Hypoparathyroidism
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Introduction

Background: Parathyroid hormone (PTH) works in conjunction with vitamin D to regulate total body calcium. The body secretes PTH in response to hypocalcemia or hypomagnesemia; the hormone then stimulates osteoclasts to increase bone resorption. PTH also acts indirectly through the stimulation or adenyl cyclase to increase renal tubular calcium resorption and phosphate excretion. Finally, it activates the conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D, the active form of vitamin D that stimulates calcium and phosphates absorption from the GI tract.

Hypoparathyroidism can result in hypocalcemia, and it commonly is diagnosed during the workup for hypocalcemia.

Pseudohypoparathyroidism describes hereditary conditions that cause end organs to be resistant to PTH.

Pathophysiology: Hypoparathyroidism can result from congenital disorders, iatrogenic causes (eg, drugs, removal of the parathyroid glands during thyroid or parathyroid surgery, radiation), infiltration of the parathyroid glands (eg, metastatic carcinoma, Wilson disease, sarcoid), suppression of parathyroid function, or idiopathic mechanisms.

Hypocalcemia is the most important consequence of hypoparathyroidism. Approximately half of serum calcium is ionized; the other half is bound to plasma proteins and other substances. The ionized calcium is physiologically active, and a significant reduction in ionized calcium level causes the signs and symptoms of hypocalcemia.

Frequency:

- In the US: The exact incidence is not known, but primary hypoparathyroidism is rare.

Mortality/ Morbidity: Hypocalcemia resulting from hypoparathyroidism can be treated with good outcome. Overall, mortality rate depends on the cause of the hypoparathyroidism.

Sex: Prevalence is equal in men and women.

Age: All ages may be affected.

Clinical

History: Symptoms occur when ionized calcium levels drop to less than 2.5-3 mg/100 ml. The symptoms are mainly neurologic, secondary to the hyperexcitability of neuronal membranes that develops in a low-calcium environment.

- Cardiac effects are limited because cardiac Tetany occurs at levels of hypocalcemia lower than those causing neurologic effects; therefore, the patient usually comes to medical attention prior to the onset of cardiac disturbances. At presentation, electrocardiogram (ECG) changes may be noted, but generally the heart is functioning normally.
- Neurologic effects in adults
  - Extremity and periorbital paresthesias
  - Muscle cramping and spasms
  - Altered mental status
  - Psychosis
- Pain
- Difficulty walking

- Neurologic effects in infants
  - Hyperirritability
  - Muscle rigidity with normal mental status
  - Seizures

**Physical:** The clinical manifestation of hypoparathyroidism is hypocalcemia.

- Neurologic effects
  - Hyperreflexia (Positive Chovostek or Trousseau sign is a classic sign of hypocalcemia.)
  - Tetany
  - Seizures
  - Altered level of consciousness

- Cardiovascular – Decreased contractility that can result in heart failure

- Infants
  - Vomiting
  - Abdominal distention
  - Apneic spells
  - Intermittent spells
  - Twitching, tremors, and seizures

**Causes:** Hypoparathyroidism has multiple etiologies.

- Congenital
  - Parathyroid aplasia
  - DiGeorge syndrome (dysgenesis of thymus and parathyroid glands)

- Iatrogenic
  - Surgery is the most common cause of hypoparathyroidism.
  - Hypoparathyroidism can occur after surgery resection of parathyroid adenoma. (This phenomenon often is transient, secondary to suppression of the other parathyroid glands.)
  - Total parathyroidectomy leads to hypoparathyroidism.
  - Thyroidectomy can lead to hypoparathyroidism because of parathyroid gland removal or destruction of the parathyroid vascular supply.

- Infiltration or destruction
  - Sarcoidosis
  - Wilson disease
  - Hemachromatosis
  - Metastatic carcinoma
  - Infarction
  - Radiation

- Suppression of the parathyroid gland
  - Hypomagnesemia – May be caused by pancreatitis, aminoglycosides, pentamidine, loop diuretics, cisplatin, and amphotericin B
  - Hypermagnesemia
  - Drugs – aluminum, asparagines, doxorubicin, cytosine, arabinoside, cimetidine
  - Idiopathic – Likely an autoimmune disorder; can occur is conjunction with other endocrine anomalies
  - Early onset – Autoimmune polyglandular syndrome type 1
  - Late onset – Kenny syndrome
• Hypoparathyroidism also can be sporadic.

**Differentials**

Candidiasis  
Hypermagnesemia  
Hyperphosphatemia  
Hyperventilation Syndrome  
Hypocalcemia  
Hypomagnesemia  
Hypoparathyroidism  
Renal Failure, Acute  
Renal Failure, Chronic and Dialysis Complications

**Other Problems to be considered:**

Increased protein binding of calcium  
Pseudohypoparathyroidism  
Vitamin D deficiency  
Rickets and osteomalacia  
Addison disease  
Pernicious anemia

**Workup**

**Lab Studies:**

- Findings supporting the diagnosis of hypoparathyroidism must include hypocalcemia, Hyperphosphatemia, and low parathyroid hormone levels in the absence of renal failure or intestinal malabsorption.  
- Total and ionized calcium are decreased. Normal total serum calcium levels range from 9-10.5 mg/dl (2.2 – 2.6 mmol/L). Normal ionized calcium levels are 4.5-5.6 mg/dL (1.1-1.4 mmol/L).  
- Radioimmunoassay (RIA) shows decreased PTH.  
- Serum magnesium can be low, high, or normal.  
- Serum phosphorous is increased.

