Child With Suspected Hypocalcemia

Suggestive history and physical findings	Initial laboratory and/or radiologic work-up can include:	When to refer	Items useful for consultation	Additional information
Symptoms: Neuromuscular irritability: paresthesias, muscle cramps, perioral numbness, carpopedal spasm, laryngospasm, seizures **Signs:** • Chvostek's sign – contraction of ipsilateral facial muscles upon tapping the facial nerve – may be seen in up to 10% of normal children • Trousseau's sign – carpopedal spasm elicited by inflating a blood pressure cuff above the systolic blood pressure for 3 minutes • QT interval prolongation Differential Diagnosis	**Blood tests:** • Total and ionized calcium • Albumin • Phosphorus • Magnesium • Alkaline phosphatase • Intact PTH • 25-OH Vitamin D • 1, 25-dihydroxy-vitamin D **Urine tests:** • Urine calcium to creatinine ratio **X-ray:** • Chest x-ray to look for thymus in DiGeorge syndrome • Wrist x-ray to rule out rickets	**Urgent:** If symptomatic, child needs to be admitted urgently and started on intravenous calcium therapy. **Routine:** Any asymptomatic child with persistently low calcium levels should be referred to a pediatric endocrinologist for further evaluation. Find a Pediatric Endocrinologist	Previous growth data/growth charts Pertinent medical records Recent laboratory and radiologic studies	Additional Information Vitamin D Deficiency and Rickets: A Guide for Families References

Differential diagnosis for hypocalcemia

The etiology of hypocalcemia is manifold. It is helpful to classify the etiology broadly into 3 categories:

- Parathyroid hormone related:
  - Hypoparathyroidism due to various causes either congenital or acquired
  - Pseudohypoparathyroidism : the parathyroid hormone is not able to act due to defective PTH receptor
- Vitamin D related
  - Vitamin D deficiency: Due to poor nutritional intake, malabsorption, liver disease or kidney disease leading to defective 25-hydroxylation and 1, α-hydroxylation respectively.
  - 1, α-hydroxylase deficiency leading to deficient active form of vitamin D.
  - Vitamin D resistance: Due to defective vitamin D receptor
- Nutritional calcium deficiency

Additional Information:

When evaluating a child for possible hypocalcemia, initial consideration should be:
1. Is it true hypocalcemia? Calcium is bound heavily to albumin in the blood stream. Hypoalbuminic states can cause hypocalcemia. In these cases however, the ionized calcium levels are maintained and thus the child is asymptomatic.
2. Is the child symptomatic? If child is having seizures or spasms due to hypocalcemia, then intravenous calcium therapy is indicated (doses are listed later in this section).

What to think about urgently:
If symptomatic, child needs to be admitted and started on intravenous calcium therapy. Since intravenous calcium is very irritating to the veins, care should be used. Preferably, therapy should be given using a central line.

Laboratory work up:

- Magnesium levels: Hypomagnesemia will result in hypocalcemia which will not respond to calcium treatment alone.
- Serum phosphorous level is a very important part of the work up and will help to establish the diagnosis. Low serum phosphorous is consistent with pathology in the vitamin D pathway. Deficient or ineffective vitamin D levels lead to elevated

parathyroid hormone which then increases the phosphorous excretion in the kidney leading to low phosphorous levels. An elevated phosphorous level is seen with poor kidney function or pathology in the parathyroid hormone pathway.

- Other blood tests to be considered are: Intact PTH, 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D level. Low 25-hydroxyvitamin D levels are consistent with nutritional Vitamin D deficiency. In this situation, 1,25-dihydroxyvitamin D levels may be normal or elevated due to the elevated PTH.

Treatment

Intravenous Calcium Therapy: Only indicated in symptomatic children or in children with prolonged QT interval. Two forms of intravenous calcium preparations are available, calcium gluconate (9% elemental calcium) and calcium chloride (27% elemental calcium) which are typically dosed according to elemental calcium content. Calcium gluconate is preferred as calcium chloride tends to cause more local irritation.

Calcium elemental ion concentration is each of these is as follows:

Calcium chloride: 10% solution	1 gram (10ml) =273mg of elemental calcium =13.6meq =6.8mmol
Calcium gluconate: 10% solution	1 gram (10ml) =93mg of elemental calcium =4.65meq =2.325 mmol

Maintenance Intravenous Therapy:

Maintenance intravenous therapy may be needed for a few days to maintain the serum calcium levels in a safe range. Urine calcium creatinine ratio should be monitored to prevent nephrocalcinosis and should be below 0.2. Children should be transitioned onto oral calcium when stable.

Oral therapy:

Asymptomatic children can be treated with oral calcium and vitamin D therapy. Until the cause of hypocalcemia is found, children may benefit from treatment with the active form of vitamin D (1, 25-dihydroxyvitamin D) at a dose of 20-40 ng/kg/day.

Usual treatment dose for oral calcium treatment is 50-100mg of elemental calcium/kg/day. The elemental calcium content of the various formulations is as follows:

CALCIUM SALT	% CALCIUM	mEq/g (CALCIUM)
Calcium acetate	25	12.5
Calcium carbonate	40	20
Calcium citrate	21	10.5
Calcium glubionate	6.5	3.3
Calcium gluconate	9	4.5
Calcium lactate	13	6.5
Calcium phosphate, dibasic	23	11.5
Calcium phosphate, tribasic	39	19.5

Suggested References and Additional Reading:

1. Allen W Root, Frank B. Diamond. Disorders of Mineral Homeostasis in children and adolescents. Pediatric endocrinology textbook by Mark A Sperling. Fourth edition.
2. Ping Zhou, Morri Markovitz. Pediatrics in Review Vol 30, No5, May 2009
3. Mark S Cooper, Neil J L Gittoes. Diagnosis and management of hypocalcemia. BMJ, 2008, 336:1298-302

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