Approach to Hypocalcemia

M. Hashemipour

Pediatric Endocrinologist

Isfahan university of medical sciences

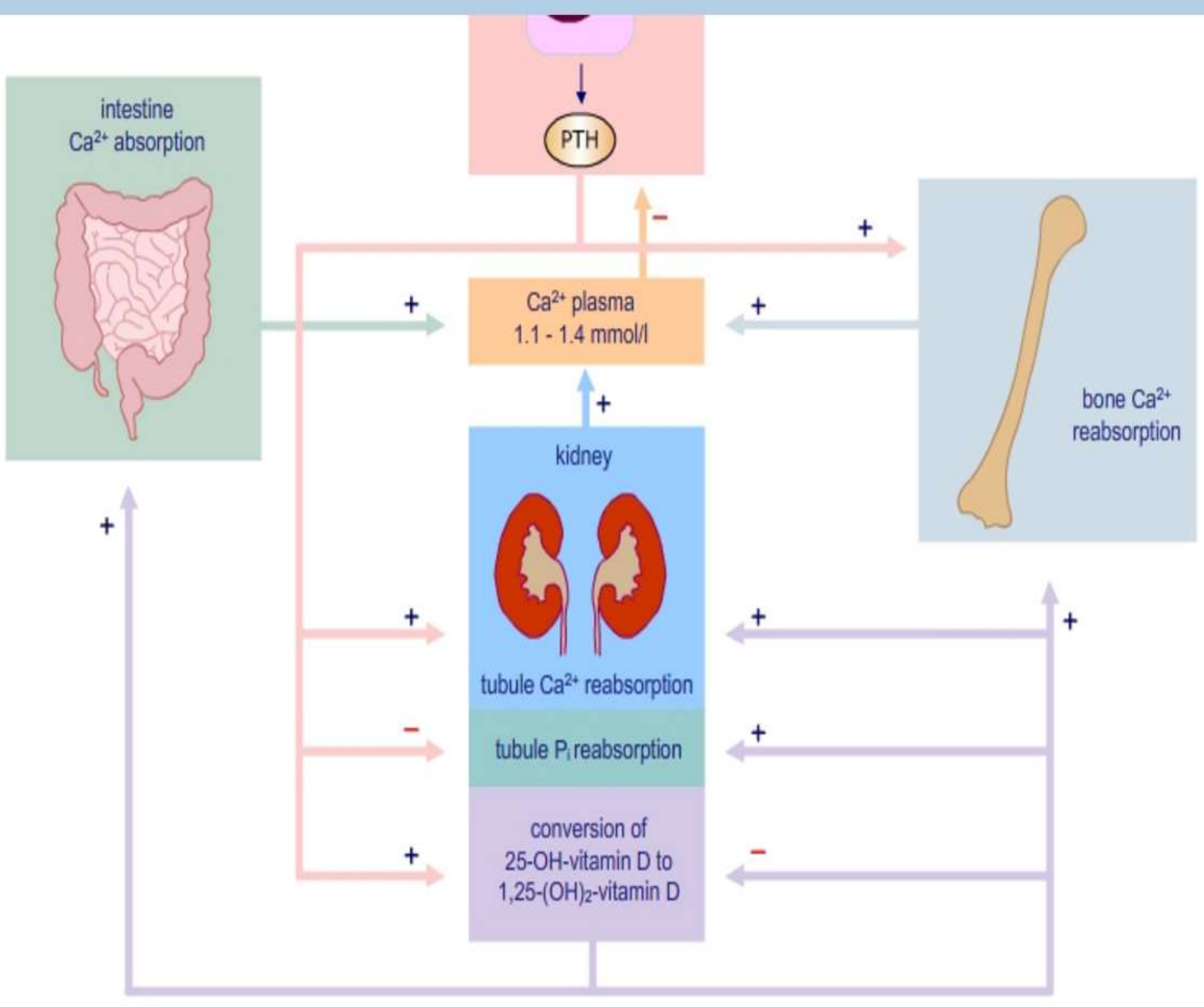
Content

- Calcium homeostasis
- Normal level of Calcium
- The effect of drugs on calcium level
- Definition of Hypocalcemia
- Etiology of hypocalcemia
- Clinical manifestation of hypocalcemia
- Physical Examination
- Approached to hypocalcaemia
- Therapeutic approach
- What patients should take intravenous calcium?
- Warnings during calcium therapy
-

