Treatment of Osteoporosis

Dr Mirfeizi
THE TIP OF THE ICEBERG

ASSESSMENT

MANAGEMENT
The main goal of osteoporosis treatment is fracture prevention.
Goals of Therapy

- Prevent first fragility fracture or future fractures if one has already occurred
- Stabilize/increase bone mass
- Relieve symptoms of fractures and/or skeletal deformities
- Improve mobility and functional status
- Initiate lifestyle changes to enhance prevention of fractures
  - Smoking
  - Alcohol
Pharmacotherapy

In each patient the clinician should assess:

- benefits of therapy
- risks of therapy
- effectiveness of osteoporosis treatment on reduction of vertebral & nonvertebral fractures.
Pyramid for Osteoporosis Prevention and Treatment

Pharmacotherapy (antiresorptives and anabolics)

Address Secondary Factors (drugs and diseases)

Lifestyle Changes (nutrition, physical activity, and fall prevention)

Leading the Effort to Help Prevent and Treat Osteoporosis

What does this mean for your patients?

UNIVERSAL RECOMMENDATIONS FOR ALL PATIENTS

- An adequate intake of calcium and vitamin D.
- Lifelong participation in regular weight-bearing and muscle-strengthening exercise.
- Cessation of tobacco use.
- Identification and treatment of alcoholism.
- Treatment of other risk factors for fracture such as impaired vision.
Management of Osteoporosis

Treatment / Secondary Prevention

Lifestyle
- Diet
- Exercise
- Smoking
- Alcohol Intake
- Sunlight Exposure

Pharmacological
- Drugs altering BMD
- Analgesia

Non-pharmacological
- Physiotherapy
- Pain Relief
- Hip Protectors

Prevention / Primary Prevention

Lifestyle
- Diet
- Exercise
- Smoking
- Alcohol Intake
- Sunlight Exposure

Pharmacological
- Drugs altering BMD

Non-pharmacological
- Physiotherapy

Prevention of Falls
Lifestyle Advice

Diet
- Balanced diet containing adequate calcium
  - 1000 mg/day

Exercise
- Regular weight-bearing exercise
  - 3 times a week for 20 minutes minimum

Smoking
- Stop smoking

Alcohol
- Avoid alcohol

Sunlight Exposure
- 15-20 minutes on face, hands, and forearms twice weekly from April to October
Adequate Intake of Calcium & Vitamin D

- The NOF:
  - Women age 51 & older:
    - 1,200 mg per day of calcium.
  - Men age 50-70:
    - 1,000 mg per day of calcium
  - Men age 71 and older:
    - 1,200 mg per day of calcium.
Intake of Calcium

- excess of 1,200 to 1,500 mg per day:
  - have limited potential for benefit and
  - may increase the risk of developing
    - kidney stones
    - cardiovascular disease
    - stroke
Adequate Intake of Calcium and Vitamin D

- combination of supplemental calcium and vitamin D can reduce the risk of fracture

- Increasing dietary calcium is the first-line approach, but calcium supplements should be used when an adequate dietary intake cannot be achieved

- A balanced diet rich in low-fat dairy products, fruits and vegetables provide calcium
Who need calcium pill supplementation

- Patient treated for osteoporosis
- Patient treated with glucocorticoids
- Individuals with low calcium intake
Calcium

- Carbonate with meals & need acid for absorption

- Calcium citrate don’t need acid & don’t produce renal stones

- Night is good time for calcium supplementation

- If over 500 mg must used divided dose especially breakfast

- Calcium supplementation reduce iron absorption by 50%
Calcium carbonate is also poorly absorbed in patients taking proton pump inhibitors or H2 blockers or acholoridria.

