

Impact of newborn screening on survival and developmental outcome in classic isovaleric aciduria: a meta-analysis

Anna T. Reischl-Hajjibadi^{*}, Sven F. Garbade^{*}, Florian Gleich^{*}, Elena Schnabel-Besson^{*}, Roland Posset^{*}, Matthias Zielonka^{*}, Georg F. Hoffmann^{*}, Stefan Kölker^{*}, and Ulrike Mütze^{*}

^{*}Heidelberg University, Medical Faculty of Heidelberg, Department of Pediatrics I, Division of Pediatric Neurology and Metabolic Medicine, Im Neuenheimer Feld 430, 69120 Heidelberg, Germany

Introduction and Aim

Classic isovaleric aciduria (cIVA) is a rare inherited metabolic disorder characterized by recurrent life-threatening metabolic decompensations and neurocognitive impairment in untreated patients. This meta-analysis aims to assess the impact of early diagnosis by newborn screening (NBS) on mortality and neurocognitive outcome.

Methods

A systematic literature search for articles published until 2022 was conducted following PRISMA protocol guidelines. We investigated effects on clinical outcome and survival, analyzing outcome parameters using meta-analytical measures and estimating effect sizes with a random-effects model.

Results

Overall, 20 studies were included, reporting on 240 individuals with cIVA. Individuals identified by NBS presented with a lower frequency of neurological symptoms (13.0% versus 44.9%; $P = 0.0040$) and developmental delay (6.1% versus 51.2%; $P < 0.0001$), and had a lower mortality rate (1.1% versus 10.9%; $P = 0.0320$). The quality of healthcare systems did not have a measurable impact on neurocognitive outcome and mortality. Despite the beneficial effect of NBS on clinical outcome and mortality, it could not reliably prevent the manifestation of neonatal decompensation in all individuals with cIVA identified by NBS.

Conclusions

Early diagnosis through NBS is essential for the timely initiation of therapy and for improving outcomes and survival rates in individuals with cIVA.