Role of Calcium Channel Blockers as Anti-Neuroinflammatory Agents in Paraphenylene Diamine-Induced Neuroinflammation in Rats

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ABSTRACT

Introduction: Kala Pathar (Paraphenylene diamine; PPD) poisoning is a new kind of deliberate suicide with a significant death rate. This hair colour is often chosen for suicide due of its simple availability, low cost, and swiftly detrimental effects. PPD is an organic compound with chemical formula $C_6H_4(NH_2)$. It is an aromatic amine, solid and white in color, which turns black on oxidation. It is a main ingredient of many locally produced hair dyes. It is produced in Germany, Japan, and the United Kingdom. If ingested it is metabolized in the body cytochrome P450 system, and is further oxidized to a toxic product that can lead to multi organ failure. PPD poisoning is very lethal, quick treatment can save the lives, but till now no antidote is available, symptomatic treatment is only the choice, signs and symptoms include, skin rash, respiratory distress, anaphylactic reaction, swelling of face/neck, rhabdomyolysis cardiovascular effects, gastrointestinal issues, neurological symptoms, renal dysfunction, hepatic dysfunction hematological effects. Calcium channel blockers (CCBs), a class of drugs primarily used to treat hypertension and cardiovascular conditions, have shown promising anti-inflammatory properties. The modulation of inflammation through CCBs, particularly in the context of neuroinflammation, has emerged as a captivating area of investigation. Neuroinflammation present in neurodegenerative diseases is the toxicants, poses a substantial risk to general population health. One such toxicant, paraphenylenediamine (PPD), has been implicated in neuroinflammation, sparking interest in exploring CCBs as potential anti-inflammatory agents. The aim of this research was to explore the feasibility of CCBs as potential anti-inflammatory drugs and the underlying mechanisms of their anti-inflammatory effects.

Objective: The aim of this research was to explore the feasibility of CCBs as potential anti-inflammatory drugs against PPD-induced neuroinflammation.

Methodology: The study conducted to assess the effects of calcium channel blockers in neuro-inflammation in 64 male Wistar rats. The rats were housed in a controlled environment for 8 weeks, including a 2-week acclimatization period, and were randomly divided into an intervention group receiving calcium channel blockers and a control group receiving a placebo. Neuroinflammation was induced using PPD. Rat brain samples were collected to evaluate pro-inflammatory cytokines via ELISA, and tissue samples were analyzed for histological examination, antioxidant biochemical tests were done to analyses the inflammation preventing effects of CCBs (Verapamil and Nimodipine) and behavioral tests were carried out to assess the positive treatment effects of CCBs in PPD-induced neuroinflammation.

Key Findings: Showed that PPD treated group had deranged results in open field test, tail suspension test, and social interaction tests as compared to control group which were attenuated in CCBs treatment groups that received Verapamil 15 and 20 mg and Nimodipine 1.5 and 3 mg. Histopathology of rat brain also

showed the decreased inflammatory cells count as compared to PPD treated rats. IL-6 and TNF ELISA tests showed the anti-inflammatory effects in CCBs treated groups.

Conclusion: This concluded that CCBs have promising anti-neuroinflammatory properties and can be used in neuroinflammatory diseases and an add in treatment option in PPD poisoning.

Keywords: Paraphenylene Diamine, Neuroinflammation, Verapamil, Nimodipine.

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