DEPARTMENT OF CLINICAL CHEMISTRY
SHEFFIELD CHILDREN'S NHS FOUNDATION TRUST

FATTY ACID OXIDATION SCREEN

Relevant disorders

Fatty acid oxidation defects

Related Metabolic Tests

Acylcarnitine profile
Organic acids

Indication for Test

Disorders of mitochondrial fatty acid oxidation are important inherited metabolic defects presenting primarily in neonates, infants and children, often acutely as life threatening hypoglycaemic, hypoketotic crisis with hepatic and sometimes cardiac involvement. The commonest fatty acid defect in Western Europe is medium chain acyl-CoA dehydrogenase deficiency (MCAD) with an estimated incidence as high as 1:9,000 live births. There are around 16 other described disorders of fatty acid oxidation and cumulatively they are as important as MCAD. Early diagnosis is important in order to minimise mortality and morbidity, as treatment, particularly for MCAD is easy and effective. However, some long chain defects carry a poor prognosis, but accurate diagnosis can offer the chance of prenatal diagnosis for future pregnancies.

Methodology

Cultured monolayers of intact fibroblasts in multiwell plates release $^{3}H_2O$ from [9,10-^{3}H] myristate, palmitate or oleate during the process of fatty acid β-oxidation. The released label is separated from unmetabolised fatty acids by an ion exchange column and subsequently counted in a liquid scintillation counter. The activity of the fatty acid oxidation flux is calculated in relation to the initial amount of fibroblast protein. Cell lines from patients with fatty acid oxidation defects will release less label as $^{3}H_2O$ than simultaneous controls. ***Please note that most fat oxidation assays entail the simultaneous assay of each cell line in duplicate using all three substrates (myristate, palmitate & oleate) i.e. 6 wells of fibroblast monolayer per patient. However in certain circumstances only one or two substrates may be used.***

Assays at elevated temperature
Growing and assaying cell lines at temperatures above 37^{o}C (i.e. 39^{o}C & 41^{o}C) from patients with "mild" mutations (i.e. cell lines that exhibit some residual enzyme activity) will often result in a significant lowering of activity as compared to the same cells assayed under standard conditions (37^{o}C).

This instability of mutant protein can be used to "unmask" certain defects and also potentially may give some insight into patient susceptibility to febrile episodes.

Sample requirements

Skin biopsy for fibroblast culture or cultured fibroblasts.

Transport information/Contact details

Send by first class post to:

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

Simon Olpin (Consultant Clinical Scientist)
0114 2717267

Turn Around Time

6 – 8 weeks. This may be longer if the cells do not grow adequately.

Reference Ranges

Interpretation will be provided with the report.

References

- Manning NJ, Olpin SE, Pollitt RJ, Webley J. A comparison of [9,10-^{3}H] Myristic acids for the detection of fatty acid oxidation defects in intact cultured fibroblasts. J. Inher. Metab. Dis; 13, 58-68, 1990.

- Olpin SE, Manning NJ, Carpenter K, Middleton B, Pollitt RJ. Differential diagnosis of hydroxydicarboxylic aciduria based on release of $^{3}H_2O$ from [9,10-^{3}H]myristic and [9,10-^{3}H]palmitic acids by intact cultured fibroblasts. J. Inher. Metab. Dis; 15, 883-890, 1992

- Olpin SE, Manning NJ, Pollitt RJ, Clarke S. [9,10-^{3}H]Oleic acid - for the improved detection of long chain fatty acid oxidation defects in intact cells. J. Inher. Metab. Dis: 20, 415 - 419, 1997.