A rare case of intestinal malabsorption: glucose-galactose malabsorption

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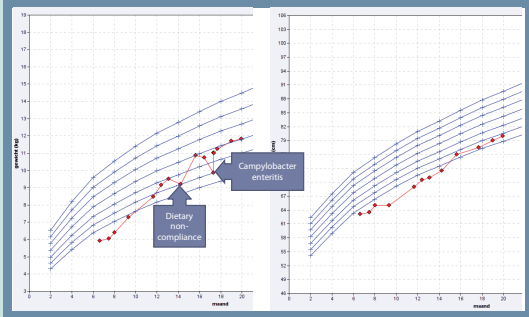
INTRODUCTION

- Cotransporters are a major class of integral membrane proteins responsible for the absorption of various solutes across the plasma membrane.
- The sodium/glucose cotransporter (SGLT1) couples the transport of sodium and glucose across the brush border of the small intestine.
- Glucose/ galactose malabsorption (GGM) is an autosomal recessive disorder caused by defects of SGLT1 (SLC5A1 gene)

Case Report

Clinical presentation

- A boy, born to non-consanguineous Belgian parents
- After a normal full-term pregnancy
- Shortly after birth his stools became progressively frequent and watery, and he was hospitalized with life-threatening dehydration with hypernatremia
- After discontinuing the enteral diet, his diarrhea stopped, and subsequent attempts to introduce lactose, dextrin maltose or glucose containing foods resulted in further bout of diarrhea
- The pediatrician thought of a GGM and referred the child to our unit of inherited metabolic diseases.
- A carbohydrate-free formula (Basic-CH, Nutricia, The Netherlands) with added fructose was started, and he has thrived since without further episodes of diarrhea under Basic-CH, fructose.
- After 9 months of age fruits and some vegetables were introduced in his diet
- Small amounts of other foods that contain glucose, galactose and starch are not tolerated



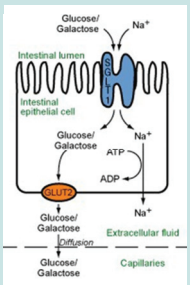
Growth charts: before and under dietary treatment

Diagnosis

- The SLC5A1 gene (chrom 22q12.3) was completely sequenced* and he was found to be heterozygous for the missense mutations c706T>G (exon 8) (p.Y236D) and c.1012C>G (exon 9)(p.L338V)
- Both mutations are not yet published: They are considered pathogenetic as at both sides a well-conserved amino acid is altered
- The molecular genetic testing confirmed the diagnosis of GGM or SGLT1

* Center for Nephrology and Metabolic Disorders Molecular Genetic Laboratory (Germany)

Co-Transporter SGLT1



Co-transport of sodium and glucose or galactose by SGLT1.

For every two sodium ions SGLT1 moves inside the cell down the sodium concentration gradient, one glucose or galactose molecule moves with it.

The glucose/galactose is then transported Into the extracellular fluid by GLUT2, and diffuses into the capillaries.

Sodium is actively transported out of the cell into the intercellular space so as to maintain the intracellular sodium concentration gradient.

SGLT1 deficiency/glucose galactose malabsorption (GGM)

- A very rare inherited (autosomal recessive) metabolic disease
- Half of the 200 severe GGM cases found worldwide result from familial intermarriage
- Usually the mutations carried by GGM individuals result in **nonfunctional truncated SGLT1 proteins** or in the **improper placement of the proteins** such that they can not transport glucose and galactose out of the intestinal lumen
- Infants will thrive on a fructose-based replacement formula and will later continue their "normal" physical development on a fructose-based solid diet.
- Older children and adults with severe GGM can also manage their symptoms on a fructose-based diet and may show improved glucose tolerance and even clinical remission as they age
- Half of the 200 severe GGM cases found worldwide result from familial intermarriage
- Usually the mutations carried by GGM individuals result in nonfunctional (truncated) SGLT1 proteins or in the trafficking of the proteins such that they can not transport glucose and galactose out of the intestinal lumen
- Differential diagnosis:
  - Congenital lactose intolerance
  - Infantile lactase deficiency
  - Sucrase/isomaltase deficiency

Dietary treatment: specifications

- Diet restricted in lactose, glucose, dextrin maltose, starch
- Bottle feeding with Basic-CH (Nutricia) and fructose-module (Nutricia)
- MCT oil (Nutricia) was given to provide enough calories
- Limited amount of vegetables with <0.5g CH/100g (allowed vegetables see list)
- A small amount of bread and fruit is tolerated
- Home-made 'pancake' and 'pudding' with Basic-CH
- Pitfalls:
  - Very restricted diet, limited options to extend diet
  - Diet compliance is difficult, resulting in diarrhea with the risk of dehydration

CONCLUSION

- We report a case of a very rare inherited metabolic disease causing a severe intestinal malabsorption syndrome
- Glucose galactose malabsorption was diagnosed on clinical base and confirmed by molecular analysis
- Very restricted diet with avoidance of glucose, dextrin maltose, galactose, lactose and starch with limited options to extend the diet
- Diet compliance is difficult, resulting in diarrhea with the risk of dehydration
- Older children and adults with severe GGM can also manage their symptoms on a fructose-based diet and may show improved glucose tolerance and even clinical remission as they get older