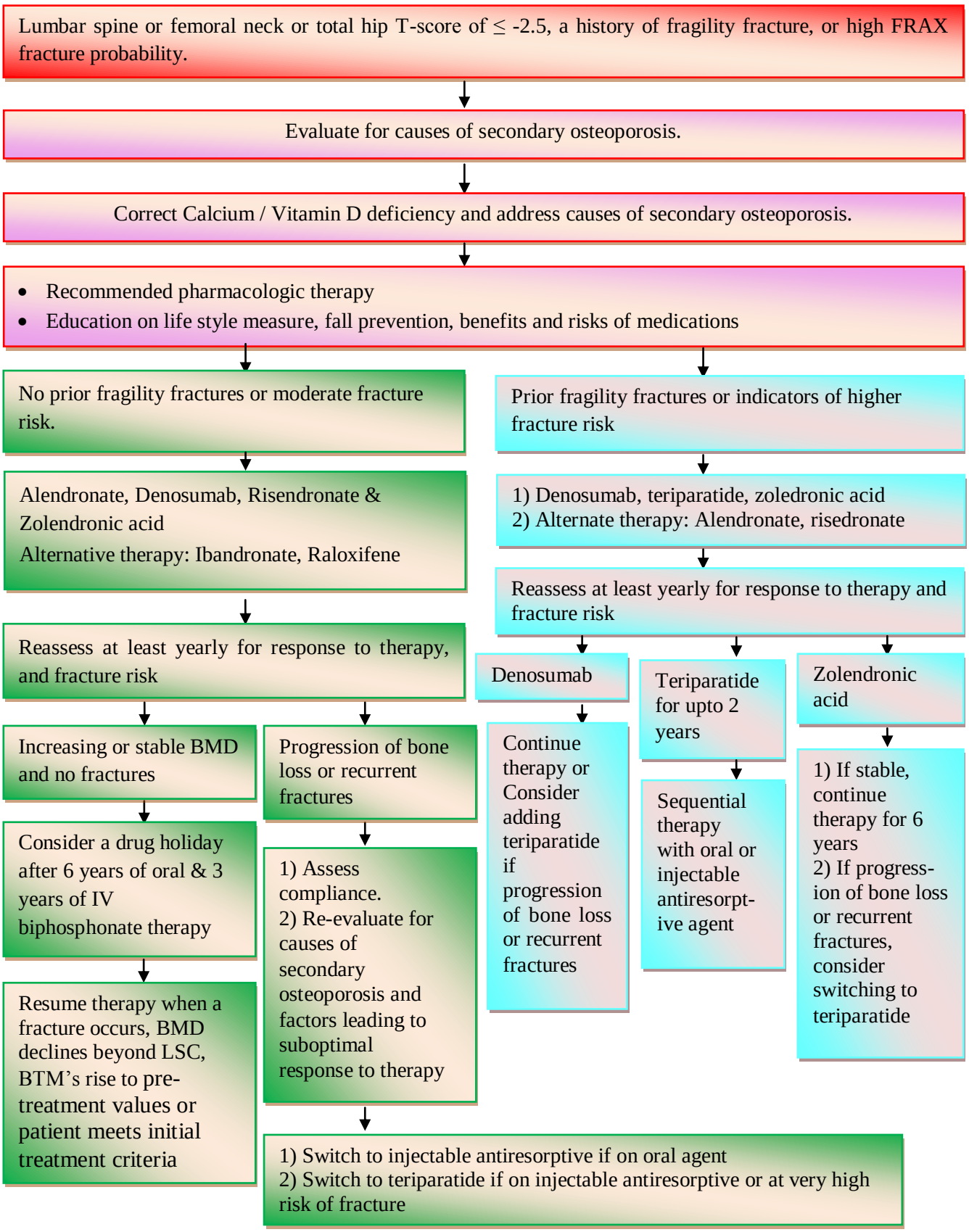

Figure 2: A systematic algorithm for the management of Osteoporosis.[59]

Patient Counselling

Patients with osteoporosis may require adequate physical therapy and other non-pharmacological measures to improve bone strength and reduce fracture risk. In addition to maintain adequate amounts of calcium and Vitamin D, a balanced diet throughout life is important for bone health.[49]

Calcium: Adequate calcium intake is an important aspect of any osteoporosis prevention or treatment program for a healthy life style issue. For women aged 50 and above daily recommended calcium intake is 1200 mg.[49]

