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Glucose Galactose Malabsorption: A Case Report

M ***Mutlu***, M ***Cakir***, Y ***Aslan***

Abstract Glucose-galactose malabsorption (GGM) is a rare autosomal recessive disorder of intestinal transport of glucose and galactose, leading to watery diarrhoea, dehydration, failure to thrive, or early death. It is caused by mutations in the gene coding for the intestinal brush border of sodium-glucose co-transporter. Treatment includes the elimination of glucose and galactose from diet. We report a female newborn with suspected GGM. She presented with the classical features of the disease including severe recurrent hypernatremia. Her symptoms rapidly improved with fructose based diet.

Key words Glucose-galactose malabsorption; Hypernatremia

Introduction

Lactose is present in breast milk and infant formula. It is broken down into the glucose and galactose in the intestinal tract. These sugars are absorbed from intestinal tract by sodium-glucose co-transporter (SGLT). Three types SGLT have been identified. SGLT1 is responsible for glucose and galactose absorption from the intestinal tract. SGLT2 is localised to the renal tubules and lesser degree in ileum. SGLT2 together with SGLT1 are responsible for glucose absorption in the renal tubules. SGLT3 is localised to the plasma membrane of enteric neurons and skeletal muscle.[1-3] Glucose-galactose malabsorption (GGM) is caused by mutations in the gene coding for the intestinal brush border SGLT1.[4] It is characterised by neonatal onset of profuse osmotic watery diarrhoea secondary to accumulation of unabsorbed glucose and galactose in the intestinal lumen and can lead to severe dehydration, metabolic acidosis and death if left untreated. Typically, the diarrhoea immediately improves by the elimination of glucose and galactose from diet.[5] Herein, we report an infant with GGM presented with the classical feature of the disease in addition to severe recurrent hypernatremia.

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Case Report

A 16-day-old Turkish girl was admitted to our newborn outpatient clinic with diarrhoea, poor feeding, fever and moaning. She was born at 35 gestational weeks after an uneventful pregnancy with a birth weight of 2600 g. She was the second child of a consanguineous parents and her elder brother was healthy. Antenatal history was normal, and she was healthy at birth. She was fed with breast milk soon after the birth and her initial neonatal period were uneventful. Watery and profuse diarrhoea (15 to 20 times/day and approximately 150 ml/kg, measured by weighing the napkin) was developed within one week after birth. Fever and moaning was then noted three days before the admission. On admission, she was ill looking and had the

signs of dehydration such as lethargy, confusion, tachypnea and hypotension. Laboratory examination at initial examination revealed the followings: haemoglobin of 11.4 g/dL, glucose 148 mg/dL, sodium 182 mmol/L, potassium 5.3 mmol/L, chloride 158 mmol/L, blood urea nitrogen (BUN) 58 mg/dL, creatinine 1.5 mg/dL, calcium 13.9 mg/dL, magnesium 3.5 mg/dL, phosphate 5.0 mg/dL, bilirubin 7.4 mg/dL. Arterial blood gas analysis showed severe metabolic acidosis with a pH of 7.121, serum bicarbonate (HCO3) 10.6 mmol/L, base excess (BE) -21 mmol/L, pCO2 26.1 mmHg and pO2 102 mmHg. Urine analysis was normal.

Hypernatremic dehydration, metabolic acidosis and pre-renal azotemia were treated with appropriate intravenous fluid (hydration, bicarbonate and to decrease serum Na by about 8-10 mEq/L/day). The clinical findings and biochemical parameters of the patient improved without any complication. However, watery diarrhoea, hypernatremic dehydration and biochemical abnormalities recurred after the infant was re-fed with breast milk. At this time, she was fed with lactose free glucose as carbohydrate content, (Bebelac LF®), soya (corn starch as carbohydrate content, Aptamil Som Soya®) and amino-acid based formula (corn starch as carbohydrate content, Neocate®) sequentially; but diarrhoea did not improve and biochemical abnormalities recurred. Laboratory findings of the patient during the different feeding regimens are shown in Table 1.

Thyroid function tests and sweat tests were within the normal limits, and both echocardiography and abdominal ultrasonography were normal. Ophthalmologic examination for the cataract was negative. Metabolic tests for abetalipoproteinemia, lysinuric protein intolerance, **disorders of bile acid synthesis**, autoimmune markers for autoimmune enteropathy and tests for polyendocrinopathy were normal. Microscopy and stool culture were negative. Infectious agents including CMV, HIV, rotavirus and adenoviruses were ruled out. Stool pH was 6, and stool sugar testing by Clinitest was positive. No fat droplet was detected in stool examination. Stool osmolarity was compatible with osmotic diarrhoea (osmotic gap: 145 mOsm/kg).

Fecal sugar chromatography could not be performed because of failure to acquired appropriate stool samples due to excessive watery diarrhoea. Glucose loading test with 2 g/kg oral glucose revealed a flat serum glucose curve with fasting. Blood glucose was measured 0, 30, 60, 90, 120 minute after the loading of glucose and blood glucose levels were 79, 97, 101, 96, and 87 mg/dL, respectively.[6]

Glucose-galactose-free, fructose-based formula (Galactomin B-19®, Nutricia), was initiated for the suspected GGM at the age of 32 days; and diarrhoea improved rapidly, compliance to fructose- based formula was excellent and the patient increased from 2800 g to 3400 g within two weeks.