- **Hypocalcemia is a laboratory and clinical abnormality that is observed with relative frequency, especially in pediatric patients.**

Regulation of calcium homeostasis

- parathormone (PTH)
- vitamin D
- liver
- Renal function
- phosphate
- Magnesium
- Calcium-sensing receptor
- Calcitonin


intestine
Ca2+ absorption
PTH
Ca2+ plasma
1.1 - 1.4 mmol/l
bone Ca2+
reabsorption
kidney
tubule Ca2+ reabsorption
tubule Pi reabsorption
conversion of
25-OH-vitamin D to
1,25-(OH)2-vitamin D

Role of PTH in calcium homeostasis

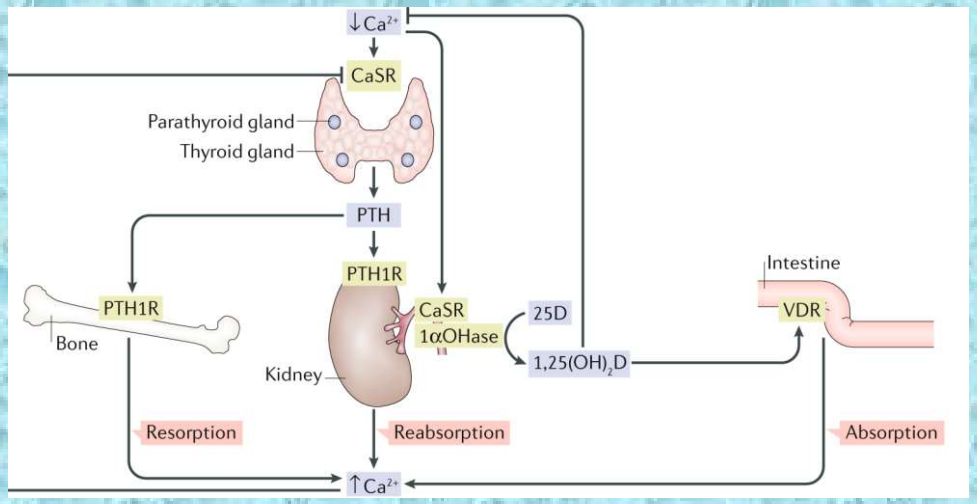
- *When serum levels of calcium fall*, the signal is transduced through the calcium-sensing receptor and *secretion of PTH increases*
- PTH stimulates activity of **١α-hydroxylase** in the kidney, enhancing production of ١’٢٥-dihydroxycholecalciferol ١’٢٥[OH]٢D٣.

Role of PTH in calcium homeostasis

- The increased level of ١’٢٥[OH]٢D٣ induces synthesis of a calcium-binding protein (calbindin-D) in the intestinal mucosa with resultant absorption of calcium.
- PTH also mobilizes calcium by directly enhancing bone resorption, an effect that requires ١’٢٥[OH]٢D٣.

The role of calcium-sensing receptor

- The calcium-sensing receptor regulates the secretion of PTH and the reabsorption of calcium by the renal tubules in response to alterations in serum calcium concentrations



The relationship between calcium&PTH

- In the normally, hypocalcemia induces increased secretion of PTH
- Hypercalcemia depresses PTH secretion

Normal level of Calcium

- **ionized calcium** → **٤-٥ mg/dL**

Calcium level ⇨ ٨٫٥-١٠٫٥ mg/dL

Falsely elevated calcium

- Elevated acetaminophen
- Alcohol
- Hydralazine
- Hemolysis
- Acidic states

Falsely depressed calcium

- Excessive exposure to air
- oxalate
- Citrate
- Hyperbilirubinemia
- Free fatty acids
- Heparin
- Bicarbonate

Definition of Hypocalcemia

- In term infants or preterm infants with BW ≥١٥٠٠g
- Hypocalcemia is confirmed when the total serum Ca is **less than ٨ mg/dL**

Definition of Hypocalcemia

- in very low birth weight preterm infants

BW <١٥٠٠ g

- Hypocalcemia is diagnosed when the total serum Ca is less than **٧ mg/dL**

Definition of Hypocalcemia

- **In children, hypocalcemia is defined as a total serum calcium concentration less than ٨/٥ mg/dL.**

Etiology

infants &Children

- ✓ Abnormal vitamin D production or action
- ✓ Hyperphosphatemia
- ✓ Hypoparathyroidism
- ✓ Hypomagnesemia

Hypomagnesemia

- End-organ unresponsiveness to PTH
- Impaired release of PTH

- Impaired formation of ١’٢٥-dihydroxyvitamin D.

