



A. Darwishi



TREATMENT OF HYPOCALCEMIA

HOSEIN MORAVEJ, MD
PEDITRIC ENDOCRINOLOGIST
SHIRAZ UNIVERSITY OF MEDICAL
SCIENCES

- Oral or parenteral treatment?



ORAL OR PARENTERAL TREATMENT?

- Treatment of hypocalcemia varies with its **severity** and the **underlying cause**.
- The **severity** of symptoms (paresthesias, carpopedal spasm, tetany, seizures) and signs (Chvostek's or Trousseau's signs, bradycardia, impaired cardiac contractility, and prolongation of the QT interval) **depends upon the absolute level of calcium, as well as the rate of decrease**.

ORAL OR PARENTERAL TREATMENT?

- Patients with **acute hypocalcemia** will be symptomatic at serum calcium values that would not cause symptoms in patients with **chronic hypocalcemia** (eg, hypoparathyroidism).
- Clinical manifestations also vary with other factors such as the **arterial pH** and the cause of hypocalcemia.

- Treatment of severe acute and/or symptomatic hypocalcemia



INTRAVENOUS CALCIUM

- Intravenous (IV) calcium for the treatment of hypocalcemia is recommended in patients with:
- **Symptoms** (eg, carpopedal spasm, tetany, seizures)
- Prolonged **QT** interval
- **Asymptomatic** patients with an **acute decrease** in serum corrected calcium to **≤ 7.5 mg/dL** or ionized calcium to ≤ 3 mg/dL, who may develop serious complications if untreated.

- Acute hypocalcemia can occur when there is a **rapid and progressive** reduction in serum calcium (eg, acute hypoparathyroidism **following post-radical neck dissection** for head and neck cancer).

INTRAVENOUS CALCIUM

Intravenous calcium dosing:

- **2 ml/kg** of 10% ca. gluconate (elemental ca 9.3 mg/ml) (**max. 10 ml**) at the rate of 0.5-1 ml/min with heart monitoring (**rate and rhythm**).
- Initially, IV calcium, **in 50 mL of 5% dextrose or normal saline** can be **infused over 10 to 20 minutes.** (**uptodate**)

INTRAVENOUS CALCIUM

- The calcium should not be given **more rapidly**, because of the risk of serious cardiac dysfunction, including **systolic arrest**.
- Patients receiving **digoxin** should be monitored closely for **acute digitalis toxicity**, which can develop with calcium infusion.

INTRAVENOUS CALCIUM

- This dose of calcium gluconate will raise the serum calcium concentration for **only two or three hours**; as a result, it should be followed by a slow infusion of calcium in patients with persistent hypocalcemia. ([uptodate](#), [sperling](#))
- Calcium gluconate is usually preferred because it is less likely to cause tissue necrosis if extravasated.

CALCIUM INFUSION

An **IV solution** containing **1 mg/mL of elemental calcium** is prepared:

- Ca. gluconate 10 ml (93 mg elemental, **1 ampule**) in **100 ml dextrose 5%/0.25 normal saline** may be infused intravenously at rate sufficient to maintain ca level in the asymptomatic low-normal range. ([sperling](#))
- For adults: adding 11 g of calcium gluconate (equivalent to 1000 mg elemental calcium) to normal saline or 5% dextrose water to provide a final volume of 1000 mL. ([uptodate](#))

CALCIUM INFUSION

- This solution is administered at an **initial infusion rate of 50 mL/hour (equivalent to 50 mg elemental, 1/2 ampule/hour)**. The dose can be **adjusted** to maintain the serum calcium concentration at the lower end of the normal range (**uptodate**).
- **Patients typically require 0.5 to 1.5 mg/kg of elemental calcium per hour.**
- **Over 8-10 hours**, this protocol will deliver as much as 15 mg/kg body weight, raising the serum calcium levels by approximately **2 mg/dL**.

CALCIUM INFUSION

- The IV solution **should not contain bicarbonate or phosphate**, which can form insoluble calcium salts. If these anions are needed, **another IV line (in another limb)** should be used.

