Osteoporosis

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*Patel N. Osteoporosis In Wagh S. (Ed). Rheumatology in Primary Care 1st Edition KYA Foundation 2012; pp 81-90*

Osteoporosis or fragile bones is usually a silent disease until it results in a low trauma or spontaneous fracture. Primary osteoporosis is usually an age related problem due to bone loss in post-menopausal women and elderly men. Secondary osteoporosis is less common.

Osteoporosis is a major public health problem due to higher incidence of fragility fractures and subsequent morbidity. An estimated 1.3 million osteoporotic fractures occur in India every year. This number is likely to increase with an increase in the elderly population. Though osteoporosis affects the entire skeleton, almost half of these fractures are vertebral fractures; hip and Colles' fractures are also common. Hip fractures are responsible for maximum morbidity and increased mortality. The incidence of fragility fractures increases sharply in women after menopause and in men over 60 years of age. These fractures occur as a result of minimal trauma or spontaneously (as in vertebral and occasionally hip fractures). In fact, any fracture in older adults may represent osteoporosis. Loss of independence and lower quality of life are most commonly seen in hip and vertebral fractures. The increase in health care cost is also significant.

Osteoporosis is defined as a skeletal disease characterized by low bone mass and deterioration of bone micro-architecture with subsequent increase in bone fragility and susceptibility to fractures. Bone turnover implies constant remodeling with formation of a 'pit' (resorption) by osteoclasts and subsequent 'filling of the pit' by osteoblasts. Decreased bone mass and micro architectural deterioration are due to increased bone resorption without proportionate increase in bone formation. Loss of both trabecular and cortical bone is seen in these patients. World Health Organization (WHO) definition of osteoporosis is based on measurement of bone mass (Bone Mineral Density - BMD) which is compared with the peak bone mass of a young adult of same race and sex. T score is calculated as the difference between BMD of the patient and reference normal BMD expressed in terms of standard deviation. T score up to -1.0 is considered normal, between -1.0 and -2.5 as osteopenia and less than -2.5 as osteoporosis. WHO Classification of osteoporosis is based on studies in white postmenopausal women and may not be applicable in India. This classification is not applicable to premenopausal females, non-white postmenopausal females and men.
Causative and risk factors

Approximately 95% of post-menopausal women and a majority of older men have primary osteoporosis. Estrogen deficiency plays a major role in primary osteoporosis. There is a threefold increase in the rate of bone loss in postmenopausal women due to increased osteoclast activity (high turnover). Thus, an early menopause is a prominent promoter of osteoporosis. This results in an exponential increase in low trauma fractures. Advanced age is another important risk factor for the development of osteoporosis (senile osteoporosis). Senile osteoporosis is due to decreased osteoblast activity (low turnover). Additional risk factors for osteoporosis include - Caucasian race, age more than 50, family history of osteoporosis, nulliparity, alcoholism, tobacco use and low physical activity. Low calcium intake and vitamin D deficiency are contributing factors.

Secondary osteoporosis is due to various causes including drugs (glucocorticoids, psychotropic drugs, anticonvulsants, heparin and oral anticoagulants, proton pump inhibitors and anti-retroviral drugs), endocrinopathies (hyperparathyroidism, hyperthyroidism, hypogonadism and diabetes mellitus), immobilization, liver cirrhosis, malabsorption syndromes, chronic inflammatory disorders (rheumatoid arthritis, ankylosing spondylitis, Crohn's disease) and malignancies. Glucocorticoids, with their extensive use, contribute to a very important and large group of patients with secondary osteoporosis.

Osteoporosis is common in elderly men. Reference BMD data for women are presently applied to men too. Osteoporosis in men is often secondary; most common underlying conditions being hypogonadism, alcoholism, use of glucocorticoids and hormone deprivation therapy used in carcinoma of prostate.