Other causes of hypocalcemia

- Malabsorption syndromes
- Pancreatitis
- Pseudohypocalcemia (hypoalbuminemia)
- Hungry bones syndrome
- Liver disease
- Drugs (anticonvulsants)
- Kidney disease

Genetic

- **DiGeorge's syndrome**
- Mitochondrial disorders
- Hypoparathyroidism

Acute manifestations

- Neuromuscular irritability(Tetany)
  ٧٫٠ to ٧٫٥ mg/dL
- Paresthesias (peri-oral, extremities)
- Muscle twitching
- Carpopedal spasm
- Trousseau's sign
- Chvostek'ssign
- Seizures
- Laryngospasm

Clinical manifestation

- **Abdominal pain**
- Bronchospasm
- Prolonged QT interval
- Hypotension
- Heart failure
- Arrhythmia
- Papilledema
- **Psychiatric manifestations**

Physical Examination

- Trousseau sign
- Chvostek sign
- Nasal speech
- micrognathia
- Ear anomalies
- short philtrum
- Heart murmur
- Short stature.
- Hyperreflexia.

Trousseau's sign

- Trousseau's sign is the induction of carpopedal spasm by inflation of a sphygmomanometer ١٠mmHg above systolic blood pressure for three minutes .

- Carpopedal spasm, as indicated above, is characterized by adduction of the thumb, flexion of the metacarpophalangeal joints, extension of the interphalangeal joints, and flexion of the wrist.
- It may also be induced by voluntary hyperventilation for one to two minutes after release of the cuff.

Chvostek's sign

- **Contraction of the ipsilateral facial** muscles elicited by tapping the facial nerve just anterior to the ear .
- The response ranges from twitching of the lip to spasm of all facial muscles and depends upon the severity of the hypocalcemia.
- Chvostek's sign occurs in about ١٠ percent of normal subjects .
- Although **Trousseau's sign is more** specific than Chvostek's sign,
- Both may be negative in patients with hypocalcemia .

Approached to hypocalcaemia

- serum calcium
- Albumin
- Phosphorus

- The serum total calcium concentration falls approximately ٠٫٨ mg/dL for every ١ g/dL reduction in the serum albumin concentration