- **Calcium citrate** as a first line calcium supplement in these patients.
## Difference between Calcium in diet & supplementation

<table>
<thead>
<tr>
<th>Diet</th>
<th>Supplementation</th>
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</thead>
<tbody>
<tr>
<td>Slow intestinal absorption</td>
<td>Fast intestinal absorption</td>
</tr>
<tr>
<td>Increase calcium for 1h</td>
<td>Increase calcium for 3-4h</td>
</tr>
<tr>
<td>Decrease absorption of oxalate</td>
<td>Increase risk of renal calculi</td>
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</tbody>
</table>
Medications should be given several hours before or after calcium supplements

- Levothyroxine
- fluoroquinolones
- tetracycline
- phenytoin
- angiotensin-converting enzyme inhibitors
- iron
- bisphosphonates
### Calcium/D Product Selection

<table>
<thead>
<tr>
<th>Product (% elemental Ca)</th>
<th>Elemental Calcium (mg)</th>
<th>Vitamin D (units)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium carbonate (40)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Tums Ultra</td>
<td>400</td>
<td>200</td>
<td>Requires acidic environment for dissolution and disintegration. Best to take with meals. Greater risk for constipation with carbonate form.</td>
</tr>
<tr>
<td>- Caltrate 600 Plus</td>
<td>600</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Oscal Plus D</td>
<td>500</td>
<td>125</td>
<td></td>
</tr>
<tr>
<td>- Viactiv Chews</td>
<td>500</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Calcium citrate (24)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Citracal Plus D</td>
<td>315</td>
<td>200</td>
<td>Take without regard to meals. Serving size usually equals 2 capsules so label can be misleading to patients.</td>
</tr>
<tr>
<td>- Citracal Petites with VitD</td>
<td>200</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>Vitamin D</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Multivitamin (D₃)</td>
<td>120-450</td>
<td>400</td>
<td></td>
</tr>
<tr>
<td>- Vitamin D</td>
<td>100-400</td>
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Vitamin D plays a major role:

- In calcium absorption
- Bone health
- Muscle performance
- Balance
- ↓ Risk of falling.
Consequences of vitamin D insufficiency

- Calcium absorption
- Parathyroid hormone
- Bone mineral density
- Risk of fracture
- Appropriate neuromuscular function
- Falls
Adequate Intake of Vitamin D

- NOF recommends:
  - intake of 800 to 1,000 IU of vitamin D per day for adults age 50 & older.
  - Vitamin D supplements should be recommended in amounts sufficient to bring the serum 25(OH)D level to approximately 30 ng/ml
  - a maintenance dose recommended to maintain this level, particularly for individuals with osteoporosis.
Adequate Intake of Vitamin D

- Adults who are vitamin D deficient may be treated with 50,000 IU of vitamin D2 or vitamin D3 once a week for 8-12 wks to achieve a 25(OH)D blood level of approximately 30 ng/ml.

- This regimen should be followed by maintenance therapy of 1500–2000 IU/d.
Benefits of Exercise

What type?

- Weight-bearing
- Muscle-strengthening

Expected benefits?

- Small (1% to 2%) effect on adult BMD
- Reduces the loss of muscle mass
- May reduce risk of falls by improving strength and balance
- Regular walking decreases risk of hip fractures

Regular Weight-Bearing and Muscle-Strengthening Exercise

- walking
- jogging
- Tai-Chi
- stair climbing
- dancing
- tennis

Before an individual with osteoporosis initiates a new vigorous exercise program, such as running or heavy weight-lifting, a clinician’s evaluation is appropriate.
Fall prevention

90% of all non vertebral fractures are related to fall

Correction of decreased visual acuity

Reduction of drug consumption that altered wakefulness & balance

Improve cardiac & neurologic function

Improve muscle strength

Improving home environment

Wearing hip protectors
Pharmacologic Options
Leading the Effort to Help Prevent and Treat Osteoporosis

Pyramid for Osteoporosis Prevention and Treatment

Pharmacotherapy (antiresorptives & anabolics)

Address Secondary Factors (drugs and diseases)

Lifestyle Changes (nutrition, physical activity, and fall prevention)

What does this mean for your patients?

Current treatments in OP

- **Antiresorptive**
  - Estrogens and SERMs
  - Calcitonin
  - Bisphosphonates
  - Denosumab

- **Anabolic (stimulate bone formation)**
  - Parathyroid hormone

- **Dual action agents**
  - Strontium ranelate
Mechanism Of Treatment

- Bisphosphonates
- Miacalcic
- EPT
- SERM
- Denosumab
- Strontium ranelate
- Teriparatide
- Anabolic hormones
- Rocaltrol
- Statins
- Fluoride
## FDA-Approved Therapeutic Options