Features

Osteoporotic fractures can be painless (vertebral fractures). A third of patients with vertebral fractures remain undiagnosed due to this reason. It is not uncommon to find osteoporotic vertebral fractures in X-rays of spine done for other reasons. Multiple osteoporotic fractures can result in loss of height or dowager's hump. Vertebral fractures can cause back pain and impair breathing. These fractures usually occur during routine daily activities or as a result of minor trauma. Hip fractures most commonly occur after a small fall or on missing a step while walking or due to tripping. Colles' fracture usually occurs after a fall on the outstretched hand and is often the first indicator of osteoporosis. Hip fractures lead to significant increase in morbidity and mortality.
Diagnosis

Osteoporosis can be clinically suspected with some certainty in a patient with low trauma fracture(s) or those who have radiographic evidence of fracture. A good history and systemic examination is needed to screen for secondary osteoporosis. Laboratory tests such as haemogram, ESR, hepatic and renal function tests should be done in all cases. Other tests can be ordered depending on clinical suspicion of a secondary cause for osteoporosis. Bone markers have recently been used to monitor efficacy of treatment of osteoporosis. These show a change earlier than that seen in BMD. Use of bone markers is not practical and is not advocated in routine clinical practice.

Clinical diagnosis of asymptomatic early osteoporosis can be confirmed by measuring BMD. Bone density is measured for the diagnosis of osteoporosis, prediction of fracture risk and to monitor response to therapy. Conventional X-ray is not suitable for measurement of BMD as it is observer dependant and shows abnormality only after loss of 30-50% of bone mineral. Ultrasound technique is gaining popularity due to low cost, portability and lack of radiation. Ultrasound measurements are usually limited to peripheral bones (calcaneum). It is a good screening test for osteoporosis but needs confirmation by DXA at present. Quantitative computed tomography (QCT) measures true bone density. Its use is limited due to its cost, higher radiation dose and lower reproducibility than DXA.

WHO has derived FRAX questionnaire (www.shef.ac.uk/FRAX) to determine 10-year probability of fracture in post-menopausal women or men over 50 years of age. FRAX tool uses following factors for calculation of 10-year fracture risk: Femoral neck T-score, age, sex, low BMI, previous low trauma fracture, glucocorticoid use, family history of hip fracture, rheumatoid arthritis, secondary osteoporosis, current cigarette smoking, high alcohol intake (> 2 units/day).

Bone mineral density

BMD is the gold standard to diagnose osteoporosis today. BMD is measured using DXA (Dual energy X-ray absorptionometry) method. DXA scan is a non-invasive test with negligible radiation exposure. Standard DXA measurements are done at the lumbar spine and left hip in the antero-posterior views. Costly infrastructure is the limiting factor for this test being freely available in our country. The drawback of this investigation, in addition to cost, is that it measures apparent bone density and does not indicate bone quality. DXA results are not reliable in the presence of conditions such as osteomalacia, osteoarthritis (osteophytes), previous fractures and vascular calcification (senile).
Indications for BMD determination are as under:

1. Women aged 65 years and older
2. Postmenopausal women under age 65 years with risk factors for fracture (rheumatoid arthritis, long term glucocorticoids and other drugs, low body mass index, previous fracture, family history of fragility fracture)
3. Men aged 70 years and older
4. Men under age 70 years with clinical risk factors for fracture (e.g. hypogonadism)
5. All adults with a fragility fracture*

* Fragility or low trauma fracture is one that occurs after a fall from height equal to that of the individual.

Management

Prevention of osteoporosis starts in childhood. A higher peak bone mass developed at 25-30 years of age has lesser possibility of developing osteoporosis following age-related bone loss. Balanced nutritious diet with adequate calcium and vitamin D as well as adequate exercise (preferably impact sports) should be advised to all children and young adults for development of high peak bone mass.

General lifestyle measures should be emphasized to all patients likely to develop osteoporosis. Regular exercise, good general nutrition as well as avoiding tobacco and excess alcohol should be advised. Lower intake of sodium is advisable as higher dietary sodium increases urinary calcium excretion. Identification and treatment of cause of secondary osteoporosis, especially drugs, is necessary in all cases.

Adequate calcium intake is essential. There appears to be no difference in various calcium preparations available in market. Calcium carbonate (400 mg elemental calcium per gram) is the cheapest one and should be used in most cases. The recommended daily intake for different age groups (NIH consensus conference) is as follows:

<table>
<thead>
<tr>
<th>Age</th>
<th>Elemental Calcium intake per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children</td>
<td>1200-1500 mg</td>
</tr>
<tr>
<td>Adolescents</td>
<td>800-1200 mg</td>
</tr>
<tr>
<td>Adults</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Older adults</td>
<td>1000-1500 mg</td>
</tr>
</tbody>
</table>

In patients with Vitamin D deficiency, replacement with vitamin D 60,000 IU once a week is advisable for eight weeks. Daily supplement of 1000 IU is advised thereafter.
Prevention of fall in people at risk is an important aspect of osteoporosis management. Wearing well fitting shoes, reducing clutter on floor, installing grab rails in bathroom and toilet, ensuring adequate light in passage areas and correcting problems of vision are some of the important measures. Dizziness, vertigo, syncope and drop attacks are common in elderly. These should be appropriately investigated and treated. Alcohol and certain drugs (diuretics, antihypertensive agents, anxiolytics, antidepressants, hypoglycemic agents etc) can also increase incidence of falls in the elderly.

