acta medica

TECHNICAL NOTE

Symptomatic hypocalcemia due to Shohl's solution in a newborn with galactosemia and a solitary kidney

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Received 7 December 2014; accepted 22 December 2014; published online 13 January 2015

ABSTRACT

Proximal tubular defects (renal Fanconi syndrome) may occur secondary to some inborn errors of metabolism. Shohl's solution is used in renal Fanconi syndrome for the treatment of metabolic acidosis. Herein, we report a newborn with galactosemia, a solitary kidney and renal Fanconi syndrome who developed hypocalcemic convulsions under Shohl's solution treatment. Experience and knowledge regarding treatment with Shohl's solution in neonates is limited. We thus recommend that clinicians should be cautious regarding the possibility of hypocalcemia while administering Shohl's solution in newborns.

Key words: Hypocalcemia, Shohl's solution, newborn.

Introduction

Proximal tubular defects may occur secondary to some inborn errors of metabolism, such as cystinosis, tyrosinemia type 1, galactosemia, oculocerebrorenal syndrome (Lowe's syndrome), Wilson's disease, and hereditary fructose intolerance. This condition is referred to as renal Fanconi syndrome and is associated with impaired reabsorption of amino acids, phosphate and glucose as well as bicarbonate. Administration of alkali treatment such as sodium bicarbonate, Shohl's solution may be required to normalize plasma HCO_3^-levels (1).

Herein, we report a newborn with galactosemia, solitary kidney and renal Fanconi syndrome who developed seizures due to hypocalcemia while under Shohl's solution treatment.

Case presentation

A male infant from the first gestation of an 18 –year-old mother was delivered by cesarean section subsequent to a 39 weeks of gestation, weighing 3250 g. There was no consanguinity between parents. The baby was fed with breast-milk only. On the third day of life, jaundice developed, and he received phototherapy until the seventh day of life. He was admitted to a local hospital for unresolved jaundice and weight loss and during the subsequent evaluation hepatomegaly and cholestasis were detected, as additional pathologies. At 17 days of age, he was referred to our hospital. On admission, his body weight was 2810 g (3rd percentile), length 50 cm (10th percentile) and head circumference 35 cm (10–25th percentile). The physical examination revealed body weight loss (440 g, 13.5 %), yellow-green discoloration of the skin and hepatomegaly; other signs were normal.

Laboratory examination on admission revealed cholestasis (total/direct bilirubin 7.7/6.24 mg/dl), mild hypertransaminasemia (alanine/aspartate aminotransferase [ALT/AST] 49/127 mg/dl), and elevated alkaline phosphatase (813 IU/L). Serum biochemical analysis revealed sodium 145 mEq/L, potassium 3.7 mEq/L, chloride 116 mEq/L, urea 14.1 mg/dL, creatinine 0.72 mg/dL, calcium 9.8 mg/dL, ionized

calcium 1.2 mg/dL, phosphorus 2.6 mg/dL, blood glucose 56 mg/dL, and gamma glutamyl transpeptidase 25 mg/dL. Blood gas analysis was normal (pH7.33, PCO_2 36.8 mmHg, HCO_3 19.3 mEq/L). Urine analysis revealed low pH (5.5), proteinuria (300 mg/dL), generalized aminoaciduria, glucosuria (200 mg/dL), and normal density. Urinary reducing substances were detected as positive (++++) and wide galactose spot was shown by urine chromatography. A diagnosis of galactosemia was made, breastfeeding was stopped, and lactose-galactose-free formula was started. Shohl's solution (140 g citric acid and 98 g sodium citrate in 1000 mL distilled water) at a daily dose of 2 mEq/kg was initiated to prevent development of metabolic acidosis with a diagnosis of renal Fanconi syndrome. Abdominal-renal ultrasonography demonstrated hepatomegaly, contracted gallbladder and enlarged right kidney (vertical length 64 mm), but the left kidney was not visualized. There was no bacterial growth on urine culture. After seven days (on the 28th day of life), the patient developed a generalized seizure. We detected hypocalcemia (total calcium 6.49 mg/dL, ionized calcium 0.88 mEq/L, phosphorus 10.6 mg/dL) as the underlying etiology leading to seizure; other serum biochemical findings were normal. Plasma parathormone level was 200 pg/mL (normal range 10-60 pg/mL), plasma magnesium 1.51 mg/dL (normal range 1.6-3 mg/dL), serum pH 7.37, plasma HCO_3 29.9 mmol/L. Urine pH 7.0 and density 1002, and no proteinuria or glucosuria were detected concomitantly. Lumbar puncture was performed, showing normal protein and glucose levels (63.7 mg/dL, 46 mg/dL, respectively); no leukocytes or bacteria were detected, and culture was negative. Dietary daily intake of elementary calcium was 140 mg/kg and of phosphorus was 68 mg/kg. Symptomatic hypocalcemia was treated with intravenous calcium gluconate infusion (50 mEq/kg/day), and Shohl's solution was stopped and was not given again. No seizures were observed after calcium infusion initiation. The calcium infusion treatment was stopped by the 2ndday. The patient was discharged on the 30th day of life with normal blood calcium and phosphorus levels. Homozygous galactose-1-phosphate uridyl transferase mutation was detected in genetic analysis.

