

Glutamine supplementation for congenital glutamine deficiency

Supplementation with glutamine can possibly prevent the development of mental retardation, multiple organ failure and death in defects of glutamine synthetase.

Glutamine contributes to neurotransmitter synthesis, pH homeostasis, immune response and wound healing. Glutamine synthetase catalyses the synthesis of glutamine (an essential amino acid), and helps in the detoxification of glutamate and ammonia (NH₃). Glutamine synthetase deficiency results in multiple organ failure, spontaneous abortion and/or premature death, and is generally incompatible with life (1).

We have recently discussed a child who developed general hypotonia and hyperreflexia postpartum and treatment-resistant seizures at 13 days old. The child had very low serum and cerebrospinal fluid concentrations of glutamine and glutamate. The cause was an autosomal recessive mutation.

At the age of four, the child showed mental retardation and had frequent epileptic seizures. With funding from the Qatar Foundation, an international research group (Drs. T. Ben-Omran, K. Ibrahim, N. Shabeck, all Doha, Qatar; Dr. J. Häberle, Switzerland; Dr. F.A. Chaudhry, Norway) was set up to intervene. Under strict monitoring, the child was administered glutamine via a gastrostomy tube (up to ~ 1 g/kg/day) (2). Serum levels of blood glutamine normalised, while corresponding values in the central nervous system approached normal and ammonia toxicity was also prevented. The child became more alert and the frequency of seizures abated. EEG showed significant improvement.

Defects of glutamine synthetase normally result in spontaneous abortion because the growth and function of the embryo and placenta are dependent on glutamine. The condition is probably underdiagnosed. Although we did not succeed in normalising brain function – MRI showed long-term cerebral atrophy – this case history indicates

that glutamine supplementation may compensate for a defect of glutamine synthetase. We may also find that glutamine supplementation is beneficial for post-operative wound healing and foetal development. The study demonstrates the importance of translational research and the strength of international research collaboration.

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References

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2. Häberle J, Shahbeck N, Ibrahim K et al. Glutamine supplementation in a child with inherited GS deficiency improves the clinical status and partially corrects the peripheral and central amino acid imbalance. *Orphanet J Rare Dis* 2012; 7: 48.