

Calcium disorders & Osteoporosis

Mohsen Eledrisi, MD, FACP, FACE

Department of Medicine

Hamad Medical Corporation

Doha, Qatar

www.eledrisi.com

Causes of hypercalcemia

VITAMIN-TRAP

Vitamin intoxication (D, A)

Immobilization

Thiazide, Theophylline, Tamoxifen,
Lithium

Addison's disease, **A**cromegaly

Milk-alkali syndrome

Inflammation/infection
(TB, sarcoidosis, fungal)

Neoplasia (kidney, lung, breast, MM,
esophagus, lymphoma, leukemia..)

Thyrotoxicosis

Rhabdomyolysis

AIDS

Parathyroidism (1^{ry},3^{ry})

Pheochromocytoma

Parenteral nutrition

FHH:

Familial hypocalciuric
hypercalcemia

Primary hyperparathyroidism

- High serum calcium & non-suppressed PTH level
- Most often caused by a single parathyroid adenoma
- Evaluation:
 - Serum creatinine, eGFR
 - 24-hour urine calcium excretion
 - Bone density (including the distal third of the radius)
 - Renal ultrasound to detect stones
 - 25-hydroxyvitamin D

Indication for surgery in primary hyperparathyroidism

- Serum calcium > 0.25 mmol (1.0 mg) the upper limit of normal
- Osteoporosis (spine, hip, femoral neck, or distal 1/3 radius)
- Vertebral fracture
- eGFR < 60 mL/min
- 24-hour urinary calcium > 400 mg/day (> 10 mmol)/day
- Nephrolithiasis
- Age < 50 years
- If follow up is not desired or possible

Follow up if no surgery

- Patients who refuse or are not candidates for surgery
- Monitor the following:
 - Serum calcium every year
 - Bone density every 1-2 years (spine, hip, radius)
 - Spine imaging if height loss or symptoms of a vertebral fracture
 - Serum creatinine, eGFR annually
 - If history or suspected kidney stones:
 - 24-hour urine calcium, renal imaging (X-ray, U/S or CT) yearly

Medical management of primary hyperparathyroidism

- Deficiencies in vitamin D and dietary calcium worsen hyperparathyroidism
- It is not recommended to limit dietary calcium intake
- Adequate calcium diet (1000-1200 mg/day) & vitamin D (serum 25-hydroxyvitamin D >20 ng)
- Cinacalcet:
 - Mild ↓ PTH, ↓ serum calcium. No effect on bone density
 - Approved for use
- Bisphosphonate:
 - Improves bone density, but no data on fracture

Approach to hypocalcemia

1) Repeat test

2) Check serum albumin

- Correct calcium if albumin is low

- Calcium ↓ by 0.8 mg/dL (0.2 mmol/L) for every 1 g/dL (10 g/L) ↓ in albumin (normal 4 g/dl)

- example: calcium 8 mg, albumin 2 g/dL

 - Corrected calcium $8 + (0.8 \times 2) = 9.6$ mg

3) Can check ionized calcium, but expensive

Causes of hypocalcemia

- Post-surgical (thyroid, parathyroid surgery)
- Autoimmune hypoparathyroidism
 - Can be isolated
 - Or with chronic mucocutaneous candidiasis + adrenal insufficiency (polyglandular syndrome type 1)
- Vitamin D deficiency
- Pseudohypoparathyroidism (PTH resistance)
- Acute or chronic kidney disease
- Acute pancreatitis
- Tumor lysis syndrome
- Hypomagnesemia, hyperphosphatemia
- Acute illness, sepsis

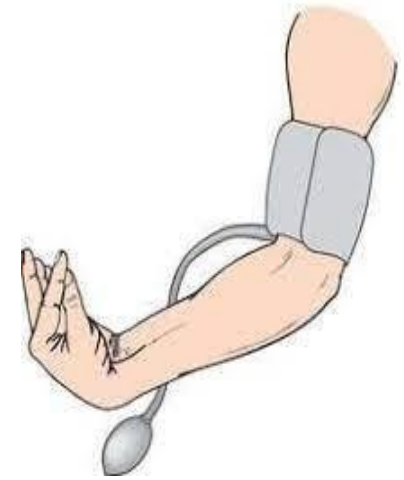
Manifestations of hypocalcemia

- Perioral numbness
- Paresthesia of hands and feet
- Muscle cramps & pains
- Carpopedal spasm
- Laryngospasm
- Seizures (focal or generalized)
- Fatigue, irritability, anxiety, depression
- Some have no symptoms

