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Technical Report

Do ointments really cause glyceroluria?

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Glycerol is present in many medications, ointments, suppositories, and emollient solutions. Therefore, many cases of glyceroluria may be due to contamination of the sample by exogenous sources. Glycerol, also known as glycerin or 1,2,3-propanetriol, is an important intermediate in lipid and carbohydrate metabolism. It is utilized as a gluconeogenetic precursor and for re-esterification of free fatty acids [1, 2]. Normally, glycerol is not present in urine, but excretion in the urine can be observed primarily in 2 metabolic diseases: glycerol kinase deficiency and fructose 1,6-bisphosphatase deficiency. There are some reports that link glyceroluria with hemochromatosis and an aquaporin 7 gene mutation [2, 3]. In addition, as a non-disease reason, the use of perineal lotions or suppositories is thought to cause glycerin-induced contamination and lead to the detection of secondary glycerol as a preanalytical defect in urine organic acid analysis [4]. However, as far as we know, this information obtained from experience has not been adequately tested; the aim of this study was to investigate whether ointments used in infants actually lead to glyceroluria.

Since glycerol is a neutral compound, it can be detected by gas chromatography/mass spectrometry (GC-MS) of urine performed using the usual protocols [5] if a solvent extraction procedure is used. In this experimental study, after urine organic acid analysis in the metabolism laboratory, residual urine samples of 2 patients with no finding of glycerol were used (Fig. 1). Each patient sample was divided into 3 portions and about 3 mg each of 3 different brands of ointment obtained from the market were mixed in. The creams were numbered 1, 2 (containing glycerol or its derivatives), and 3 (containing no glycerol or its derivatives). Organic acid analysis was performed on vortexed urine samples. The organic acids were extracted with ethyl acetate and derivatized with N-Trimethylsilyl-N-methyl trifluoroacetamide for analysis. The prepared extract was analyzed using a Thermo Scientific Trace GC Ultra/Thermo Scientific ISQ (GS/MS) (Thermo Fisher Scientific, Inc., Waltham, MA, USA). The quantity of the internal standard (4-phenylbutyric acid) was used to calculate the glycerol level and the units were provided as mmoL/moL creatinine. Glycerol >0 mmoL/moL creatinine in the urine was evaluated as positive.

Of the 6 samples analyzed, only 1 (urine sample containing ointment category 2) was found to have glycerol (5.2 mmoL/

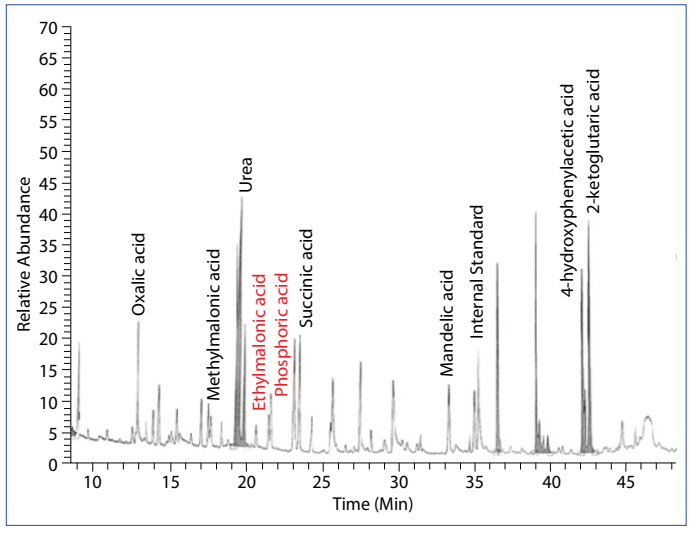

Figure 1. Patient's first chromatogram, before contamination of sample.

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moL creatinine) (Fig. 2). No glycerol was detected in the other urine specimens.

The use of perineal lotions or suppositories is thought to cause glycerin-induced contamination and lead to the detection of secondary glycerol as a preanalytical defect in urine organic acid analysis. In our study, glycerol was detected in 1 urine specimen of 4 specimens mixed with lotions containing glycerol or its derivatives. This finding shows that perineal lotions may cause a false positive finding of glyceroluria. This is consistent with general practical knowledge of metabolic laboratories. The absence of a glycerol finding in the other contaminated samples may be related to the different ointments used and the non-standardization of the added amount. Although in our study, contamination led to a low concentration of urinary glycerol and metabolic diseases are generally expected to be associated with higher levels of glycerol, since glycerol

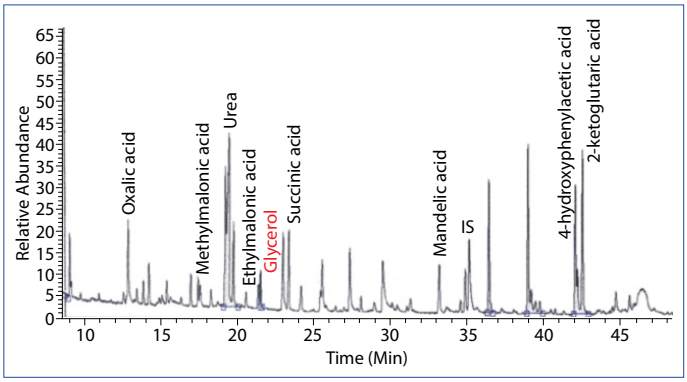

Figure 2. Patient's chromatogram after contamination of sample.

in any amount is not expected in normal urine, even low-level positives from contamination can lead to confusion during interpretation and diagnosis in laboratories.

Laboratory specialists should be aware of glycerol contamination from ointment while interpreting urine organic acid analysis, especially when it is isolated (without ketosis and lactic acidosis) and excreted in minimal quantities. In cases where contamination cannot be excluded, it is necessary to ask for a repetition of the sample with a new one obtained in a controlled sampling process.

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