Case Reports

Hypocalcemia Complicating Bicarbonate Therapy for Salicylate Poisoning

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SALICYLATES are an important cause of both accidental poisoning in children and suicidal overdoses in adults. Sodium bicarbonate ($NaHCO_3$) therapy has been widely recommended in the literature. A recognized but infrequently mentioned complication of alkali therapy is a reduction of ionized calcium.[1] The following case illustrates the development of symptomatic hypocalcemia with a low total serum calcium level during treatment of salicylate ingestion.

Report of a Case

The patient, a 14-year-old boy, ingested approximately 30 325-mg aspirin tablets. He began vomiting, had headache, tinnitus, orthostatic dizziness and symptomatic tachypnea, and arrived at the emergency room about six hours after ingestion. No other medications were taken. The patient had no prior history of drug overdose, was taking no maintenance medication and did not smoke or drink alcohol. Past medical history was unremarkable, with no evidence of growth disturbance, malabsorption or endocrinopathy.

On physical examination he was well developed and afebrile with a pulse rate of 100, respirations 28, blood pressure 120/80 mm of mercury and weight about 50 kg (110 lb). The patient was tachypneic with no neurologic abnormalities. There was no clinical evidence of pancreatitis or bone abnormality. Ipecac syrup was given with resultant emesis, followed by the administration of activated charcoal and cathartics.

Emergency room laboratory studies gave the following values: arterial pH of 7.44; oxygen partial pressure (tension; Po_2), 95 mm of mercury; carbon dioxide partial pressure (tension; Pco_2), 26 mm of mercury; bicarbonate (HCO_3), 18 mEq per liter (normal, 28 ± 4), and salicylate concentration, 60 mg per dl. Sodium bicarbonate, 50 mEq, was administered intravenously and a regimen of 5% dextrose in water with 100 mEq per liter of $NaHCO_3$ was begun at 100 ml an hour. Admission laboratory studies of specimens drawn about an hour after initiation of $NaHCO_3$ therapy gave the following values: serum calcium, 8.7 mg per dl (normal, 9.5 ± 1); phosphorus, 5.2 mg per dl (normal, 4 ± 1.5); sodium, 141 mEq per liter (normal, 140 ± 5); potassium 3.7 mEq per liter (normal, 3.5 to 5.0); chloride, 107 mEq per liter (normal, 100 ± 5); alkaline phosphatase, 309 IU per liter (normal, 30 to 300); albumin, 4.8 grams per dl (normal, 4.4 ± 0.9), and total protein, 7.0 grams per dl (normal, 7.0 ± 1). Glucose was 141 mg per dl (normal, 90 ± 15) and creatinine, 1.1 mg per dl (normal, 1.1 ± 0.5). Other laboratory studies showed no abnormalities. The serum salicylate concentration 2½ hours after admission declined to 48 mg per dl.

About nine hours after admission, the patient began having numbness and paresthesias of his face and extremities with pain in his extremities. He was afebrile and normotensive with a pulse of 100 per minute and respirations 24. He was alert, oriented and hyperpneic. Hypertonus, hyporeflexia, Chvostek's and Trousseau's signs were noted. The arterial pH was 7.52; Po_2, 88 mm of mercury; Pco_2, 29 mm of mercury, and HCO_3, 28 mEq per liter. Total serum calcium was 6.4 mg per dl; magnesium, 1.3 mg per dl (normal, 2.1 ± 0.3), and potassium, 3.1 mEq per liter. Phosphate and total protein levels were not rechecked; serum hormone levels and urinary electrolytes were not measured. An electrocardiogram (ECG) showed a rate of 88 with a very prominent U wave. Intravenous administration of HCO_3 was discontinued and the patient was given 200 mg of calcium as calcium gluconate intravenously over the next hour. The calcium therapy was continued over the ensuing five hours at 100 mg an hour. Potassium chloride replacement was also given intravenously, and magnesium sulfate was administered intramuscularly. Calcium and potassium were later administered by mouth.