Discussion

Glucose-galactose malabsorption is an inherited metabolic disorder characterised by the small intestine's

Table 1 Laboratory findings of the patient during different feeding regimens

	At admission	Breast feeding	Lactose free or soya based diet	Glucose-galactose free diet
Sodium (mmol/L)	182	168	169	139
Chloride (mmol/L)	158	138	138	114
BUN (mg/dL)	58	42	27	17
Creatinine (mg/dL)	1.5	0.3	0.4	0.2
Calcium (mg/dL)	13.9	11.8	11	9.5
Phosphate (mg/dL)	5.0	7.8	5.9	4.2
Arterial pH	7.12	7.38	7.39	7.40
HCO3 (mmol/L)	10.6	14.9	17.4	22.4
BE (mmol/L)	-21	-10.2	-7.5	-2.6
Urine Ca (mg/dL)	20.5	59.4	35.4	4.5
Urine Cr (mg/dL)	14.5	27.3	18.9	29.6
Urine Ca/Cr	1.41	2.17	1.87	0.15
Stool reducing substance	+	+	+	-

inability to transport and absorb glucose and galactose (simple sugars or monosaccharide). Affected infants experience severe diarrhoea resulting in life-threatening dehydration, increased acidity of the blood and tissues (acidosis), and weight loss when fed breast milk or regular infant formulas. Diagnostic criteria for congenital GGM are: 1) onset of diarrhoea shortly after initiating glucose galactose containing feeds; 2) glucose-galactose malabsorption evidenced by presence of reducing substance in stool; 3) a normal intestinal biopsy (no evidence of enteropathy); 4) flat blood glucose curve or positive glucose breath hydrogen test following oral glucose load and diarrhoea promptly stopped after initiating fructose containing feeds.[1,7,8] Contrary to glucose and galactose, fructose is transported across the brush border by the facilitated fructose transporter (GLUT5).[1,8] Diagnosis of GGM may also be made by measuring sugar and amino acid evoked potential differences in the jejunum in vivo.[7] Our patient was diagnosed to have GGM because of the onset of diarrhoea shortly after breast feeding, acidic stool pH and positive reducing substance, flat blood glucose curve following oral glucose load, non response to lactose free and amino acid based diet and improving in diarrhoea promptly after starting fructose-based formula, but we could not able to perform genetic study. There have been very few reports of GGM in Turkish population, but this is the first case in our center.

Differential diagnosis of GGM should have been made with congenital chloride diarrhoea, congenital sodium diarrhoea, microvillus atrophy, acrodermatitis enteropathica, hormonally mediated secretory diarrhoea, short bowel syndrome, disorders villous architecture such as microvillus inclusion disease, intestinal epithelial dysplasia (tufting enteropathy), milk protein allergy, autoimmune enteropathy, disaccharidase deficiencies and cystic fibrosis.[1,8-13] Our patient did not have skin lesions for acrodermatitis enteropathica, stool chloride levels and sodium levels were not compatible with congenital chloride diarrhoea, congenital sodium diarrhoea, respectively. **Additionally, she did not have the clinical features of phenotypic diarrhoea**. We could not perform intestinal biopsy because of no suitable endoscope such a small infant, but improvement in diarrhoea only after fructose-based formula support the diagnosis of GGM in our patient. Primary or secondary lactase and sucrose deficiency may also present with intractable diarrhoea in the early infancy but diarrhoea generally improves after hydrolyzed formulas. Sweet chloride test were negative for cystic fibrosis.

Hypernatremic dehydration in general is common in breast-fed infants. Most of them underwent sepsis evaluations. Non-metabolic complications occurred in 17% of these infants, with the most common being apnoea and/or bradycardia.[14] Findings of hypernatremic dehydration in breast-fed infants with watery diarrhoea and sugar in the stool should lead to the consideration of monosaccharide intolerance such as glucose-galactose malabsorption. Hypernatremic dehydration occurs because of excessive water losses from the body due to osmotic diarrhoea. The frequency of hypernatremic dehydration in children with GGM has been reported to be 25%.[7] Hypercalcemia probably results from either metabolic acidosis or enhanced calcium absorption in the ileum, as facilitated by non-absorbed lactose. Hypercalcemia improves after initiating glucose and galactose free diet. Nephrocalcinosis, nephrolithiasis and renal tubuler acidosis in patients with GGM have been described previously.[5,8-10] In long term, patients may have renal or cardiovascular complications, but none have reported in patients under strict diet adherence.

In the early infancy, fructose based formulas are sufficient for the nutritional management. After weaning period; strained fruits or vegetables with higher fructose content may be introduced such as pears, applesauce, peas, potatoes and creamed corn. As children get older, meats, eggs, fats and small amount of glucose can be added to the diet. Affected children learn to adjust the amount of glucose they can eat in order to limit their diarrhoea.[15]

GGM is a rare disorder and leads to osmotic diarrhoea, recurrent hypernatremia and dehydration in early days of life. Neonatologists must keep in mind GGM in cases with severe diarrhoea associated with hypernatremia and metabolic acidosis in the neonatal period. If diagnosed early, fructose based formula can promptly improve the symptoms.

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