When the patient was five-months-old 1.7 mCi ^{99m}TcDMSA scintigraphy was performed and left renal agenesis was confirmed. It was detected by scintigraphy that the right kidney was in normal dimension and location, with no cortical damage. No uptake was observed at the left renal region and at any ectopic location.

The last time the patient came to our outpatient clinic for control was at 3.5 years of age. The blood calcium, phosphorus, PTH, 25-OH vitamin D levels and urinalyses performed during the outpatient follow-up has remained normal.

Discussion

Shohl's solution is used in tubular function defects such as distal renal tubular acidosis (dRTA) and renal Fanconi syndrome for the treatment of metabolic acidosis in pediatric patients (1,2). In this case, we thought that renal Fanconi syndrome developed secondary to galactosemia, and Shohl's solution was initiated to prevent the occurrence of metabolic acidosis.

As these diseases are not frequently observed in the neonatal period, experience and knowledge regarding treatment with Shohl's solution in neonates is limited. In the literature, there are a few case reports about some adverse effects of Shohl's solution administration in children (3). Vomiting and diarrhea in a newborn with distal renal tubular acidosis during Shohl's solution treatment has previously been reported which was reversed by the cessation of the Shohl's solution (3). In our patient in the current report, gastrointestinal symptoms were not observed.

Shohl's solution includes citric acid and sodium citrate. Profound hypocalcemia caused by parenteral citrate was reported in an elderly adult patient with multiple organ failure and rhabdomyolysis. This patient had received parenteral citrate treatment to provide regional anticoagulation of the extracorporeal circuit. On follow–up, the patient had developed hypocalcemia requiring increasing amounts of intravenous calcium replacement. The cause of hypocalcemia was related to the binding of citrate with ionized calcium, in addition to sequestration of intracellular calcium due to the rhabdomyolysis in this particular patient (4).

It is known that the ionized calcium level decreases in an alkaline environment. As the plasma pH values were in normal ranges during the treatment with Shohl's solution in this case, we attributed the symptomatic hypocalcemia to binding of citrate to calcium.

To our knowledge, there is no data in the reported literature about the effect of oral Shohl's solution on calcium absorption from the intestine and

additionally no data regarding the action mechanism of Shohl solution affected by lactose-galactose-free diet. However, in our case, the orally administered citrate may have caused hypocalcemia due to the prevention of calcium absorption from the intestine. A similar mechanism was discussed in a previously reported case (4). We thus recommend that clinicians should be cautious regarding the possibility of hypocalcemia while administering Shohl's solution in newborns.

A congenital solitary functioning kidney may be an isolated congenital malformation or it may be associated with various chromosomal or non-chromosomal anomalies such as cardiac, genital, skeletal, gastrointestinal, urological, and respiratory abnormalities (6). Both congenital solitary kidney and galactosemia are very rare and separate entities (5,6). To date, no previous case with congenital solitary kidney accompanied to galactosemia has been reported in the literature.

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