Leucine levels in maple syrup urine disease (MSUD) from a single centre in the United Kingdom

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Background: Optimal control of leucine concentrations in MSUD disease is essential for maximising neurocognitive outcomes. In 2014 Frazier et al. published guidelines recommending lowering the leucine treatment range to 75–200 μmol/L for patients ≤5 years and 75–300 μmol/L for >5 years. In 2015, the UK Expanded Newborn Screening (ENBS) guidelines recommended the range 200–400 μmol/L. In 2013, this was later reduced to 150–300 μmol/L and reported the typical leucine intake for classical MSUD as 300 mg/day (6 × 50 mg leucine exchanges). We have adopted these guidelines for our MSUD patients aged 5 years and under.

Aim: To audit leucine monitoring results to determine if the lower treatment range was achievable.

Methods: A 12 month retrospective review of all blood spot leucine levels (including during illness), number of 50 mg leucine exchanges per day and frequency of samples. All classical MSUD patients 5 years and under were included.

Results: Six patients were identified (median age 4.75 years, range 0.7–8 years). All diagnosed in the neonatal period (median age 13 days, range 7–17 days), median screening level 3635 (range 1153–4600 μmol/L). The mean of each patient’s 12 month leucine monitoring results was determined (median 210, range 178–290 μmol/L). The proportion of leucine concentrations below 300 μmol/L for each patient was also determined (median 75 %, range 60–92 %). The median number of samples per patient received in 52 weeks was 64 (range 37–76). The median number of mean 50 mg leucine exchanges per day for each patient was 7 (range 5–13). The median peak leucine level during illness was 765 (range 554–895 μmol/L).

Discussion: Our data shows that the UK ENBS lower treatment range of 150–300 μmol/L is achievable without having to overly restrict leucine exchanges.

A novel BCAT2 mutation causes hypervilaminaemia/hyperleucine-isoleucinemia in a boy with a developmental disorder with autism

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The biochemical findings suggested MAAI deficiency due to a defect in the GSTZ1 gene. The Illumina HiSeq platform was used to sequence the gene captured by the TruSight One Panel target enrichment system (Illumina). Analysis was performed with an in-house pipeline. Quality analysis of coverage data revealed a pattern consistent with a homozygous deletion of exons 3, 4, 5 and 6. This was confirmed by targeted microarray analysis (Affymetrix CytoScan HD array). This deletion has not been previously described in the literature or in any database; as it removes a big part of the gene it is likely to be pathogenic.

Discussion: Although it is not clear whether MAAI deficiency has caused the neurodevelopmental problems, this case adds to our knowledge of the phenotype of MAAI deficiency.