

Newborn Screening for Arginase Deficiency in the U.S. – Where Do We Need to Go?

"Arginase 1 deficiency is a rare inborn error of metabolism, which if detected at birth is amenable to intervention and effective therapy. The major identifying metabolic abnormality in the newborn period is an elevated level of plasma arginine, an amino acid that is readily detected by the screening methods in universal use. Its utility is limited by the overlap in arginine levels between unaffected and affected individuals. The object of this study was to determine if a screening algorithm could be devised that minimized both false positive and false negative cases and which make newborn screening for the disorder prohibitively expensive.

We tested the utility of different algorithms in their ability to analyze arginine elevations and accurately identify arginase 1 deficiency in the newborn screens. Some states did not screen, others used approaches that missed cases, and others generated false positives. Some states used ratios between amino acids, but with different cutoff levels that resulted in differing probabilities of false positives or negatives.

Ratios between arginine and any of a number of different amino acids provided the most accurate results. The best ratios were applied to archived and blinded data from the California newborn screening program. The chosen ratio of arginine to the product of phenylalanine and leucine resulted in the ascertainment of all known cases of arginase 1 deficiency over a ten-year period with no false positives. The high sensitivity and specificity of this approach makes it appropriate to include arginase 1 deficiency as a primary target on newborn screening panels using one of these effective ratios to aid identification of newborns with this condition."

Contact: scederbaum@mednet.ucla.edu