



Theophylline, adenosine receptor antagonist prevents behavioral, biochemical and neurochemical changes associated with an animal model of tardive dyskinesia

Mahendra Bishnoi¹, Kanwaljit Chopra², Shrinivas K. Kulkarni^{1,2}

¹Centre with Potential for Excellence in Biomedical Sciences (CPEBS), Panjab University, Chandigarh, 160014 – India

²Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, 160014 – India

Correspondence: Shrinivas K. Kulkarni, e-mail: skpu@yahoo.com

Abstract:

Tardive dyskinesia is considered to be the late onset adverse effect of prolonged administration of typical neuroleptic drugs. Adenosine is now widely accepted as the major inhibitory neuromodulators in the central nervous system besides GABA. Antagonists of A_{2A} receptors are known to confer protection against neuronal damage caused by toxins and reactive oxygen species. The present study investigated the effect of adenosine receptor antagonist, theophylline (25 and 50 mg/kg, *ip*) in an animal model of tardive dyskinesia by using different behavioral (orofacial dyskinetic movements, stereotypy, locomotor activity, % retention), biochemical (lipid peroxidation, reduced glutathione levels, antioxidant enzyme levels (SOD and catalase)) and neurochemical (neurotransmitter levels) parameters. Chronic administration of haloperidol (1 mg/kg *ip* for 21 days) significantly increased vacuous chewing movements (VCMs), tongue protrusions, facial jerking in rats which was dose-dependently inhibited by theophylline. Chronic administration of haloperidol also resulted in the increased dopamine receptor sensitivity as evidenced by increased locomotor activity and stereotypic rearing. Further, it also decreased % retention time in elevated plus maze paradigm. Pretreatment with theophylline reversed these behavioral changes. Chronic administration of haloperidol also induced oxidative damage in all the brain regions which was prevented by theophylline, especially in the striatum. Chronic administration of haloperidol resulted in a decrease in dopamine levels which was reversed by treatment with theophylline (at higher doses). The findings of the present study suggested the involvement of adenosinergic receptor system in the development of tardive dyskinesia and possible therapeutic potential of theophylline in this disorder.

Key words:

adenosine, neuroleptic drugs, tardive dyskinesia, theophylline
