Second-tier Bestimmung von Methylmalonsäure – Herausforderungen bei der Detektion und Therapie des Vitamin B12-Mangels

Second-tier analysis of methylmalonic acid – challenges in the detection and treatment of vitamin B12 deficiency

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The detection of methylmalonic acid (MMA) by second-tier analysis has been shown to reduce the number of false positives in newborn screening (NBS) for genetically determined methylmalonic acidurias (MMAuria). In addition to genetic conditions, MMA is an indicator of vitamin B12 status, thus applicable to detect maternal vitamin B12 deficiency in the newborns screened. This study reviewed biochemical and clinical follow-up data of a 7.5-year pilot study with 1.2 million newborns screened. Among 1,195,850 NBS samples, 3,595 (0.3%) fulfilled criteria for second-tier analysis of MMA. In 37 (0.003%; 1/32,000) samples, elevated concentrations of MMA were detected, resulting in diagnostic workup at a metabolic center in 21 newborns. In 6 infants (1/199,000), genetic conditions were established. The remaining 15 newborns (1/79,000) displayed significantly lower concentrations of MMA and were evaluated for maternal vitamin B12 deficiency. In 9 mothers, vitamin B12 deficiency was verified, and 6 showed no indication for vitamin B12 deficiency. Treatment with vitamin B12 normalized biochemical parameters in all 15 infants. However, repeated medical appointments and blood samplings were necessary. Applying a 2-tier strategy measuring MMA in NBS identified genetic conditions of MMAuria. It was possible to separate severe, early-onset phenotypes from maternal vitamin B12 deficiency. However, the detection of genetic MMAuria with mildly elevated MMA interferes with impaired vitamin B12 status of unknown clinical relevance and thus burdens possibly healthy newborns. Regarding maternal vitamin B12 deficiency, testing and supplementing mothers-to-be is preferable. This might decrease straining follow-up of newborns and improve quality and overall perception of NBS.