The catechol-O-methyltransferase and monoamine oxidase B polymorphisms and levodopa therapy in the Iranian patients with sporadic Parkinson’s disease

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Parkinson’s disease (PD) patients vary widely in their response to levodopa treatment, and this may be partially genetic in origin. Recent studies suggest that catechol-O-methyltransferase (COMT), G1947A and monoamine oxidase B (MAOB), A644G polymorphisms might influence the risk and treatment of PD. Herein, we aimed to test the possible influence of MAOB and COMT genetic polymorphisms on the effective daily dose of levodopa administered in the fifth year of treatment. We also examined the effect of COMT and MAOB haplotypes on levodopa therapy outcome. There were 31 females and 72 males of Iranian origin diagnosed with sporadic PD included into the study. The patients were divided into two groups. Group 1: patients received daily doses of levodopa below 500 mg in the fifth year of treatment. Group 2: those patients receiving daily doses exceeding 500 mg in the fifth year of treatment. MAOB and COMT polymorphism genotyping was performed by using PCR-based restriction fragment length polymorphism (RFLP) analyses. Our data show that the first group suffered less frequently from dyskinesia than patients from the second group. No statistically significant differences were found in allele frequencies and genotype distributions of the studied genes between two groups. In addition, the incidence of the specific haplotypes between the two groups did not show any difference. The present data suggest that pharmacokinetic or pharmacodynamic factors other than the investigated genetic variants of the MAOB and COMT enzymes seem to determine the response to levodopa in the Iranian PD patients.

Key words: COMT, dyskinesia, Iranian, levodopa, MAOB, Parkinson’s disease, polymorphism

INTRODUCTION

Parkinson’s disease (PD) is a neurodegenerative disease of unknown etiology that predominantly affects the elderly (Jankovic et al. 2000). Interaction of both environmental factors and genetics has been suggested to be involved in destroying the pigmented cells of the cerebral substantia nigra (Fahn and Ciohen 1992) and development of the disease. The candidate PD pathogenic genes include those that are linked to dopamine synthesis, transport and degradation, detoxification of xenobiotics and other toxins in dopaminergic neurons. Levodopa in combination with a dopa-decarboxylase (DDC) inhibitor remains the most effective symptomatic treatment for PD (Rascol et al. 2000, Jankovic 2006). A number of studies suggested that functional polymorphisms might affect the phenomenon of ‘levodopa-nonresponse’ and levodopa-induced motor fluctuations, mainly levodopa-induced dyskinesia (Gilgun-Sherki et al. 2004, de Lau et al. 2012). Recent investigations suggest that polymorphism in catechol-O-methyltransferase (COMT) and monoamine oxidase B (MAOB) might influence the risk and treatment of PD (Goudreau et al. 2002, Bialecka et al. 2007, 2008). COMT inactivates neurotransmitters, hormones, potentially toxic metabolites, and xenobiotics contain-