Physical examination

- **Trousseau's sign:**

induction of carpal spasm by inflation of a sphygmomanometer above systolic blood pressure for 3 minutes



- **Chvostek's sign:**

contraction of the ipsilateral facial muscles elicited by tapping the facial nerve just anterior to the ear (may occur in normal persons)



Evaluation of hypocalcemia

	PTH	Phosphorus	Magnesium	25-OH vit D	creatinine
Hypoparathyroidism	↓	↑	Normal	Normal	Normal
Pseudohypoparathyroidism	↑	↑	Normal	Normal	Normal
Hypomagnesemia	Normal or ↓	Normal	↓	Normal	Normal
Vitamin D deficiency	↑	↓ or normal	Normal	↓	Normal
Chronic kidney disease	↑	↑	Normal or ↑	Normal	↑

Treatment of hypocalcemia

- 1) Acute symptoms or very low calcium [< 7 mg (1.75 mmol)]:
 - IV calcium
 - Check magnesium and potassium (replace if low)

- 2) Chronic treatment:
 - Oral **elemental** calcium 1-2 grams/day
 - Ca carbonate = 40% elemental calcium (1250 mg = 500 mg)
 - Ca citrate = 21% elemental calcium
 - Ca lactate = 13%
 - Vitamin D:
 - Calcitriol 0.25 to 2 mcg /day (higher doses can be used)
 - Or Alfacalcidol (one alpha) 0.25 to 2 mcg/day (may need \uparrow)

- 3) Target calcium is low normal [8 to 8.5 mg (2-2.15 mmol)]

Osteoporosis

- Low bone mass
- Microarchitectural disruption
- Skeletal fragility
- **This causes ↓ bone strength & ↑ risk of fracture**

Clinical manifestations of osteoporosis

- No symptoms until there is a fracture
- **Vertebral fracture**
 - Commonest manifestation of osteoporosis
 - Mostly asymptomatic
 - Found incidentally on imaging
 - May present as height loss or kyphosis
 - Pain if acute presentation
- **Other fractures:**
 - Hip fractures
 - Distal radius fractures (Colles fractures)

Risk factors for osteoporosis

- Women \geq 65 years, men \geq 70 years
- Previous fragility fracture
- Parental history of fracture
- Cigarette smoking
- Excessive alcohol use
- Low body weight ($<$ 58 kg)
- Rheumatoid arthritis
- Long term glucocorticoid therapy
- Secondary osteoporosis

When to screen for osteoporosis?

- Women \geq 65 years, men \geq 70 years
- Women < 65 years, men < 70 years if:
 - Low body weight
 - Prior fracture
 - High risk medication use
 - Disease or condition associated with bone loss

Diagnosis of osteoporosis

- **Fragility fracture:**

- Occurs spontaneously or from minor trauma (fall from a standing height)
- Generally at the spine, hip, wrist, humerus, rib or pelvis

OR

- **T-score ≤ -2.5 :**

- At any site by bone mineral density

Bone mineral density (BMD)

- Usually measured with dual-energy X-ray absorptiometry (DXA) scan
- Scores are expressed as standard deviations
- T score: bone density compared with young normal person
- Z score: bone density compared with age-matched person
- Definition of bone density depends on **T SCORE**
 - Between 0 and -1 → **Normal**
 - Between -1 and above -2.5 → **Osteopenia**
 - At or below -2.5 → **Osteoporosis**
 - At or below -2.5 with fragility fracture → **Established Osteoporosis**
- Z score is low in secondary causes of osteoporosis

Evaluation of osteoporosis

- **History and physical examination:**

- Smoking, alcohol, physical inactivity, poor nutrition
- History of a fragility fracture
- Height and weight
- Secondary causes of osteoporosis

- **Fracture Risk Assessment Tool (FRAX):**

- A calculator that estimates the 10-year probability of hip fracture and major osteoporotic fracture for untreated patients aged 40-90 years
- Region/country specific
- Information include age, risk factors, femoral neck BMD if available

