Osteoporosis

Osteoporosis

- Def: Reduction of Bone mass (density) beyond 2.5 SD
- T-score < -2.5
- T-score = -1 to -2.5 → At Risk

Osteoprosis: Clinical presentation

- Pathologic fractures esp. of Hip n Vertebrae
- Hip #....high mortality (5-20%)
  ....high morbidity (DVT n PTE; 20-50%)
- Vertebral #.....Asymptomatic
  .....Kyphosis, Spinal compression
  Chr. Backache

Osteoporosis: Risk factors

Modifiable

- Smoking
- Alcoholism
- Estrogen def.

  Early menopause (<45)

  B/L oophorectomy
- Low Ca intake

Non-modefiable

- Age
- Female sex
- p/h/o # as an adult

Osteoporosis: Pathophysiology

- Normal bone mass maintained by bone remodeling …resorption (osteoclasts) and apposition (osteoblasts)
- Imbalance in remodeling i.e. resorption more than apposition leads to net loss of bone mass

Osteoporosis: Pathophysiology

- Factors affecting bone remodeling

1. Calcium nutrition:

- Peak bone mass reduced by inadequate Ca intake during growth
- Dieatry Ca < 400 mg/d→ Osteoporosis
- Low Ca→ high S. PTH→ high osteoclast activity→ Increased bone resorption

Osteoporosis: Pathophysiology

2. Vitamin D:

- Rickets (children) n Osteomalacia (adults)
- Predisposed group→ CKD, CLD, Malabs synd
- > 50% of inpatients on general medical service have biochem e/o Vit.D def (Ca, PTH or ALP)
- Low Vit.D→ Reduced Ca absorption from gut n reabsorptio from renal tubules + high PTH leading to more resorption

Osteoporosis: Pathophysiology

3. Estrogen:

Estrogen def→ osteoblast modulation (IL-1,6 n TNF æ)→ prevent osteoclast apoptosis n activates them for bone resorption

4. Physical activity:

- immobilization→ loss of bone mass
- However with moderate exercise→ only modest rise in bone mass (1-2%)
- Physically active ppl→ less likely to fall

Osteoporosis: Pathophysiology

5. Medications:
- Steroids
- Overtreatment with thyroid supplements
- Anticonvulsants

6. Smoking:
- Direct toxic effects
- Smoker women→ early menopause

Osteoporosis: Investigations

I. Radiologic:

a) DEXA Scan….Lumbar spine, Hip, Radius, Ulna, Phalynges, Calcaneus; T-score < -2.5 and Z-score < -1.0

b) CT-scan…provides true bone density (bone mass per unit volume) however expensive & asso radiation exposure

Osteoporosis: Investigations

- Indications for BMD test:

1. Estrogen def women
2. X-ray e/o osteopenia
3. Steroids > 7.5 mg/d; > 3 mths
4. F/u during treatment of Osteoporosis > 23 months of treatment
5. HyperPTH

Osteoporosis: Investigations

II. Lab investigations:

a) S. Ca→ high in Pr. HyperPTH n PTHrP dr
→ Low in Malnutrition, Malabs synd

b) 24 hr Ca urinary excretion→
< 50 mg …Malnutrition, Malabs synd
> 300 mg …Absorptive hyperCa (CGD)
High bone turnover (hemat malig)

c) TSH (suspected Hyperthyroidism)

d) Urinary free cortisol/fasting S. cortisol
(suspected Cushing's synd)

Osteoporosis: Investigations

III. BM Bx:

Not required now….DEXA scan, hormonal evaluation & biochem markers of bone remodeling serve the purpose

IV. Biochem markers of bone remodeling:

Bone formation→ Bone spf S. ALP, Osteocalcin
Type I Procollagen peptide

Bone resorption→ Telopeptides of collagen (I)
Bone sialoproteins

Osteoporosis: Investigations

IV. Biochem markers of bone remodeling:

Fallacies…variability (circadian rhythm)

…analytic variability

…..single-point observation

Uses….not for diagnostic purposes but rather..

a) Monitoring of therapy (3-6 mthly)
b) If BMD (T-score) = -1.0 to -2.5 (to decide for therapy)

Osteoporosis: Treatment

- Risk-factor reduction:

- Smoking cessation
- Alcohol absteinance
- Visual-aids
- Review of medications (steroids, thyroxin)

Osteoporosis: Treatment

- Nutritional recommendations:

- Ca intake = 1000-1300 mg/d (elemental Ca)
- Ca Formulations→ Carbonate (400mg/1 g)
  Citrate (60 mg/ 300 mg)
  Gluconate (40 mg/500 mg)
- Monitor 24 urinary Ca excretion
- Vit.D intake = 200 IU (<50 yrs), 400 (50-70)
  & 600 IU (> 70 yrs)
- S. levels should be > 50 μmol/L (20 ng/mL)

Osteoporosis: Treatment

- Exercise:
- Î likelihood of attaining max genetically determined peak bone mass in adults
- Improves neuromuscular funcn & coordination
- Exerise at least 3 times a wk
- Swimming n water exercises for those who cant walk

Osteoporosis: Treatment

- Pharmacotherapy:

1. Estrogens
2. Progestins
3. SERMs
4. Biphosphonates
5. PTH
6. calcitonin

Osteoporosis: Treatment

- Estrogens:

- Reduce bone turnover n permanent bone loss
- Mediated by ER on osteoblasts

- Available as Oral suppl (EE 5μg/d) or Trans-dermal patch (50 μg)
- S/Es→ ACS up by 29% (HEPRS & WHI)
  - → DVT-PTE up by 100%
  - → Stroke (40%)
  - → Ca Breast (26%)

Osteoporosis: Treatment

- Progestins:
  - Used in combination with steroids
  - At least 12 days a month
  - Increased risk of Ca Breast n Uterus
- SERMs (Raloxinfene):
  - Estrogenic effect on skeleton
  - 60% decrease in Ca Breast; 40% decline in Heart ds n Stroke
  - No asso uterine malignancies

Osteoporosis: Treatment

- Biphosphonates: Induce Osteoclast Apoptosis

1. Alendronate- 70 mg/wk

For prevention n treatment of postmenopausal osteoporosis

For treatment of steroid-induced osteoporosis

2. Risedronate- 35 mg/wk

For prevention of steroid-induced osteoporosis as well (in addition to above)

3. Zolandronate- (under clinical trials only)

Advantage of monthly oral annual iv dosage

Osteoporosis: Treatment

- Calcitonin:
  - MOA: Loss of ruffled border of osteoclasts
  - Available as nasal spray (200 IU/d) or Subcutaneous injections
  - For treatment of late postmenopausal osteoporosis only (5 yrs following menopause) ….not effective in early postmenopausal osteoporosis

Osteoporosis: Treatment

- PTH:
  - Low dose supplementation along with estrogen therapy
  - MOA→ Osteoblast activation
  - Expensive

Treatment monitoring

- BMD:

1. Changes in BMD exceeding 4% (spine) or 6%(hip) considered significant
2. Hip is the preferred site→ because of greater reproducibility (larger surface area)
3. Not before 2 yrs of initiation of therapy

eatment monitoring

- omarkers of bone turnover:
- High biologic n technical variability
- eduction of at least 30-40% considered ignificant
- epeated at intervals of at least 4 mths ollowing initiation of therapy
- linical evidence to support their routine se not enough