Vitamin D: It is important to maintain sufficient levels of vitamin D among children and adults to prevent osteoporosis. It is primarily found in fish oils (cod liver oil), fortified milk, cereals, and breads. It is produced in the skin by exposure to sunlight during dawn. National academy of sciences recommends daily intake of vitamin D 400 IU / day in normal adults aged 50 to 70 years whose age more than 70 are recommended to take 600 IU / day.[49]

Essential fatty acids: Essential fatty acids are unsaturated fatty acid and saturated fatty acid. A food survey had found that unsaturated fatty acid protect BMD mean while saturated fatty acids accelerates bone loss.[60]

Vitamin K: It is essential nutrient for healthy bone mineralization involved in maintenance of adequate bone integrity, primarily found in probiotics and fermented soyas.[4]

Studies reporting a correlation between the protein intake and bone metabolism had showed that the excess of a protein deficiency causes calcium homeostasis resulting in calcium imbalance. An increase in protein intake increases the acid load to be removed by the kidney which results in urinary calcium loss.[60]

Caffeine: Patients should be advised to limit their caffeine intake to less than 1 to 2 servings (8 to 12 ounces in each serving) of caffeinated drinks per day.[49]

Lifestyle Modifications

Strategies for prevention of falls: Falls are the major causes of osteoporotic fractures; therefore, a program needs to be structured for the effective treatment of osteoporosis in order to prevent falls.[6]

- Patients with severe osteoporosis should avoid engaging in motions such as forward flexion exercises, using heavy weights, or even performing side-bending exercises because pushing, pulling, lifting, and bending exert compressive forces on the spine that may lead to fracture.[49]
- Correction of visual field may reduce risk of falling resulting in reduction of fractures.[49]
- Correction of other disease states such as postural hypotension and arrhythmias may reduce the risk of fall.[6]
- Placing hip protectors do not reduce the risk of falling. Intuitively, hip protectors should reduce the risk of fracture.[49]
- Modification of home environment may help to reduce the risk of falling by placing non slippery door mates, removing wires, using anchor rugs and minimizing clutter.[49]

Smoking: Cigarette smoking is a risk factor that has been validated by multiple studies to increase osteoporotic fracture risk and thus should be avoided.[49]

Alcohol: Excessive intake of alcohol should be avoided because studies have proved that alcohol consumption may prone to accidental falls, calcium deficiency, and CLD which in turn predisposes to vitamin D deficiency.[49]

CONCLUSION

Osteoporosis is one of the leading skeletal disorder resulting in fragility fractures. It is mostly diagnosed after the first fracture. Treatment regimens may improve BMD but not the post fracture status, the population of osteoporosis vulnerable mostly are postmenopausal women, men aged >50, long term use of glucocorticoids, recent hip fractures of other causes. It is important to maintain healthy lifestyle for better BMD status, strategies for prevention of falls to minimize the fractures. Regular follow up of BMD measurement shall decrease the risk of osteoporotic fractures. In addition, issues related to the disorder, its management related adverse drug effects and dietary consumption should be focused. Regular Calcium intake, Vitamin D intake and exercises benefit the risk group. Clinical Pharmacist can play an important role in consulting and educating patients about the investigations, for osteoporosis, treatments, related benefits and harms.

Acronyms

ABL kinase: Abelson Murine Leukemia kinase

BMD: Bone Mineral Density

BTM: Bone Turnover Marker

CLD: Chronic Liver Disease

COPD: Chronic Obstructive Pulmonary Diseases

DKK: Dickkopf

DXA: Dual X-ray Absorptiometry

ER: Estrogen Receptor

FRAX: Fracture Risk Assessment Tool

GnRH: Gonadotrophin Releasing Hormone

IBD: Inflammatory Bowel Disease

LRP-5: Low density Lipoprotien Receptor Protein-5

LSC: Least significant change

MOA: Mechanism of Action

NO: Nitric Oxide

OD: Once Daily

ONJ: Osteonecrosis of Jaw

OPG: Osteoprotogerin

PGE_2: Prostaglandin E_2

PO: Per Oral

PTH: Para thyroid Hormone

RANK: Receptor Activated Nuclear Factor Kappa Beta

RANK-L: Receptor Activated Nuclear Factor Kappa Beta Ligand

RunX2: Runt related Transcription Factor-2

SC: Subcutaneous

SERM: Serum Estrogen Receptor Modulator

SHBP: Sex Hormone Binding Protein

SNP: Single Nucleotide Protein

Src Kinase: Serine Kinase

SOST: Sclerostin

TPN: Total Parenteral Nutrition

USFDA: United States Food and Drug Administration

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