Case Reports

Hypoglycemia With Salicylate Poisoning

A Report of Two Cases

ERNEST K. COTTON, MD
AND
VERA I. FAHLBERG, MD
DENVER

The possible causal association of hypoglycemia in patients with salicylism has recently been emphasized by Mortimer and Lepow.[1] They reported four deaths in infants less than 7 months of age in whom the severe hypoglycemia was believed to be related to salicylate ingestion. They also showed that severe hypoglycemia can be produced by feeding salicylates to a starved animal.

This paper reports two infants who developed severe hypoglycemia apparently secondary to salicylate poisoning; both of the children survived.

Report of Cases

CASE 1.—A 10-month-old white girl was admitted to the hospital because of lethargy and vasomotor collapse. Three days prior to admission, she developed a fever associated with a mild upper respiratory infection. She was treated with aspirin, two 1¼ grain (75 mg) tablets being given during her waking hours every four hours over the next three days. A total of 35 grains (2,250 mg) was consumed. The last dose of aspirin was administered about three hours prior to admission. On the day before admission, she refused solid food, and by the time of admission was only taking water.

On physical examination she was a well-nourished, well-developed, but very lethargic white female who responded only to painful stimuli. While being admitted to the hospital, she vomited and aspirated some blood tinged vomitus. Her weight was 10 kg (22 lb); temperature, 36.5 C (96 F) rectally; pulse, 135/minute; respirations, 36/minute; and systolic blood pressure, 95 mm Hg. The skin was cold, clammy, and pale. A serosanguineous discharge was seen at the nostrils. The pupils were dilated and reacted only sluggishly to light. Fundi were normal. The anterior fontanel was slightly depressed. Deep tendon reflexes were hyperactive and equal.

Complete blood count and urinalysis were normal. CO_2 combining power was 16 mEq/liter. A blood salicylate level, taken approximately four hours after the last dose of aspirin was 32 mg/100 ml. Spinal fluid examination revealed a clear fluid

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Ernest K. Cotton, MD, Department of Pediatrics, University of Colorado Medical Center, 4200 E Ninth Ave, Denver, Colo 80220.

From Department of Pediatrics, University of Colorado School of Medicine.

with no white cells, 1-2 red cells, 15 mg/100 ml of protein, and 0 mg/100 ml of sugar. Shortly before the administration of intravenous fluids was begun, a blood specimen was drawn and refrigerated. The blood glucose level, performed one hour later on the refrigerated specimen, was 0 mg%.

Initially, treatment consisted of intravenous fluids containing 5% glucose and 0.45% isotonic saline. When 100 cc of this fluid had been given, the child began to move and respond to stimulation. The results of the blood sugar determinations were available one hour after admission, but 20 ml of a solution of 10% glucose in water given intravenously did not produce any additional clearing of the sensorium. Over the next 24 hours she received 1,200 cc of 0.45% NaCl in a 10% glucose solution. By the end of this period, the patient was awake and responsive. Oral fluids were then started, but over a period of eight hours she again became lethargic and began to vomit. On examination she was found to have dilated pupils, a mild facial weakness, and an esotropia of the left eye. Intravenous therapy, with the 0.45% NaCl-5% glucose solution was restarted. A glucose determination was performed on a sample of blood obtained while glucose was being administered intravenously; the level was only 25 mg%. Approximately 36 hours after the last dose of aspirin had been ingested, the salicylate level was only 8 mg%. The abnormal neurological manifestations gradually cleared over the next 24 hours, and by the fourth hospital day she was completely responsive with only a mild choreo-athetosis of the face and upper extremities being present. On the fifth hospital day blood was drawn for a prothrombin time and cephalin flocculation determination. The cephalin flocculation was 0 and the prothrombin time was 100%. On her seventh hospital day she was asymptomatic and physical examination was normal.

A three-hour oral glucose tolerance test was done on the tenth hospital day using 2.0 gm glucose/kilogram. Normal values were obtained: fasting level—74 mg%; 30-minute level—124 mg%; 60-minute level—108 mg%; 120-minute level —80 mg%; and 180-minute level 68 mg%. A repeat glucose tolerance test was done on the 16th hospital day. Prior to this test, the patient received 5 grains (300 mg) of aspirin every six hours for three doses. Blood salicylate level reached 26 mg/100 ml. The repeat glucose tolerance results were similar to the original results, fasting level being 68 mg%; 30-minute level—118 mg%; 60-minute level—110 mg%; 120-minute level—78 mg%; and 180-minute level—72 mg%.

