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Investigations of Blood Ammonia Analysis: Test Matrices, Storage, and Stability

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Abstract

An assessment of blood ammonia concentration is common medical practice in the evaluation of an individual with an unexplained mental status change or coma. The determination of a blood ammonia level is most commonly done using a glutamate dehydrogenase (GLDH)-based assay, although there are many potential sources of artifact and the literature is inconsistent regarding key preanalytic issues. Using a GLDH-based assay, we first investigated matrix effects using three anticoagulants: heparin, EDTA and oxalate. Heparin-anticoagulated plasma was substantially less precise than EDTA- and oxalate-anticoagulated plasma. Oxalate-anticoagulated plasma showed a greater baseline of apparent ammonia than either heparin- or EDTA-derived plasma, presumably due to interferants. We then evaluated the stability of EDTA-anticoagulated plasma for assessment of ammonia when stored at 4°C, -14°C or -70°C. There was a linear increase of ammonia with storage at both 4°C and -14°C. Plasma kept at -70°C for up to three weeks showed no change in measured ammonia relative to the baseline determination. This work clarifies preanalytic conditions for which a precise determination of ammonia can be accomplished using a GLDH-based assay.

Key Words: ammonia, plasma, hyperammonemia

1. Introduction

An important etiologic mechanism of both pediatric and adult encephalopathies is that of disturbances of waste nitrogen metabolism (i.e., hyperammonemic encephalopathy). For this reason, determinations of blood ammonia concentration are important for the evaluation of individuals with unexplained altered mental status.

In order to accurately measure blood ammonia levels for clinical and research purposes, there are important preanalytic and analytic parameters that must be considered. Among these are the blood collection tube type and the stability of blood ammonia levels under different storage times and temperatures. Yet, except for agreeing on the superiority of plasma over serum or whole blood,[1–3] the literature suggests significant differences regarding both matrix effects and storage times and temperatures.[1–9] While there is no gold standard method for ammonia determination, blood ammonia is most commonly determined by a glutamate dehydrogenase (GLDH)-based enzymatic method. Heparin- and EDTA-anticoagulated plasma are commonly recommended for the determination of blood ammonia concentration, but oxalate-anticoagulated plasma has also been used.[2,7–9] In light of the differences in the literature, this study aims to determine the appropriate test matrix for ammonia measurement and the stability of plasma ammonia in various storage conditions using a GLDH-based method.

2. Materials and Methods

2.1 Materials

Blood samples included de-identified leftover clinical blood samples and blood from a healthy adult male volunteer after an overnight fast, all of which had normal plasma gamma-