<table>
<thead>
<tr>
<th>Prevention</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Estrogen</td>
<td>Calcitonin</td>
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<tr>
<td></td>
<td>Alendronate</td>
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<td>Risedronate</td>
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<td>Ibandronate</td>
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<td>Zoledronic acid</td>
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<td>Raloxifene</td>
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<td>PTH (teriparatide)</td>
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<td>Denosumab</td>
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Estrogen/Hormone Therapy (ET/HT)

- ET/HT is approved by the FDA for
  - prevention of osteoporosis but not treatment of osteoporosis
    - estrogen is effective in postmenopausal women with established osteoporosis and vertebral fractures
  - Relief of vasomotor symptoms
  - vulvovaginal atrophy associated with menopause.
Estrogen

- ERT increases BMD > SERM
- E2 still approved for hot flashes
- Low-dose ERT at menopause will delay bone thinning not as first-line therapy
- Raised concerns about CV risks
- Breast Ca 2-6/1000 women treated with HRT for 5 years
HRT: A CONSENSUS

- Review need annually (esp aged>60)
- Can give up to age 50 if pre menopause
- Do not use in IHD/CVA, or Alzheimer's
- Transdermal E2 has lower DVT risk
- Low-dose estrogen — The dose of estrogen required to prevent bone loss had been thought to be **0.625 mg of conjugated estrogens**.
The Concept of a **SERM**
Selective Estrogen Receptor Modulator

- **Estrogen-like** medications — Certain medications, known as selective estrogen receptor modulators (SERMs), produce some estrogen-like effects in the bone.

- **SERM** provide protection against postmenopausal bone loss.

- Currently available SERMs include raloxifene (Evista) and tamoxifen.

- SERMs are not recommended for premenopausal women.
Raloxifene (Evista)

- for both prevention and treatment of osteoporosis in postmenopausal women.

- for the reduction in risk of invasive breast cancer in postmenopausal women with osteoporosis.
RALOXIFENE - SERMS

- Reduces vertebral (not hip) fracture risk
- Reduces development of new breast Ca
- No increased risk of CVD (reduces CV events!)
- Increased risk of DVT/PE & may worsen hot flushes
- Well tolerated, easy dosing: 60 mg OD
Calcitonin

- A less popular choice for treatment of osteoporosis is nasal spray
  - 200 units (1 spray) alternating nares daily
  - IM/SQ
    - 100 units/every other day
    - Should perform skin test prior to initiating therapy
Calcitonin

- We prefer other drugs to calcitonin
  - Anti fracture efficacy compared with bisphosphonates & parathyroid hormone. Weak.
  - Because of its relatively modest effect on BMD
  - Beneficial, short-term effect on acute bone pain after osteoporotic fracture (vertebral)
- No significant effect in the hip
Bisphosphonates

- Alendronate (Fosamax) generic
- Risedronate (Actonel) better GI profile
- Ibandronate (Boniva) no hip protection
- Zoledronic Acid (Aclasta) once a year
Bisphosphonates

- **Alendronate**: 10 mg daily (tablet) or 70 mg weekly (tablet or liquid) for treatment, 5 mg daily or 35 mg weekly for prevention

- **Risedronate**: 5 mg daily or 35 mg weekly (tablet); 150 mg monthly (tablet)

- **Ibandronate**: 150 mg monthly by tablet; 3 mg intravenously over 15 to 30 seconds every 3 months

- **Zoledronic acid**: 5 mg by intravenous infusion over a minimum of 15 minutes once every year for treatment—and every other year for prevention
Bisphosphonates: Indications

- Treatment and prevention of postmenopausal osteoporosis
  - Alendronate, risedronate, ibandronate, zoledronic acid

- Prevention and/or treatment of glucocorticoid-induced osteoporosis
  - Risedronate, zoledronic acid, alendronate

- Treatment of men with low bone density
  - Alendronate, risedronate, zoledronic acid
Bisphosphonates
Oral dosing requirements

- Tablets (with exception of delayed release risedronate) taken on an empty stomach after overnight fast with 6 to 8 oz of plain water while in an upright position.

- Patients should not eat or lie down for at least 30 minutes (alendronate & risedronate) or 60 minutes (ibandronate).

- Calcium and vitamin D supplements, if needed, should be taken at a different time of day than the oral bisphosphonate.
Bisphosphonate Holidays

- In patients at **high risk** for fractures, continued treatment seems reasonable. Consider a drug holiday of **1 to 2 years after 10 years** of treatment.

