Erroneous glucose recordings while using mutant variant of quinoprotein glucose dehydrogenase glucometer in a child with galactosemia

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ABSTRACT
We report a 2-month-old child with galactosemia and falsely high glucose readings with a glucometer using mutant variant of quinoprotein glucose dehydrogenase (MutQ-GDH) chemistry. Potentially fatal hypoglycemia could have been induced in the child if insulin infusion had been initiated as per glycemic management protocol. Even though, the product information with the glucometer carries warning regarding interference by high galactose levels, the awareness regarding this interaction is generally poor in many practice settings. Although, false readings have been reported with glucose dehydrogenase pyrroloquinoline quinone (GDH-PQQ) glucometers, to our knowledge this is the first case report of a falsely high glucose reading due to high galactose in a proven case of galactosemia with a glucometer using the MutQ-GDH chemistry (a modified GDH-PQQ chemistry). Our experience has prompted us to write this case report and we suggest avoiding these glucometers in neonates and infants when a metabolic disease is suspected.

Key words: Galactosemia, glucose dehydrogenase pyrroloquinoline quinone glucometers, hypoglycemia, mutant variant of quinoprotein glucose dehydrogenase chemistry, neonate

INTRODUCTION

Glucometers, which employ the glucose dehydrogenase pyrroloquinoline quinone (GDH-PQQ) are known to produce falsely high recordings of capillary glucose in the presence of interfering substances like maltose and galactose.[1] The food and drug administration (FDA) did recommend that these meters should not be used in hospital settings.[2] Following this public health notification GDH-PQQ glucometers have been supplanted by glucometers using mutant variant of quinoprotein glucose dehydrogenase (MutQ-GDH) chemistry which is a maltose independent advanced chemistry.

We report a child who had falsely high capillary glucose values with a MutQ-GDH glucometer.

The child was later proven to have galactosemia and the falsely high capillary glucose was due to a cross reaction with galactose.

CASE REPORT

A 2-month-old male child was admitted to our hospital for jaundice and failure to thrive. The child was the first child born of a third degree consanguineous marriage. His birth weight was 3.5 kg. At 1 month of age, the child was noticed to have a yellowish green discoloration of the conjunctiva. The parents reported feeding difficulties and poor weight gain. His current weight was 2.8 kg. He was anemic, icteric and had hepatomegaly. The liver function tests revealed a cholestatic pattern. Admission arterial blood gas was suggestive of compensated metabolic acidosis with a high anion gap. His urine examination revealed ketonuria. Upon
admission, random capillary glucose was performed, which revealed a value of 310 mg/dL [Table 1].

Subsequent readings taken every hour for the next 6 h were above 250 mg/dL. Capillary glucose testing was performed using Accu-Check® Performa (Roche diagnostics, Mannheim, Germany) glucometer. In view of suspected diabetic ketoacidosis, an endocrinology consultation was sought and hydration and insulin infusion were considered. However, the corresponding random venous plasma glucose was 67 mg/dL (performed using glucose oxidase method) and there was an absence of glucosuria. Hence, it was decided to withhold insulin infusion and potentially fatal hypoglycemia was avoided. In view of a possible cross reaction of high galactose with the glucometer, which employs a MutQ-GDH chemistry further testing was not performed using the same glucometer. A Benedict’s test of urine showed the presence of reducing sugars. A quantitative test for galactose-1-phosphate uridyl transferase in whole blood showed a value of 3.85 U/g Hb (normal range 11-41.0 U/g Hb).

Quantitative test for galactose 1-phosphate in red blood cell was 1.8 mg/dL (normal range 0-1 mg/dL). A liver biopsy revealed macrovesicular steatosis with bile duct proliferation and a fibrosis score of 4/6 [Figure 1].

The child was started on a galactose free formula. He showed steady improvement with resolution of jaundice and weighed 4.0 kg on repeat examination 1 month later.

**DISCUSSION**

Galactosemia is a rare condition with a prevalence of 1 in 60,000 live births among caucasians. Diagnosis of galactosemia is usually made by a new born screening test in western countries. In India, new born screening for galactosemia is not widely prevalent.

A prospective screening study for galactosemia in 18,000 newborns in India identified a single case of galactosemia with an estimated prevalence of 1:10,300.[3] However, the exact prevalence of galactosemia in India is still not clear.

Point of care testing devices like glucometers are increasingly being used in hospital care settings. Hence, it is important that the practicing clinician is aware of the technical deficiencies associated with these devices. There are mainly four sources of errors associated with glucometers. Pre-analytical errors include damage to the test strip or incomplete deposition of reagent on the test strip. Analytical errors deal with the technique of testing and includes insufficient or excessive blood loading, miscoding, calibration errors and those arising from contamination. Post-analytical errors result from misleading of the result display. Operator dependent errors can be divided into two, namely those involving glucometers using glucose oxidase chemistry and those involving GDH-PQQ chemistry.

Hypertriglyceridemia, hyperuricemia, hypoxia and acetaminophen can interfere with glucometers using the glucose oxidase chemistry. Diet or medication containing excessive galactose, maltose, xylose and vitamin C can interfere with glucose dehydrogenase (GDH) biosensor.[4]

A previous analysis of the food and drug administration’s (FDA) manufacturer and user facility device experience (MAUDE) data base for GDH-PQQ glucometer has listed two cases of severe hypoglycemia (non-fatal) in children with galactosemia and these events happened despite warnings by both manufacturers and regulatory authorities.[1] To our knowledge, this is the first clinical case report of a falsely high glucose reading due to high galactose in a proven case of galactosemia with a glucometer using the MutQ-GDH chemistry (a modified GDH-PQQ chemistry). The package insert of the glucometer cautions that galactose levels greater than 15 mg/dL (0.83 mmol/L) can cause overestimation of glucose values. According to a previous biochemical study galactose levels more than 39 mg/dL (2.2 mmol/L) had significant interference with the glucometer test strips and can produce a falsely high reading.[5] In developing countries where there is no new born screening for galactosemia a sick infant with high galactose levels is at risk for developing iatrogenic hypoglycemia. Based on our experience, we suggest precautionary measures to prevent a medical misadventure. All stakeholders including doctors, nurses, diabetic educators and caregivers of galactosemia patients

![Figure 1: Liver biopsy showing macrovesicular steatosis (white arrow) and bileduct proliferation (black arrow)]
should be made aware of the pitfalls of MutQ-GDH-PQQ chemistry based glucometers. Secondly all glucometers with potential galactose interference should carry prominent warning information. Finally, these glucometers should not be used in a neonatal care setting.

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