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Determination of Plasma α-Galactosidase A Activity in Patients with Fabry's Disease and Its Normal Reference Range in Chinese

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A method to diagnose hemizygotes and heterozygotes of Fabry's disease by measuring α-galactosidase A activity in plasma was studied. The 4-methylumbelliferyl-α-D-galactopyranoside was used as the artificial substrate and the N-acetyl-D-galactosamine was used to inhibit the α-galactosidase B activity. Plasma α-galactosidase A activity showed an optimum pH at 4.6. The within-run and between-run precision of this method were determined to be around 1.5-2.7 % and 2.7-3.4% (coefficient of variation), respectively. The reference range of plasma α-galactosidase A activity in Chinese adults was estimated to be 7.6-16.5 nmol/hr/ml (n=202). There was no significant difference between males and females. The plasma α-galactosidase A activity in hemizygotes (0.4-0.8 nmol/hr/ml ; n=3) and heterozygotes (4.5-4.8 nmol/hr/ml ; n=2) of Fabry's disease was found significantly lower than those of normal subjects. The results indicated that this assay could be applied for diagnosis of Fabry's disease in Chinese and may be used for detection of heterozygotes.

Key words: Fabry's disease , a-galactosidase A , lysosomal enzyme

INTRODUCTION

Fabry's disease (MIM 301500) is an inborn error of glycosphingolipid metabolism (1), characterized by the deposition of the glycosphingolipid with terminal α-galactosyl moieties and trihexosyl ceramides in tissues (2,3), primary in the cardiovascular-renal system. The primary metabolic defect resulting in the accumulation of these substrates is the defective activity of the lysosomal enzyme, ceramide trihexosidase (4,5), which is a specific X-linked α-galactosyl hydrolase (6,7). The activity of this enzyme could be analyzed by utilizing an artificial substrate, 4-methylumbelliferyl-α-D-galactopyranoside (7), which provided reasonably reliable determinations of the deficient enzymatic activity in patients with Fabry's disease (8-12). However, the artifical substrate can be hydrolyzed by two α-galactosidase (EC 3.2.1.22) isoenzymes, namely α-galactosidase A and α-galactosidase B (12,13). The α-galactosidase B, which is not deficient in the tissues of Fabry's disease (11), also has α-N-acetyl-

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