Differential diagnosis

Cause of low Ca&IP

Cause of low Ca&IP

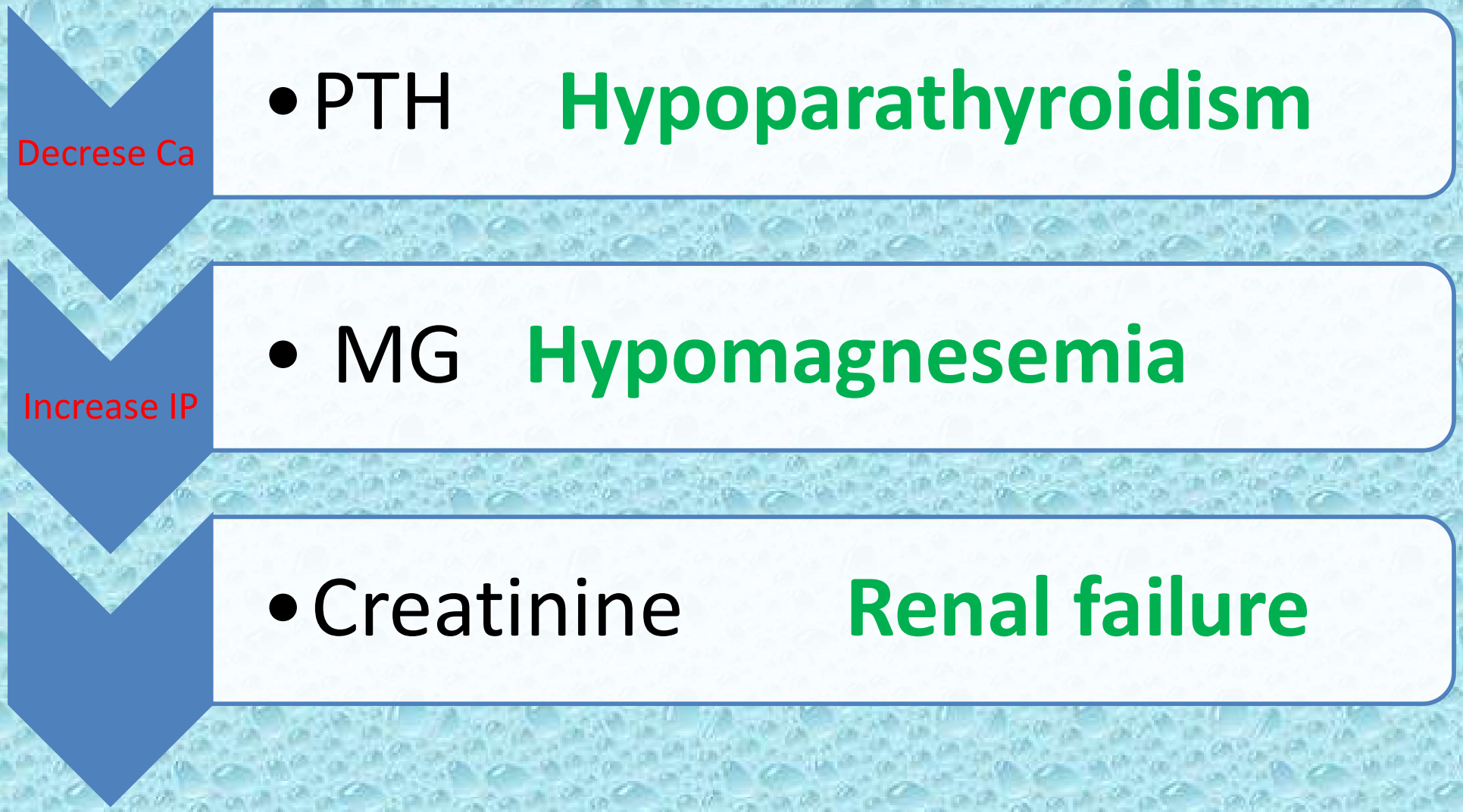
- vitamin D deficiency

Cause of low Ca&IP

- Defect in renal tubular function

Hypophosphatemia& Hypocalcemia

- vitamin D deficiency
- Liver disease
- Drugs (anticonvulsants)
- Celiac disease
- Cystic fibrosis
- Malabsorption
- Renal tubular acidosis


Decrese Ca
• PTH Hypoparathyroidism
Increase IP
• MG Hypomagnesemia
• Creatinine Renal failure

Hyperphosphatemia& Hypocalcemia

- Renal failure
- Tissue breakdown
- Hypoparathyroidism
- Pseudohypoparathyroidism.
- Chemotherapy
- **Mg deficiency**

Hypocalcemia & increase PTH

- **In hypocalcemic states due to** Rickets
- **Defect in renal tubular function**

- Renal failure
- Psudohypoparathyroidism

Hypocalcemia & Decrease PTH

- Severe hypomagnesemia
- Hypoprathyroidism

Hypocalcemia & A low serum calcidiol

٢٥(OH)D٣

- Decrease vitamin D intake or absorption
- Phenytoin therapy
- Hepatobiliary disease
- Nephrotic syndrome .

low serum calcitriol

١’٢٥-(OH)٢ –Vitamin D

- Renal insufficiency
- Vitamin D-dependent rickets, type ١
- Hypoparathyroidism

Imaging study

Imaging Studies

- Chest radiography
- Renal ultrasonography
- Left hand and wrist radiography
- There is a prolongation of the QT interval

Imaging Studies

- **Echocardiography**
- Electrocardiogram
- Non-contrast head CT, which revealed bilateral basal ganglia and subcortical white matter calcifications

Imaging Studies

In patients with hypoparathyroidism

- increased density limited to the metaphyses
- increased density of the lamina dura.

Therapeutic approach

Goal of treatment

- **The overall goal of therapy is to maintain serum calcium in the low-normal range.**

۸-۸/۵ mg/dl

What patients should take intravenous calcium?