**Imaging Studies:**

- X-ray: Bone density is increased; tooth roots are absent.  
- CT scan: Calcifications of cerebellum, choroids plexus, and basal ganglia can occur.

**Other Tests:**

- Electrocardiogram
  - ST and QT prolongation  
  - Terminal T-wave inversion

- Serum beta-carotene (normal)  
- D-xylose absorption  
- 72-hour stool fat absorption

**Procedures:**

- Slit-lamp examination may reveal early, posterior, lenticular cataract formation.

**Treatment**

**Prehospital Care:**

- Address and stabilize ABCs.  
- Obtain intravenous (IV) access.  
- Control seizures with benzodiazepine.
**Emergency Department Care:** In an emergent situation, treat empirically with calcium if severe hypocalcemia is suspected, and if seizures, Tetany, life-threatening hypotension, or cardiac arrhythmia are present.

- IV Calcium
  - 100-300 mg elemental calcium diluted in 150 mL D5W over 10 minutes (10-30 mL of 10% calcium gluconate [9.2 mg/mL elemental calcium]. This solution raises ionized calcium level by 0.5-1.5 mmol. Calcium chloride can be used but is irritating if extravasated.
  - Initial rate of infusion is 0.3-3 mg elemental calcium/kg/h. This scale is not exact; base subsequent adjustments on serial calcium measurements every 2-4 hours.
  - Infuse children with 2-mg/kg elemental calcium, or about 0.2 mL of 10% calcium gluconate/kg, IV.

**Consultations:** An endocrinologist may be consulted.

**Medications**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Calcium gluconate (Kalcinate) – Can be given IV initially, then maintained as high-calcium diet. Some patients require calcium supplementations.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adult Dose</strong></td>
<td>100-300 mg elemental calcium IV (10-30 mL of 10% calcium gluconate) diluted in 150 mL D5W over 10 min; initial rate of infusion is 0.3-2 mg of elemental calcium/kg/h</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>2 mg/kg of elemental calcium or about 0.2 mg of 10% calcium gluconate/kg</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Renal calculi; hypercalcemia; hypophosphatemia; renal or cardiac disease; digitalis toxicity</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>May decrease effects of tetracyclines, atenolol salicylates. Iron salts, and fluoroquinolones; when administered IV, antagonizes effects of calcium channel blockers; large intake of dietary fiber may decrease absorption and levels.</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>B – Usually safe but benefits must outweigh the risks.</td>
</tr>
<tr>
<td><strong>Precautions</strong></td>
<td>Caution when administering digitalized patients or to those with respiratory failure or acidosis or severe Hyperphosphatemia; closely monitor IV calcium supplementation because it can cause cardiac dysrhythmias.</td>
</tr>
</tbody>
</table>

**Drug Category:** *Vitamin D Supplement* – Vitamin D enhances absorption of calcium and maintains calcium homeostasis.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Ergocalciferol, Vitamin D-2 (Calciferol) – Stimulates absorption of calcium and phosphate from small intestine and promotes release of calcium from bone into blood.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adult Dose</strong></td>
<td>25,000-200,000 IU PO qd</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>50,000-200,000 IU PO qd</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Hypercalcemia or malabsorption syndrome</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>Colestipol, mineral oil, and cholestyramine may decrease absorption from small intestine; thiazide diuretics may increase effects of vitamin D</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>A – Safe in pregnancy</td>
</tr>
<tr>
<td><strong>Precautions</strong></td>
<td>Caution in impaired renal function, renal stones, heart disease, or arteriosclerosis.</td>
</tr>
</tbody>
</table>

**Further Inpatient Care:**

- Effects of 1 bolus of IV calcium will wane after 2 hours; therefore, subsequent continuous infusion is required to control hypocalcemia.
- Cardiac monitoring

**Further Outpatient Care:**

- Vitamin D-2 (calciferol) supplements
- Calcium supplementation

**Transfer:**

- May be considered after acute hypocalcemia is treated, if a specialist is needed
Complications:
- Neuromuscular symptoms (reversible)
- Cataracts
- Basal ganglia calcifications
- Growth stunting, tooth malformation, and mental retardation, if the condition starts early in childhood
- Hypothyroidism
- Parkinsonian symptoms
- Ossification of paravertebral ligaments

Prognosis:
- With appropriate monitoring and calcium and vitamin D supplementation, prognosis is fair.

Patient Education:
- Educate patients concerning regulation and effects of calcium on the body.
- Educate patients about the importance of periodic blood chemistry evaluation.

Bibliography

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