- **Laboratory evaluation**

- Biochemistry (electrolytes, calcium, phosphorous, albumin)
- 25-hydroxyvitamin D
- Complete blood count

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: **Kuwait**

Name/ID:

[About the risk factors](#)

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth

Age:

Date of Birth:

Y:

M:

D:

2. Sex

Male

Female

3. Weight (kg)

4. Height (cm)

5. Previous Fracture

No

Yes

6. Parent Fractured Hip

No

Yes

7. Current Smoking

No

Yes

8. Glucocorticoids

No

Yes

9. Rheumatoid arthritis

No

Yes

10. Secondary osteoporosis

No

Yes

11. Alcohol 3 or more units/day

No

Yes

12. Femoral neck BMD (g/cm²)

Select BMD

▼

Clear

Calculate

BMI: 27.5

The ten year probability of fracture (%)



without BMD

Major osteoporotic

5.1

Hip Fracture

1.5



Weight Conversion

Pounds kg

Convert

Height Conversion

Inches cm

Convert

00026060

Individuals with fracture risk assessed since 1st June 2011



Print tool and information

Causes of secondary osteoporosis

- Endocrine disorders (hyperparathyroidism, hyperthyroidism, hypogonadism, Cushing's syndrome, DM)
- GI disorders (celiac disease, IBD, chronic liver disease)
- Nutritional disorders (vitamin D deficiency, parenteral nutrition)
- Medications (glucocorticoids, cyclosporine, heparin, phenytoin, phenobarbital, GnRH agonists & antagonists)
- Rheumatoid arthritis
- Multiple myeloma, leukemia, lymphoma, sickle cell disease
- Organ transplantation (kidney, liver, bone marrow, lung, heart)

When to consider drug therapy for osteoporosis?

◆ Postmenopausal women or men ≥ 50 years with:

- History of fragility fracture
- Osteoporosis
- High risk with osteopenia:
 - Using FRAX tool
 - Defined as:

A 10-year probability of hip fracture $\geq 3.0\%$

OR

A 10-year probability of major osteoporotic fracture $\geq 20\%$

Treatment of osteoporosis

- Lifestyle measures:

- Adequate calcium intake (1200 mg/day)
- Adequate vitamin D intake (800 units/day)
- Exercise
- Smoking cessation
- Avoidance of alcohol use

Treatment of osteoporosis

• Bisphosphonates:

- Mostly recommended as 1st line agent
- Reduce vertebral & hip fractures (Ibandronate did not ↓ hip fractures)
- Oral: Alendronate, risedronate (daily or weekly dosing),
Ibandronate (once monthly)
 - Stay upright for 30-60 minutes after taking the medication
 - Do not use if esophageal disorders, inability to follow the instructions
- IV: Zoledronic acid (every year), Ibandronate (every 3 months)
- Not recommended if eGFR <30

Treatment of osteoporosis

- Denosumab:

- Inhibits osteoclast formation, ↓ bone resorption
- Reduced rates of vertebral and hip fractures
- May be used as an alternative (especially if there is intolerance to bisphosphonates or CKD)
- Subcutaneous injection once every 6 months
- There is an increased risk of vertebral fractures after stopping it
- If denosumab is discontinued, an alternative therapy should be given (usually a bisphosphonate)

Treatment of osteoporosis

• Anabolic agents:

- Generally used for severe osteoporosis:
 - T-score of ≤ -3.5 , T-score of ≤ -2.5 with a fragility fracture, severe or multiple vertebral fractures
- Teriparatide, Abaloparatide, Romosozumab
- Teriparatide & abaloparatide (once daily subcut.) for up to 2 years
- Romosozumab (once monthly subcut.) for up to 1 year
- Bisphosphonates are usually given after those agents

Treatment of osteoporosis

- Selective Estrogen Receptor Modulators (SERMs):
 - In postmenopausal women with osteoporosis at high risk of fracture
 - Reduce the risk of vertebral fractures (not hip)
 - Reduce the risk of breast cancer
 - Raloxifene, Bazedoxifene (oral)
 - Used if low risk for deep vein thrombosis and for whom bisphosphonates or denosumab are not appropriate or with a high risk of breast cancer