A prolonged QT interval

Carpopedal spasm

Tetany

Seizures

What patients should take intravenous calcium?

in patients with mild or chronic hypocalcemia who unable to take or absorb oral supplements

An asymptomatic patients with an acute decrease in serum corrected calcium to ≤۷٫۵ mg/dL or ionized calcium to ≤۳ mg/dL

What patients should take intravenous calcium?

Corrected calcium >٧٫٥ mg/dLIf symptoms don't improve with oral supplementation

Emergency Treatment

١٠% calcium gluconate

- **١٠cc** = ٩٣mg Elemental calcium
- **١cc** =Elemental calcium ٩/٣ mg
- **١٠cc =** ١ gram calcium gluconate = ٩٣ mg elemental calcium

Emergency Treatment

The infant was given infusion of ١-٢ ml/kg of ١٠% calcium gluconate

At a rate of ٠/٥-١ ml/min. slowly, over a ١٠ minute period. Approximate ١٠ ml

Emergency Treatment

Total dose not to exceed ٢ cc of calcium gluconate/kg/dose

Approximate ٢٠ ml

May repeat every ١٠ to ٢٠ minutes for ٣ to ٤ additional doses if no response occurs

Emergency Treatment

This dose may be repeated every

٣-٦ hr

How long does it take for the patient to improve ?

- The treatment resulted in immediate termination of seizures and the normalization of consciousness of the infant
- **Serum concentrations of Ca improve within three to five days after starting therapy**

Duration of intravenous calcium therapy

- Intravenous calcium should be continued until the patient is receiving an effective regimen of oral **calcium** and **vitamin D**.
- Calcitriol is the preferred preparation of vitamin D for patients with severe acute hypocalcemia because of its rapid onset of action (hours).

Mildly asymptomatic or chronic hypocalcemia

- it is likely that the hypocalcemia, even when very severe, has been longstanding and **oral therapy** should be the first line of therapy
- **IV calcium** is **not** warranted as initial therapy for asymptomatic hypocalcemic patients

Maintenance therapy

- We also provide oral **calcium supplements** such as **calcium glubionate (٣٠ to ٥٠ mg/kg per day PO** in four- six divided doses.
- .Although its high osmolality and sugar content can cause **gastrointestinal irritability or diarrhea**
- Alternatively, ١٠ percent Ca gluconate can be divided and given in **four to six feedings**.

- We discontinue Ca supplements gradually after **٢-٤ week** , also depends on etiology

warnings

Avoid too-rapid IV administration

- vasodilatation
- Hypotension
- Bradycardia
- Arrhythmias
- Syncope
- Cardiac arrest

ECG or cardiac monitoring

Legal pitfall

- The calcium can be diluted in dextrose and water or Saline because concentrated calcium solutions are irritating to veins.
- The IV solution should not contain bicarbonate or phosphate, which can form insoluble calcium salts.

Medical/Legal Pitfalls

- Ensure proper catheter or needle position prior to and during infusion
- Central access is preferred if possible.

Medical/Legal Pitfalls

- Tissue necrosis
- Necrosis of liver
- Arterial spasm
- intestinal necrosis.
- Constipation, bloating, and gas are common with oral calcium supplements
- Extravasation into subcutaneous tissues, resulting in necrosis and subcutaneous calcifications

Warnings/Precautions *Concerns related to adverse effects*

- **Hyperphosphatemia:** Use with caution in patients with severe hyperphosphatemia as elevated levels of phosphorus and calcium may result in soft tissue and pulmonary arterial calcium-phosphate precipitation.
- **Hypokalemia:** Use with caution in patients with severe hypokalemia as acute rises in serum calcium levels may result in life-threatening cardiac arrhythmias.

Warnings/Precautions *Concerns related to adverse effects*

- **Kidney stones** :Use caution when administering calcium supplements to patients with a history of kidney stones.
- **Renal impairment**: Use with caution in patients with chronic renal failure to avoid hypercalcemia; frequent monitoring of serum calcium and phosphorus is necessary.
- **Hypomagnesemia:** Hypomagnesemia is a common cause of hypocalcemia; therefore, correction of hypocalcemia may be difficult in patients with concomitant hypomagnesemia.
- If there is **refractory hypocalcemia**