CASE REPORT

# Trihexyphenidyl-induced Hypersexuality: A Case Report

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## Abstract

Anticholinergics such as trihexyphenidyl are widely prescribed for the prophylaxis and treatment of antipsychotic-induced extrapyramidal symptoms. Although prescribed commonly with the typical antipsychotics, they may also be prescribed to counteract the extrapyramidal side effects of atypical antipsychotics rarely. These drugs may sometimes cause euphoria as a side effect. We report a case of a 29-year-old male suffering from schizophrenia who developed features of hypersexuality on starting trihexyphenidyl, which resolved on its discontinuation only to re-emerge on re-challenging the patient with the same drug.

**Keywords:** Anticholinergics, Hypersexuality, Trihexyphenidyl.

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## Introduction

Anticholinergic drugs are used in the prophylaxis of extrapyramidal reactions caused by antipsychotic drugs.[1] The inhibitory effects of dopaminergic neurons are normally balanced by the excitatory effects of cholinergic neurons. Blocking dopamine receptors by antipsychotics alters this balance, which causes a relative cholinergic excess resulting in extrapyramidal symptoms.[2] Blocking of cholinergic activity by anticholinergic drugs restores a near normal balance and extrapyramidal symptoms are ameliorated.[3] On the contrary, anticholinergic drugs also act as a potent indirect dopamine agonist in the limbic system, which is involved in motivation, learning, memory, and reward.[4] The euphoric and probable mood-elating effects of anticholinergics are explained by this mechanism.

Trihexyphenidyl binds with high affinity to the $M_1$ muscarinic receptors and possibly with the dopamine receptors. The blockade of the muscarinic peripheral receptors results in reversible and minor side effects such as dryness of the mouth, drowsiness, constipation, and blurred vision; the blockade of the central nervous system receptors yields major psychiatric symptoms such as euphoria, visual, and auditory hallucinations.[5] However, no known mechanism exists, which could explain hypersexuality as its side effect. We report herewith the case of a 29-year-old male patient with schizophrenia who developed hypersexuality with trihexyphenidyl.

## Case Description

A year ago, a 29-year-old Hindu graduate, self-employed, married male had presented to our outpatient department with complaints of suspiciousness against his family members, muttering to self, and hearing of voices inaudible to others since 4 months prior to presentation. On clinical interview, the patient stated that his family members were plotting to kill him and get his wife remarried to his younger brother. On asking as to what made him believe this, he stated that he could hear voices of three males unknown to him warning him of the same. Although he could not see any of them, he believed them to be real and would talk to them in return. He further stated that the entire neighborhood was involved in the plot as they would talk about him among themselves. He gradually started remaining withdrawn from his family members, refused to eat food cooked by them, and began preparing his own meal instead. He stopped going to work and confined himself to his room following which he was brought for a psychiatric consultation.

There was no history suggestive of any other psychopathology or substance use. There was no history suggestive of any medical/surgical comorbidity or family history of psychiatric illness. On examination of mental status, the patient was oriented to time, place, and person; was ill-kempt and unshaven; and had unclean nails. He had persecutory and referential delusions and also expressed death wishes as he was fed up of being monitored by his family members. He also had second person auditory hallucinations. A diagnosis of paranoid-type schizophrenia was made per International Classification of Diseases, Tenth Revision and the patient was started on olanzapine 5 mg at night and clonazepam 0.5 mg twice a day was added because of anxiety. The patient was followed up regularly every 15 days and the dose of olanzapine being titrated on subsequent follow-ups to 20 mg at night. Clonazepam was withdrawn in a span of 2 months.

The patient exhibited marked improvement in symptoms, starting with improved sleep, reduction in anxiety to disappearance of auditory hallucinations and fragmentation of his delusional beliefs. Three months later, the patient and his relatives perceived around 100% improvement and he had developed grade IV insight. The patient resumed his work and assured that he would come for follow-ups regularly alone. After a year on medication, the patient started having tremulousness of his hands with slurred speech following which an examination was done, which demonstrated postural tremors, rigidity, and slurring of speech, suggestive of olanzapine-induced extrapyramidal symptoms, and

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trihexyphenidyl 2 mg twice a day was added. In the subsequent follow-up, there was improvement in his extrapyramidal symptoms, but he started complaining of an abrupt increase in his libido, having repeated urges to masturbate, watch pornography, force his wife to have intercourse daily often 2 to 3 times a day, which was not present before and this would make him anxious and distressed. On assessment, trihexyphenidyl was stopped and the dose of olanzapine reduced to 15 mg. Fifteen days later in the next follow-up, the patient reported complete resolution of hypersexual symptoms though tremors were noted. A decision to rechallenge the patient with trihexyphenidyl was taken after his consent; and in view of tremors, he was started with a dose of 2 mg at night. The patient, however, came back the next week with recurrence of hypersexual symptoms following which trihexyphenidyl was stopped. Olanzapine was reduced to 10 mg and the patient was shifted to aripiprazole 10 mg over 3 weeks. There was immediate resolution of hypersexual symptoms in the next follow-up and removal of olanzapine led to an amelioration of his extrapyramidal symptoms. The patient is currently maintained and following up well.

## Discussion

To the best of our knowledge, hypersexuality as a side effect of an anticholinergic drug has not been reported previously. An extensive literature search revealed no case reports in this domain. However, clinicians must be aware of this potential adverse reaction as trihexyphenidyl is a commonly used drug in clinical practice. There is also a clinical potential to consider whether combining antidepressants with this drug as used in polypharmacy may precipitate hypersexuality as a side effect. There have been case reports of antidepressant-induced hypersexuality but none with anticholinergics.[6] Clinicians must be aware of this adverse effect, and it is worthwhile noting that the neurobiological mechanisms of this phenomenon need to be still elucidated.

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