

CARNITINE = Levocarnitine (rINN)

Use

L-Carnitine is used in the management of a range of rare genetic conditions associated with carnitine deficiency.

Nutritional factors

Carnitine (3-hydroxy, 4-N-trimethylaminobutyric acid) is a small water-soluble molecule. It is essential for the entry of long-chain fatty acids into the mitochondria, where they are oxidised. Most of the body's carnitine is found in skeletal and cardiac muscle. Carnitine can be synthesised in the body from lysine and methionine, although synthetic pathways are relatively immature at birth, but most is usually provided by dietary red meat and dairy produce. Human milk and whey-based formula milks all contain L-carnitine, but soya based preparations seldom do, making primary nutritional deficiency a possibility. Dialysis and defects of renal tubular reabsorption (Fanconi syndrome) can cause secondary dietary deficiency.

Pharmacology

Primary systemic carnitine transporter deficiency is an extremely rare condition resulting from a defect in the uptake of carnitine across cell membranes. It usually presents with hypoglycaemia, cardiomyopathy or myopathy and is generally associated with a total plasma carnitine level of less than 10 µmol/l. It is diagnosed on the basis of carnitine uptake by fibroblasts *in vitro*.

Secondary systemic carnitine deficiency occurs in fatty acid oxidation defects and organic acidaemias. In these conditions carnitine binds to accumulating intermediate metabolites and is excreted with them in the urine. The commonest fatty acid oxidation defect is medium-chain acyl-CoA dehydrogenase (MCAD) deficiency, which presents with hypoglycaemic encephalopathy, sometimes in the neonatal period. Other fatty acid oxidation defects present similarly, or with cardiac or skeletal myopathy. Organic acidaemias usually present with encephalopathy, often within a few days of birth. In all these conditions treatment should be managed under the guidance of a consultant experienced in the management of metabolic disease. All the conditions are recessively inherited.

Carnitine is of proven value in primary carnitine deficiency, and it is also often used in the management of organic acidaemias (such as isovaleric, methylmalonic, and propionic acidaemia and glutaryl-CoA dehydrogenase deficiency). Its use in fatty acid oxidation defects is more controversial. Reports of supplementation in patients on dialysis, on valproate (q.v.) or with Fanconi syndrome have suggested only variable or equivocal benefit. Treatment should always be with the naturally occurring L isomer and not the racemic (DL) mixture. The main dose-related adverse effects of oral treatment are nausea, vomiting, abdominal cramp, diarrhoea and a fish-like smell. A number of controlled trials have failed to show that routine supplementation reduces apnoea, makes episodic hypoglycaemia less common, or improves growth, either in orally or in parenterally fed preterm babies. Women requiring carnitine supplementation should not stop treatment during pregnancy or lactation.

Treatment

Urgent IV treatment: Give 100 mg/kg (5ml of a solution made up as described below) as a slow loading dose over 5 to 10 minutes, followed by a continuous infusion of 4 mg/kg per hour (0.2 ml per hour of the same solution) during acute metabolic decompensation.

Oral treatment: The usual dose is 25 mg/kg four times a day by mouth.

Compatibility

While formal tests of compatibility do not seem to have been done, problems have not been encountered when carnitine is terminally co-infused with arginine, sodium benzoate and sodium phenylbutyrate.

Supply and administration

An oral preparation in sucrose, dispensed as a 30% paediatric solution (containing 300 mg/ml of L-carnitine), is available commercially costing £1.10 per ml. It can be mixed with a flavoured drink to make it more palatable. It contains sorbitol and sucrose. For IV use, 5 ml ampoules containing 1 gram of L-carnitine, costing £12 each, are obtainable on request; to give 100 mg/kg take 1 ml of this preparation for each kilogram that the baby weighs, dilute to 10 ml with 0.9% sodium chloride, and infuse 5 ml as described above. The product is stable at room temperature for 24 hours after reconstitution in this way.

References

See also the relevant Cochrane reviews ©

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