

ASSOCIATION OF GENETIC VARIANTS OF MNSOD (ALA9/VAL) AND GLUTATHIONE REDUCTASE ACTIVITY WITH MITOCHONDRIAL DYSFUNCTION IN TYPE 2 DIABETES MELLITUS

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It has been shown that inhibition of superoxide anion accumulation prevents mitochondrial dysfunction in Diabetes Mellitus. Manganese superoxide dismutase (MnSOD) catalyzes the dismutation of superoxide radicals in mitochondria by converting anion superoxide into hydrogen peroxide, which, in turn is converted to hydrogen peroxide by glutathione peroxidase (GSH-Px). It has been suggested that the substitution of C to T, which results in an amino acid change from alanine to valine at 9 position, modulates MnSOD transport into mitochondria. The mitochondrial pool of glutathione (GSH) is considered to be vital for cell to protect itself against oxidative stress and the principal functional mitochondrial antioxidant. The enzyme responsible for GSH regeneration is glutathione reductase (GSH-Rd). In the light of these findings, we decided to examine the association of Ala9Val polymorphism of MnSOD gene and the activity of GSH-Rd with mitochondrial dysfunction in type 2 Diabetes Mellitus (DM) patients. Ninety-nine type 2 DM patients and 67 normal healthy subjects were included in the study. The frequency of Ala/ala homozygote genotype was significantly higher in patients than in controls ($p < 0.05$). The activity of GSH-Rd was significantly reduced in patients as compared with controls. When MnSOD genotype were compared with GSH-Rd activity in patients or controls, the activity of GSH-Rd was significantly lower in patients carrying Val/Val than in controls carrying the same genotype ($p < 0.05$). In conclusion, genetic variants of MnSOD and GSH-Rd activity might be associated with mitochondrial dysfunctions in type 2 DM.

Key Words:

Mitochondrial dysfunction, MnSOD, GSH-Rd, Type 2 Diabetes Mellitus