Drugs

The recommendations for the use of approved drugs for the treatment of osteoporosis for post-menopausal women and men over 50 years of age are:

1. A hip or vertebral fracture
2. T-score less than or equal to -2.5 at the hip or lumbar spine
3. Patients with high 10 year probability of fragility fracture (FRAX)
4. Patients with medical conditions that increase risk of osteoporosis (e.g. rheumatoid arthritis)

Various drugs such as bisphosphonates, teriparatide, calcitonin and others are available for the treatment of osteoporosis. Bisphosphonate drugs act by decreasing bone resorption and have been shown to decrease fracture risk. Oral bisphosphonates include alendronate (70 mg once a week), risedronate (35 mg once a week) and ibandronate (150 mg once a month). Ibandronate (3 mg every 3 months) and zolendronic acid (5 mg once a year) are available for intravenous use.

Oral bisphosphonates are poorly absorbed. It is recommended to take these drugs on an empty stomach with a glass of water. Patients are advised not to take anything orally and to remain upright for 45-60 minutes after taking this drug.

The adverse reactions to this group of drugs are nausea, oesophagitis, arthralgias, myalgias, hypocalcaemia and osteonecrosis of the jaw (ONJ). ONJ is a rare but dreaded complication of high dose bisphosphonate therapy. All patients on bisphosphonates must maintain good dental hygiene and inform dentist about drug usage prior to any dental procedure. Bisphosphonates are to be avoided in women of childbearing age and during pregnancy. Vitamin D deficiency should be corrected before starting bisphosphonate therapy. Adequate calcium intake is essential.
Teriparatide is a parathyroid hormone analogue and the only anabolic agent approved by FDA for the treatment of osteoporosis. It has been shown to decrease incidence of vertebral as well as nonvertebral fractures. The drug is administered subcutaneously daily for a maximum period of 24 months. It is relatively contraindicated in patients who have had skeletal irradiation, Paget's disease, history of bone cancers, patients with hypercalcemia and pregnant or nursing women. Cost of the drug is a limiting factor to its use. Teriparatide is probably more effective than bisphosphonates, although bisphosphonates remain the first choice in the treatment of osteoporosis.

Calcitonin has been shown to reduce pain of acute vertebral compression fractures. It reduces incidents of vertebral fractures but not that of non-vertebral fractures. It is available as a nasal spray in India but it is less potent drug than the ones mentioned above and is not used to treat osteoporosis.

Hormone replacement therapy may decrease the rates of hip and vertebral fractures by 25-50%. The risk of breast and uterine cancers, stroke, heart disease and thromboembolism is high. This risk outweighs the benefit of using these drugs as first line treatment for osteoporosis. These drugs are very effective in controlling menopausal symptoms. Raloxifene, a selective estrogen receptor modulator, has been approved by the FDA for the treatment of osteoporosis. This drug reduces the risk of vertebral fractures but not that of non-vertebral fractures. The risk of thromboembolic disease remains the same as HRT and it does not control menopausal symptoms.

Denosumab, lasofoxifene, basodoxifene and odanacatib are some of the newer drugs which may become available in future.

Osteomalacia

Osteomalacia (soft bones) is characterized by defective mineralization of mature bone and cartilage leading to an accumulation of unmineralized bone matrix. It results from inadequate calcium or phosphorus due to vitamin D deficiency or abnormal vitamin D metabolism.

The main symptoms are generalized bone pain, weakness of proximal muscles and difficulty in walking. Patients have a waddling gait with difficulty in climbing stairs and getting out of bed. The pathognomonic radiologic feature of osteomalacia is pseudo fracture (also called Looser's zones).

Osteomalacia is treated with high dose vitamin D (calcitriol in cases of renal impairment) along with calcium supplementation.