Mitochondrial complex-1 in Parkinson’s disease

Parkinson’s disease (PD) is the most common neurodegenerative movement disorder. The classical form of the disease is characterized clinically by rigidity, resting tremor, bradykinesia and postural instability. Its pathological hallmarks are the preferential loss of dopaminergic neurons of the substantia nigra pars compacta and formation of Lewy bodies; intraerytoplasmic inclusion bodies that are mainly composed of fibrillar \( \alpha \)-synuclein. The clinical symptoms of PD arise by a threshold effect, whereby denervation of the corpus striatum by dopaminergic neuronal loss reduces dopamine levels to below 70% of wild type.

Mitochondrial dysfunction has long been implicated in the pathogenesis of PD. Evidence first emerged following the accidental exposure of drug abusers to 1-methyl-4-phenyl-1,2,3,4-tetrahydropyridine (MPTP), an environmental toxin that results in an acute and irreversible parkinsonian syndrome. The active metabolite of MPTP, the 1-methyl-4-phenylpyridinium ion (MPP\(^+\)) is an inhibitor of complex I of the mitochondrial electron transport chain and a substrate for the dopamine transporter. It therefore accumulates in dopaminergic neurons, where it confers toxicity and neuronal death through complex I inhibition. This has many deleterious consequences, including increased free radical production and oxidative stress, and decreased ATP production.

PD is the second most common neurodegenerative disease after Alzheimer disease. About 1% of the population over 60 have Parkinson’s disease. As the people grow older no of PD patients will increase. The number of patients likely to grow in India with increasing mature population and affordable medical care. Despite its high rate, there is number diagnostic test that can confirm PD. Laboratory testing of the blood of patients with the symptoms typical of Parkinson’s only rarely uncovers any abnormality. PD may be identified by clinical tests, imaging studies, blood tests, cerebrospinal fluid tests and genetic tests.

In an attempt to develop some biochemical tests, investigators focused on oxidative stress measurement in blood and cerebrospinal fluid. Oxidative stress is considered one of the causes of Parkinson’s pathophysiology other is environmental toxin and genetic factor. Mitochondrial complex 1 level was found low in substantia nigra of PD brain. To identify the peripheral marker, investigators have studied the mitochondrial complex 1 levels and 8-hydroxy-2-deoxyguanosine as a sign of oxidative stress. However platelets show no difference in complex 1 levels and 8-hydroxy-2-deoxyguanosine levels. Other investigators found low platelets levels of complex 1 which co-relate with Parkinson’s disease levels. All these genetic and bio-chemical studies have increased our understanding of PD, opinion on weather they can assist in diagnosis and prognosis of PD is mixed.

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References