She was discharged on the 18th hospital day. On follow-up examination, five months later, she was developing normally and presented no neurological abnormalities.

CASE 2.—A 2-year-old white male was admitted in coma after having ingested an unknown quantity of 5 grain aspirin tablets 24 hours previously. Prior to taking the aspirin he had been in good health and had been eating normally. Two hours after ingesting the tablets his stomach was lavaged and a bicarbonate solution instilled. Eight hours later the respiratory rate increased and he was noted to be confused. At that time he was admitted to another hospital where he received 400 ml of a 1/6 M sodium lactate solution, intravenously. Despite this treatment his sensorium gradually became more clouded and by 20 hours after ingestion he was unresponsive. On physical examination at the University of Colorado Medical Center, he was a well-developed white male who weighed 13.5 kg (29.7 lb). He was unresponsive to painful stimuli and had a fixed gaze and deep respirations. No other abnormalities were found. Initial laboratory determinations revealed a serum salicylate of 46 mg/100 ml, a serum bicarbonate content of 12.2 mEq/liter, and a blood glucose of 5 mg/100 ml. Serum sodium, chloride, and potassium levels were normal.

Ten milliliters of a 50% glucose solution was given intravenously and this resulted in an immediate return of a normal sensorium with complete clearing of the neurologic manifestations. Intravenous therapy of 1,800 ml of a 0.45 NaCl-20% glucose solution was given over the next 24-hour period. Food or liquids were not given by mouth during this period.

Twelve hours after admission, the serum salicylate level was 30 mg/100 ml and the serum glucose was 120/100 ml. Twenty-four hours later, the salicylate level had dropped to 6 mg%.

On the third hospital day, an oral glucose tolerance test was performed using 2.0 glucose/kg. The resultant curve was normal with levels of: fasting—58 mg%; 30 minute—120 mg%; and 180 minute—60 mg%. The glucose tolerance test was repeated after a period of fasting during which the patient received 10 grains (600 mg) of aspirin every four hours for two doses. The salicylate level rose only to 13 mg%; the fasting blood sugar was 58 mg%. Since the fasting blood sugar was unaltered, the remainder of the glucose tolerance test was not completed.

Six months after hospitalization the patient was reexamined by his private doctor and found to be in good health with no evident abnormalities.

Comment

Until recently the possible association of hypoglycemia with salicylate poisoning was not generally recognized. In 1942 Barnett et al [2] reported a case of hypoglycemia with

salicylism in a 20-month-old child who was treated with 740 cc of a Lactated-Ringers solution until the hypoglycemia was discovered. The report of Mortimer and Lepow,[1] in which they described four infants with varicella who died with severe hypoglycemia, focused attention on the possibility that the hypocemia might result as a complication of salicylism. They also postulated that a severe infection, such as varicella, could have played a major role in producing disturbed carbohydrate metabolism.

Mortimer and Lepow found that hypoglycemia was produced in fasted rats given salicylates while fasted rats given sodium bicarbonate failed to show an alteration in blood glucose levels.

The exact metabolic changes producing hypoglycemia in individuals with salicylism are unknown. Salicylates have been shown to influence carbohydrate metabolism by causing a marked reduction or disappearance of liver glycogen.[3,4] Interference with adenosine triphosphate formation seems to play a role whether this occurs by "uncoupling" high energy phosphate bonds or by other mechanisms has not been made clear.[5] This metabolic interference and the combination of increased glucose consumption and decreased synthesis of carbohydrate could be the cause of the reduced blood glucose.

There is no ready explanation for the rarity of this condition. Since most therapeutic regimes include the administration of glucose given intravenously this may act to prevent the symptoms of hypoglycemia from developing.[6]

Only one of our patients had any signs of infection, a mild upper respiratory infection; however, for the 24 hours prior to the time that blood salicylate levels were found to be elevated, neither child had had any appreciable intake of calories.

Since severe hypoglycemia may produce significant brain damage, it should be considered in all cases of salicylism, especially in infants whose diet has been restricted. Determination of blood glucose should be a part of the evaluation of any case of lethargy or coma where the child may have received salicylates.

Summary

Two infants with salicylism and severe hypoglycemia have been reported. Both infants survived without neurological sequelae. The possible pathogenesis of hypoglycemia in children who have received salicylates is discussed. A recommendation is made for the determination of blood glucose in any case of lethargy or coma where an infant or child may have received salicylates.

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