- For **lower risk** patients, consider a “drug holiday” after **4 to 5 years of stability**.

- Follow BMD and bone turnover markers during a drug holiday period, and reinitiate therapy if bone density declines or markers increase.
When to Stop Treatment?

After 5 years treatment with bisphosphonate

High risk of fracture (previous fractures, older age, frail, high risk for fall, etc),

continuing therapy

Low risk of fracture (stable BMD, no previous vertebral fractures, and who are at low risk for fracture in the near future)

Discontinuing therapy

In FLEX, >8% in 1 year, >10% in 2 years

monitor BMD

stable

significant loss
Teriparatide

The only treatment agent that is anabolic: stimulates bone formation rather than inhibiting bone resorption

- 20 μg daily (subcutaneously) for no more than 2 years

- Forteo® prefilled pen contains 28 daily doses
Teriparatide

Teriparatide is approved by the FDA for the

- Treatment of osteoporosis in postmenopausal women and men at high risk for fracture.

- Treatment in men and women at high risk of fracture with osteoporosis associated with sustained systemic glucocorticoid therapy.

- Indicated to increase bone mass in men with primary or hypogonadal osteoporosis who are at high risk of fracture.
Denosumab

- **Denosumab**— RANKL, a member of the TNF superfamily of ligands and receptors, is essential for the function of bone-resorbing osteoclasts.

- RANKL accelerates osteoclastogenesis when it binds to its receptor, RANK, but is blocked by osteoprotegerin, which is produced by osteoblasts.

- **Denosumab** is a humanized monoclonal antibody against RANKL that reduces osteoclastogenesis.
RANK Ligand Is an Essential Mediator of Osteoclast Activity

Many different factors can affect osteoclast activity, but most do so through the osteoblast and RANK ligand (RANKL)

TNF-α=tumor necrosis factor-alpha; PTHrP=parathyroid hormone-related peptide; PTH=parathyroid hormone; IL-1, IL-11=interleukins-1, and -11; PGE₂=prostaglandin E₂.

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Denosumab (Prolia®)
60 mg subcutaneous injection every 6 months

- Denosumab is approved by the FDA for
  - Treatment of osteoporosis in postmenopausal women at high risk of fracture.
  - To increase bone mass in men at high risk of fracture
  - Treat bone loss in women with breast cancer
  - To treat bone loss in men receiving certain treatments for prostate cancer who are at high risk for fracture.
  - Used in renal failure
Strontium ranelate (Protelos)

- Strontium ranelate is an orally active drug consisting of two atoms of stable strontium and an organic moiety (ranelic acid).

- It appears to have a modest antiresorptive effect, with little effect on bone formation.

- Protelos sachets 2 g mixed with water 2 hour after bed time meal
Protelos

- Protelos is indicated for patients with postmenopausal osteoporosis

- As a first line alternative to bisphosphonate therapy, particularly in the elderly

- In those with a history or potential for upper gastrointestinal complications

- In women who have tried/failed (intolerance or inadequate response) treatment with other osteoporosis therapies
Other therapies

Calcitriol: Effective in preventing glucocorticoid-induced and posttransplant-related bone loss.

- Vitamin K
- Tibolone
- Folate/vitamin B12
- Growth factors
- Androgens
- Isoflavones
- Fluoride
Pain control in fracture

- Oral analgesics are first-line therapy for the relief of acute pain due to vertebral compression fractures.
- For inadequate pain relief with oral analgesics, adding nasal calcitonin
- **NOT using vertebroplasty or kyphoplasty** for the acute management of pain associated with osteoporotic compression fractures
- **NOT using skeletal muscle relaxants** for the acute management of pain in patients with osteoporotic compression fractures
- If bracing is used to relieve pain, braces should be discarded as soon as possible, since they promote immobility of the spine and the potential for disuse osteoporosis
Summary of Medications

- Bisphosphonates- First line therapy
  - Must have GFR > 30

- Denosumab, 2x/yr useful in low eGFR

- Strontium 3rd line C/I IHD

- PTH 3rd line use <2yrs

- Estrogen for post-menopause symptoms

- SERM: spine only
Thanks for your attention