

PIPECOLIC ACID

Relevant disorders

Peroxisomal biogenesis disorders
Pyridoxine (vitamin B6) Responsive Epilepsy

Related Metabolic Tests

Very Long Chain Fatty Acids
Plasmalogens
Bile Acids

Indication for Test

Pipecolic acid is an imino acid derived from lysine catabolism. A minor lysine pathway passes through the peroxisomal matrix where pipecolic acid (piperidine-2-carboxylic acid) is metabolised. Pipecolate can thus be used as a marker for generalised peroxisomal function which is impaired in peroxisomal biogenesis disorders (PBD) such as Zellweger syndrome, Infantile Refsum's Disease and Neonatal Adrenoleukodystrophy. Where plasma VLCFAs are abnormal, the same sample can be used for pipecolate quantitation, although perinatal levels can be less clear for diagnosis, an effect which is more marked in urine. CSF is a good diagnostic indicator at all ages.

The more recently described application for this assay is for CSF (and plasma) pipecolate as a marker for Pyridoxine (vitamin B6) Responsive Epilepsy (PDE), where the lysine pathway is blocked at 2-aminoadipylsemialdehyde (AASA) dehydrogenase due to deficiency of the enzyme 'antiquitin'. The accumulation of the equilibrium isomer of AASA, piperidine-6-carboxylate is then responsible for the condensation and therefore sequestration of vitamin B6. The deficiency overall of B6 is responsible for seizures in the patients.

Pipecolate accumulates upstream of the block and can be used as a marker even when the patient is receiving B6 therapy but at a reduced concentration in some patients. CSF pipecolate is more reliable, seemingly unaffected by B6 therapy. Plasma values have also been reported as less reliable as spuriously high plasma pipecolate has been attributed to diet, liver disease and other factors.

Urinary pipecolate is not reliable for PDE diagnosis when B6 therapy is ongoing.

Methodology

Stable isotope dilution Gas Chromatography Mass Spectrometry

Sample requirements

Plasma – 1ml, Li Hep plasma

CSF – 0.5ml, no preservative

Urine – 5ml, plain sample

Transport information/Contact details

Send all samples by first class post to:

Department of Clinical Chemistry
Sheffield Children's NHS Foundation Trust
Western Bank, Sheffield
S10 2TH, UK

Joanne Croft (Clinical Scientist)
0114 2717307

Turn Around Time

4 – 6 weeks

Reference Ranges

Interpretation will be provided with the report

References

- Plecko et al Pipecolic acid elevation in plasma and cerebrospinal fluid of two patients with pyridoxine-dependent epilepsy. Ann Neurol. 2000 Jul;48 121-5
- Verhoeven et al. J Inher Metab Dis Vol 18 Suppl 1(1995) p58)

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