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Urea Cycle Disorders

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In the urea cycle, there are six enzymes which are involved in the conversion of ammonia to urea.There are six metabolic disorders associated with a defect or deficiency in these six urea cycle enzymes (1).These disorders are the following: 1) CPS-Carbamyl Phosphate Synthetase; 2) NAGS-N-Acetylglutamate Synthetase; 3) OTC-Ornithine Transcarbamylase; 4) AS-Argininosuccinic Acid Synthetase (Citrullinemia); 5) AL/ASA- Argininosuccinate Lyase (Arginosuccinic Aciduria); 6) AG-Arginase (2).

A urea cycle disorder (UCD) is a deficiency of one or more of the above six enzymes which are responsible for removing ammonia from the bloodstream.In a healthy individual, urea is transferred into the urine and is excreted from the body. In a UCD, hyperammonemia results from the accumulation of nitrogen in the form of ammonia. Coma, irreversible brain damage and/or death results when ammonia reaches the brain via the bloodstream (3).

The incidence of UCDs has been estimated by experts at the Urea Cycle Consensus Conference in April 2000 to be 1 in 10,000 births (3). It is imperative that an inborn error of metabolism (such as a UCD) be considered in an ill newborn as the first symptoms of hyperammonemia are failure to feed and somnolence which are symptoms in many other diseases. If hyperammonemia is present, lethargy and coma will follow quickly if therapy is not initiated (4). For long-term management of UCDs plasma glutamine levels used to measure the effectiveness of therapy (4).

A very important part of therapy is a reduced protein intake although, The Recommended Daily Allowance for dietary protein is higher than the minimum needed for normal growth (4). Parents play a very important role in the nutritional management of their children-they need to be trained in the placement of nasogastric and/or the placement of gastric tubes or buttons (4). Neonates and older individuals who do not respond to intravenous sodium phenylacetate and sodium benzoate may require hemodialysis to control hyperammonemia (5). Liver transplantation should be considered for patients with severe CPS or OTC deficiency. The 5-year survival rate for patients having a liver transplant is now approximately 80% (4).

Recently, there has been an increase in the number of adult onset cases of UCDs. The symptoms resemble stroke-like symptoms with episodes of lethargy and delirium. It has been seen after viral illnesses, childbirth, dieting, use of valproic acid and chemotherapy. It is of vital importance that these patients are diagnosed properly and then receive treatment.

UCDs have been under diagnosed in neonates and young children in the recent past and is on a rise as an adult-onset disorder. It is imperative that proper diagnostic testing is performed in a timely manner. Hopefully, with more awareness of UCDs, more research will performed thus providing a brighter future for all individuals with UCDs.

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