- IV calcium should be **continued until** the patient is receiving an **effective regimen of oral calcium and vitamin D**.

- **If hypocalcemia persists**, calcium gluconate administration in the form of **IV** boluses or as a continuous i.v. infusion, **may be continued for a week to ensure** enterocyte recovery and **adequate intestinal absorption** of oral calcium.

HYPOCALCEMIA IN RENAL FAILURE

- **IV calcium is not warranted** as initial therapy for **asymptomatic** hypocalcemia in patients with impaired renal function
- Correction of **hyperphosphatemia** and of **low circulating 1,25-dihydroxyvitamin D** are usually the primary goals.

CONCOMMITANT ORAL THERAPY

- For patients with hypoparathyroidism, calcitriol and oral calcium should be initiated **as soon as possible**.
- **Calcitriol is the preferred** preparation of vitamin D for patients with severe acute hypocalcemia because of its rapid onset of action (hours)
- Dose of Calcitriol: **0.01- 0.1 microg/kg/d**, max: 1-2 microg/day
- Starting dose: 0.25 microg/d (one capsule)

DRUG INTERACTION

- **Furosemide** and other loop diuretics can increase renal calcium clearance and **reduce serum calcium** levels.
- **Glucocorticoid** antagonizes the action of vitamin D and its analogs and may also precipitate **hypocalcemia**.
- **Estrogen** can **increase calcium absorption** directly at the level of intestine and, indirectly, through the stimulation of renal 1α -hydroxylase activity, thus estrogen therapy may alter calcium homeostasis requiring dose adjustments.

CONCURRENT HYPOMAGNESEMIA

- Hypomagnesemia is a common cause of hypocalcemia, both by inducing **resistance** to parathyroid hormone (PTH) and by **diminishing its secretion**.

CONCURRENT HYPOMAGNESEMIA

- Magnesium repletion should be continued as long as the serum magnesium concentration is **less than 1 mg/dL**.
- More careful monitoring is required in patients who have **impaired renal function** who are at greater risk of developing **hypermagnesemia**.

CONCURRENT HYPOMAGNESEMIA

- **Persistent hypomagnesemia**, as occurs in some patients with ongoing gastrointestinal (eg, **malabsorption**) or **renal losses**, requires supplementation with **oral magnesium**, typically 300 to 400 mg daily divided into three doses.

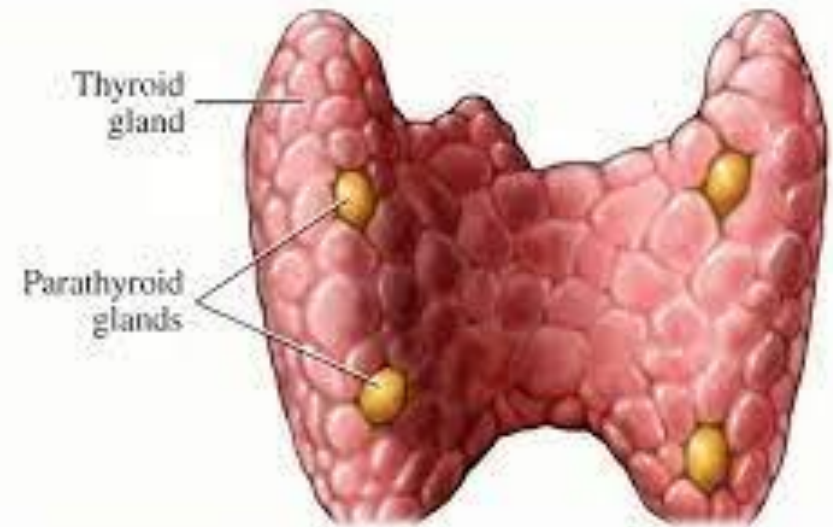
ORAL CALCIUM THERAPY

- For milder degrees of acute hypocalcemia (serum corrected calcium concentration **above 7.5** to 8.0 mg/dL or a serum ionized calcium concentration above 3.0 mg/dL) **or for chronic hypocalcemia**, oral calcium supplementation is preferred.
- Such patients are typically **asymptomatic** or, at most, mildly symptomatic (eg, **oral paresthesias**).

