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SCREENING, DIFFERENTIAL DIAGNOSIS AND PRENATAL DIAGNOSIS OF HYPERPHENYLALANIEMAIA

Screening, differential diagnosis and prenatal diagnosis of hyperphenylalaninemia

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Hyperphenylalaninemia (HPA) is the most common disorder of amino acid metabolism caused by deficiency of phenylalanine hydroxylase (PAH) or tetrahydrobiopterin (BH_4), the essential cofactor of aromatic amino acid hydroxylases. Both PAH and BH_4 deficient HPA are autosomal recessive inheritance. Early diagnosis and treatment starting at neonatal period will prevent mental retardation for HPA patient and result in normal intellectual development. BH_4 deficient-HPA should be treated with BH_4 and neurotransmitters while PAH deficiency should restrict Phe intake for dietary therapy. When treatment started, continuous monitoring of therapy should be prosecuted to ensure the patients are in well development. Neonatal screening for HPA started in January 1984 in Taiwan. The overall incidence rate of HPA was about 1/31,000 (95% confidence interval 1/23,260 to 1/46,460). The BH_4-deficient HPA in Taiwan was estimated to make up around 30% of patients suffering from HPA, which is much higher than in Caucasian populations (1.5-2% of HPA), indicating the importance of differential diagnosis in Chinese population. This presentation will emphasize on the laboratory tests for neonatal screening, differential diagnosis, and prenatal diagnosis of HPA.

For neonatal screening, a bacteria inhibition assay (BIA) was shown to be a simple method to determine blood Phe from blood spot collected on filter paper. More recently, tandem mass spectrometry was proved to be a rapid and sensitive method for mass screening of HPA. For differential diagnosis, analysis of urinary pterins, measurement of blood DHPR activity, and oral loading test of BH_4 should be done in all newborn with elevated blood Phe. For monitoring of treatment, a chemical fluorescence test for blood Phe can be applied to detect Phe level in serum and/or blood spot. For prenatal diagnosis, analysis of pterins in amniotic fluid, measurement of DHPR activity in amniocytes and/or chorionic villi could be applied to detect fetus at risk of BH_4 deficiency. In addition, molecular genetic analysis could be used for prenatal diagnosis of PAH deficient HPA as well as BH_4 deficient HPA.

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