



# Successful management of Haloperidol induced akathisia with cyproheptadine

## Introduction

Akathisia is a term used for motor restlessness along with subjective feelings of tension and discomfort. It requires both subjective and objective aspects and these behaviors are attributed to inner feelings of tension. It is due to antipsychotic drug exposure. Treatment involves lowering the dosage of the antipsychotic medications, adding propranolol, benzodiazepines like diazepam or clonazepam, clonidine, mirtazapine. Here we are presenting a case of akathisia which we found novel as the patient didn't respond to the forementioned conventional methods and developed adverse effects but responded only to cyproheptadine syrup. There should be a personalized treatment plan for akathisia, incorporating details like history, therapeutic response and side effects profile. Akathisia is a term used for motor restlessness along with subjective feelings of tension and discomfort. It requires both subjective and objective aspects and these behaviors are attributed to inner feelings of tension. Akathisia meaning "Never to sit down" is a drug induced movement disorder which develops within first 4 weeks of starting or increasing the dose of antipsychotic medications or after decreasing the dose of antiparkinsonian drugs. Prevalence of Antipsychotic induced akathisia is 20%-75%. It is also reported with Selective Serotonin Reuptake Inhibitors where it is mediated by the serotonin agonism of the dopamine system. These symptoms should not be a part of any other psychiatric illness, neurological or a general medical condition. Cholinergic, ad-

renergic, serotonergic, dopamine pathways are implicated in the etiology of akathisia. This condition is often misdiagnosed as persistent anxiety or agitation or manic excitement. The two traditional methods involved in treatment are the change in antipsychotic regimen and addition of an anti-akathisia agent. Pharmacological regimens mainly focus on the role of beta adrenergic blockers like propranolol in the treatment of akathisia. Newer research focus on the role of 5HT<sub>2A</sub> receptor mediators like mirtazapine, cyproheptadine. This activity is thought to counteract antipsychotic-induced dopamine D<sub>2</sub> receptor blockade with subsequent enhancement in dopamine neurotransmission. Lack of response to conventional methods is common but developing adverse effects with most of the first line drugs but tolerating cyproheptadine alone is quite unusual. In India, we have comparative studies between cyproheptadine and other conventional methods there are not much case reports supporting the evidence of sole response to cyproheptadine alone.

A 45 year old married female, presented to the outpatient department with complaints of inability to stay still, rocking to and fro movements, subjective and objective restlessness for the past one and half months. She was on tablet haloperidol 10mg tablet, trihexyphenidyl 4mg and tablet divalproex sodium 500mg past two months. She had agitation, aggression, increased speech and sleep disturbances past two months for which she was started on the above medications. Restlessness began 15 days after starting the treatment.

## Editorial

She is a diagnosed case of diabetic mellitus on treatment. Past history suggestive of multiple similar episodes. She was admitted in the psychiatric ward. Base line investigations done were normal her glycemc control was good. Neuroimaging CT Brain was normal. Haloperidol was stopped. She was started on tablet risperidone 4mg and divalproex sodium was increased upto 750mg. She was started on anti adrenergic agent propranolol 10mg and was titrated upto 60mg over a period of 1 week but her symptoms persisted and she developed hypotension so propranolol was stopped. Tablet clonazepam 0.5mg was started and increased upto 2mg within 5 days but her restlessness persisted, had drowsiness and so it was tapered to 0.5mg at night alone. Next she was started on alpha agonist tablet clonidine 0.1mg and was increased upto 0.3mg over a week's time, she started to have hypotension and so it was stopped. Trihexyphenidyl dose was increased upto 6mg but her symptoms continued. She was assessed with Barnes Akathisia Rating Scale. Initially her subjective and objective restlessness amounted to a score of 9 and her Global Clinical Assessment of Akathisia score was 5. After one week of cyproheptadine, her total subjective and objective restlessness scores were 2 and her global clinical assessment of akathisia score was 1. During follow up, her mood symptoms settled down and there were no movements.

Akathisia, a drug induced movement disorder if left untreated, has high morbidity as it can lead to suicidal intention. Shear reported completed suicides which occurred impulsively in schizophrenia patients with akathisia. Sculte have reported suicidal ideation attributed to akathisia. D2 receptor affinity of Haloperidol is high and its administration is found to have increased expression of fos protein in regions of high D2 expression like striatum, prefrontal cortex, nucleus accumbens, lateral septal nucleus

and dorsolateral striatum resulting in high incidence of akathisia. Conventional treatment involves lowering the dosage of the antipsychotic medications, adding benzodiazepines like diazepam or clonazepam, clonidine, mirtazapine. In few patients, the first line drugs like antiadrenergic drugs and anticholinergic medications have limitations based on tolerability and side effect profile. These treatment strategies suggest that a complicated relationship exists between the various neurotransmitter systems, including dopamine, acetylcholine, gamma-aminobutyric acid, norepinephrine, serotonin, and neuropeptides making the outcome more and more challenging. Other modalities like Cyproheptadine a 5HT receptor antagonist has demonstrated significant efficacy and adequate tolerability in small, randomized, placebo controlled trials in patients with First generation Antipsychotic induced akathisia based on the potential to counteract anti psychotic induced receptor blockade which increases dopamine release. In a double blind study done in 30 Schizophrenia patients with Neuroleptic Induced Akathisia, it was found that the reduction in severity of the akathisia was 46% in Cyproheptadine group whereas it was 42% in the propranolol group. It has also got better tolerability. When conventional method fails and adverse effects prop in, treatment with alternative options like cyproheptadine can be considered.

There should be a personalized treatment plan for akathisia, incorporating details like history, therapeutic response and side effects profile. When the initial approach like antipsychotic dose reduction, discontinuing polypharmacy, choosing of an antipsychotic agent with lower liability for akathisia and addition of an anti adrenergic agent fails, next line measures like adding cyproheptadine can be considered.