- Dosage of oral calcium for children and adolescents:
- **30-75 mg of elemental calcium/kg/day** in divided doses
- When replacing calcium, it is essential to recognize that the actual amount of elemental calcium in the supplement is of major importance. As an example, **calcium carbonate comprises 40% elemental calcium.**
- All varieties of calcium supplements are better absorbed when taken in small doses (500 mg or less) **at mealtimes.**

- If patients with milder acute hypocalcemia, do **not have symptomatic improvement** with oral calcium supplementation, we **switch to IV calcium**.
- **IV calcium** is also indicated to prevent acute hypocalcemia in patients with milder degrees of hypocalcemia or chronic hypocalcemia (due to hypoparathyroidism) who become unable to take or absorb oral supplements, as may occur **after complex surgical procedures** requiring prolonged recuperation

- Management of hypoparathyroidism



HYPOPARATHYROIDISM

- When hypoparathyroidism is the cause of hypocalcemia, administration of **calcium alone is usually only transiently effective.**
- Long-term management requires the **addition of vitamin D.**

- The **goals** of therapy in patients with hypoparathyroidism are to relieve symptoms and to raise and maintain the **serum calcium** concentration in the low-normal range, eg, **8.0 to 8.5 mg/dL**.
- Attainment of higher values is not necessary and is usually limited by the development of **hypercalciuria** due to the loss of renal calcium-retaining effects of PTH.

MONITORING

- Urinary and serum calcium and serum phosphate is required **weekly initially**, until a stable serum calcium concentration (at the low end of the normal range) is reached.
- Thereafter, monitoring at **three- to six-month intervals** is sufficient.
- **Foods with high phosphorus** content such as milk, eggs and cheese should be **reduced** in the diet.

Recombinant human parathyroid hormone

- For patients with chronic hypoparathyroidism who **cannot maintain stable serum and urinary calcium** levels with calcium and vitamin D supplementation, the addition of **recombinant human parathyroid hormone (1-84)** is an option.
- Long-term **safety** of PTH has not been established. In addition, recombinant PTH is much **more expensive** than standard therapy with calcium and calcitriol.

GOAL

primary goals of chronic management aim in maintaining an acceptable range of the following indexes:

- Serum total **calcium: low-normal range**
- Serum **phosphorus: high-normal range**
- **24-h urine calcium** excretion: <7.5 mmol/d
- **Calcium-phosphate product under 55** mg²/dl²

CHRONIC KIDNEY DISEASE

- Few patients with chronic kidney disease have symptomatic hypocalcemia. Such patients are often treated with **oral calcium to bind intestinal phosphate** and to prevent bone disease rather than hypocalcemia per se. The **addition of an active form of vitamin D is required in some** of these patients.

HYPERCATABOLIC STATE

- Unless they are symptomatic from hypocalcemia (eg, tetany or cardiac arrhythmia), patients with acute hypocalcemia and hyperphosphatemia due to a hypercatabolic state such as the **tumor lysis syndrome or massive trauma** **should not be treated with calcium until the hyperphosphatemia is corrected** to prevent calcium-phosphate precipitation.
- **Hemodialysis is often indicated** in such patients who have symptomatic hypocalcemia.

PSEUDOHYPOPARATHYROIDISM

- Similar to hypoparathyroidism
- **Infrequently develop hypercalciuria** with calcium and vitamin D therapy. Therefore, **the goal** of treatment with calcium and vitamin D is to maintain **normocalcemia** (rather than low-normal serum calcium as for other forms of hypoparathyroidism).
- Patients with PHP may also require screening for other endocrinopathies, particularly **hypothyroidism and hypogonadism**.

THANK
YOU