The patient had considerable clinical improvement after initiation of therapy. Serial serum calcium levels rose, reaching 7.3 mg per dl at 1 hour, 8.5 mg per dl at 2 hours and 8.7 mg per dl at 11 hours after initiation of infusion. The serum potassium level corrected to 4.6 mEq per liter and the magnesium level to 2.0 mg per dl. The prominent U waves disappeared from the ECG tracing with correction of the electrolyte abnormalities. The patient continued to do well with no suggestion of underlying illness during the rest of his hospital stay. Discharge occurred on the fourth hospital day, 36 hours after discontinuation of calcium supplementation, with a serum calcium value of 8.7 mg per dl. The patient failed to keep follow-up appointments.

Comment

The recommended treatment of salicylate intoxication includes hydration with administration of potas-

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ABBREVIATIONS USED IN TEXT

ECG = electrocardiogram
HCO_3 = bicarbonate
$NaHCO_3$ = sodium bicarbonate
Pco_2 = carbon dioxide partial pressure (tension)
Po_2 = oxygen partial pressure (tension)

sium chloride and sodium bicarbonate until the salicylate level is therapeutic.[2] Recommendations for HCO_3 include initial administration of 88 mEq (two ampules) over the first one to two hours, followed by a maintenance solution containing 20 to 88 mEq per liter of HCO_3, depending on hydration state and the serum potassium level. An initial urine flow rate of 10 to 15 ml per kg of body weight per hour is recommended, followed by 3 to 6 ml per kg per hour. (Initial and maintenance solutions may need to be altered depending on the patient's serum and urine pH and urinary output.) Treatment of our patient fell within these guidelines; less than three ampules of $NaHCO_3$ had been infused by the time symptoms developed.

Reviews on the pathophysiology and treatment of salicylate toxicity occasionally mention tetany during the alkalotic phases of the condition.[3] Tetany has been presumed to be due to a diminution in ionized calcium, without necessarily altering measured total serum calcium. It has been stated that tetany is rarely severe unfewer than three ampules of $NaHCO_3$ had been infused amounts. Our case suggests that tetany may occur with the usual recommended HCO_3 doses for salicylate poisoning. Although it is possible the patient's tetany was due to alkalosis from his salicylate poisoning, his initial laboratory values suggest that this was not the case. The first salicylate concentration was in the range of mild toxicity, and subsequent levels declined. The initial arterial pH was 7.44, and a simultaneously drawn calcium level was normal, indicating that alkalosis during the prehospital phase of the overdose was not a contributing factor. Only after initiation of medical therapy did hypocalcemia become evident; discontinuing the $NaHCO_3$ therapy and administering calcium rapidly reversed the patient's symptoms.

We can only speculate about the pathogenesis of hypocalcemia in this patient. The first serum calcium level of a specimen drawn after administration of about 60 mEq of sodium bicarbonate was in the low-normal range. The possibility of inapparent underlying illness exists, though the patient's history and physical examination were compatible with that of an otherwise normal teenager. Alkaline phosphatase and phosphate levels were normal for age.

Alterations in hormonal control of serum calcium could be postulated; serum parathyroid hormone and calcitonin levels were not measured. Moderate hypomagnesemia was recorded in our patient, and it is known that profound hypomagnesemia interferes with parathyroid hormone secretion in vivo.[4]

A renal mechanism is also plausible, considering that kidneys filter 5,000 to 8,500 mg of calcium a day, with 90% to 95% of filtered calcium being resorbed by the renal tubules. A change in efficiency with which calcium is resorbed can greatly alter urinary calcium excretion and plasma calcium. Calcium complexes are not resorbed by the renal tubules, and under physiologic conditions, the acidity of tubular fluid inhibits calcium-anion interactions.[5] Therefore, administration of HCO_3 may interfere with the renal conservation of calcium.

In dogs there is a linear relationship of about 1:1 between ionized calcium clearance and sodium clearance during saline infusion, independent of urine pH. Urinary calcium loss accompanying excretion of the sodium load (as $NaHCO_3$) is also possible.[6]

Few reviews of salicylate poisoning recommend routine determination of serum calcium level during treatment. The compilers of Poisindex suggest measuring electrolytes, but no specific mention is made of calcium.[2] Hypokalemia frequently complicates salicylate overdose, and it should be noted that administration of potassium to a hypocalcemic patient can precipitate or worsen signs and symptoms of hypocalcemia.

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