

# Methylphenidate for the Treatment of Erectile Dysfunction Induced By Long Acting Injectable Paliperidone Palmitate: A Case Report

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## ABSTRACT:

Methylphenidate for the treatment of erectile dysfunction induced by long acting injectable paliperidone palmitate: a case report

Erectile dysfunction is one of the common sexual adverse effects encountered in male patients treated with antipsychotics. It is associated with prolactin secretion secondary to dopamine antagonism by the antipsychotics. Methylphenidate is a psychostimulant that inhibits the reuptake of dopamine. In this case, we report a 42 year old schizophrenic male, who developed erectile dysfunction after administration of a long acting injectable antipsychotic, namely paliperidone palmitate. The erectile dysfunction did not respond to sildenafil but recovered with the treatment of methylphenidate 10mg. The current finding suggests that clinicians should be aware of the possible emergence of erectile dysfunction among patients on long acting injectable antipsychotics. Methylphenidate may be an alternative treatment option for erectile dysfunction induced by antipsychotics.

**Keywords:** erectile dysfunction, paliperidone, methylphenidate, sexual dysfunction

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## INTRODUCTION

There is often a lack of attention among clinicians on the issue of sexual dysfunction related to antipsychotics. This may be based on the notion that schizophrenic patients have difficulty in maintaining relationships and therefore the issue of sexual dysfunction will not be a concern (1). However, with the emergence of newer antipsychotic agents with better efficacy and minimal extrapyramidal adverse effects, most schizophrenic patients are able to return to society and start their own family. Among male patients, erectile dysfunction (ED) has been documented with the use of the first and new generation of

antipsychotics (2). There have also been reports of cases of galactorrhea and breast engorgement which are the result of prolactin secretion secondary to the dopamine antagonist effect at the pituitary gland. The International Index of Erectile Function (IIEF) is a commonly used self-rated tool for assessment of male sexual dysfunction (3). The abbreviated version, IIEF-5, has been developed as a diagnostic tool for ED to complement clinical judgment (4).

Sildenafil citrate was introduced in 1990's for the treatment of erectile dysfunction. Sildenafil is a potent and selective inhibitor of cGMP-specific phosphodiesterase type 5 (PDE5). Increased cGMP leads to smooth muscle relaxation (vasodilation) of

arteries, followed by increased inflow of blood into the spongy tissue of the penis which causes an erection (5). In view of the difference between the mechanism of erectile dysfunction induced by antipsychotics and the action of sildenafil, there is uncertainty about the efficacy of sildenafil in this condition. An alternative treatment option which targets the mechanism of erectile dysfunction induced by antipsychotics may be required.

There have been reports of using stimulants for treatment of sexual dysfunction (6). The following is a case of antipsychotic induced erectile dysfunction that did not respond to sildenafil but recovered with methylphenidate treatment.

## CASE REPORT

Mr AS was a 43-year-old Indian male, married patient with 7 children. He had been diagnosed as having paranoid schizophrenia since 2010. He first presented with paranoid delusions about his family members, was easily irritable and wandered naked in the temple. His initial treatment consisted of haloperidol 5mg twice daily, trihexyphenidyl 2 mg twice daily and lorazepam 1mg twice daily. He was not compliant with these medications and was readmitted to the ward with the same complaints. He also lost his job due to the illness. As a result, he was started on a long acting injectable antipsychotic. He was given depot paliperidone palmitate 150 mg on day-1 and 100 mg on day-8. He was subsequently maintained on paliperidone palmitate 100 mg monthly with no other oral psychotropics. He recovered from psychosis and able to returned to work as a construction laborer.

However, after 3 months with the depot paliperidone palmitate, Mr AS complained of erectile dysfunction. He stated that he had sexual desire and urge but was unable to achieve an erection during intercourse. This information was confirmed by his wife, who claimed his sexual function was normal prior to the depot paliperidone palmitate and she stated that they were having sexual relations 3 to 4 times per week. They did not have any marital problems. The sexual complaint was not part of the patient's

delusion and there were no changes of mental state based on the clinical assessment. Mr AS was diagnosed as having erectile dysfunction induced by depot paliperidone palmitate. His IIEF-5 score was 5. He was started on sildenafil 50 mg but Mr AS found it was not helpful even with adequate sexual arousal from his wife. He was then put on methylphenidate 5mg when necessary and advised to take it before 6 pm. After a month, Mr AS claimed that there was a slight improvement in his sexual function, and his IIEF-5 was 10. The methylphenidate was increased to 10 mg. After 3 months, Mr AS recovered from erectile dysfunction and his IIEF-5 score was 24. Throughout the period, there was no worsening of psychosis or issues of dependence. Mr AS only took the methylphenidate when necessary. Both the patient and wife were satisfied with the medications.

## DISCUSSION

To the best of our knowledge, this is the first case report on the use of methylphenidate for the treatment of erectile dysfunction induced by long acting injectable paliperidone palmitate. Many schizophrenic patients do not adhere to the recommended therapeutic regimes. One of the methods of overcoming the issue of non-adherence is the use of long acting injectable antipsychotics. Paliperidone palmitate is one of the few new antipsychotic agents available in an intramuscular formulation. Paliperidone palmitate was formulated as an aqueous suspension with low water solubility, so it can be administered monthly. Paliperidone, like risperidone, blocks both 5HT<sub>2A</sub> and dopamine D<sub>2</sub> receptors, as well as alpha 1 and alpha 2 adrenoceptors and histamine 1 receptors but not beta adrenoceptors, muscarinic cholinergic receptors or peptidergic receptors. Dopamine acts on the pituitary as an inhibitor of prolactin secretion. Due to the blockade of dopamine D<sub>2</sub> receptors, paliperidone is associated with substantial increases in serum prolactin which may lead to amenorrhea, anorgasmia, erectile dysfunction, galactorrhea, and other sexual dysfunction (7).

Methylphenidate is a piperidine-derived central nervous system stimulant. The IUPAC name for methylphenidate is methyl- $\alpha$ -phenyl-2-piperinacetate hydrochloride. Methylphenidate is marketed as a racemic mixture of the d-threo and l-threo enantiomers. Previous studies have revealed that the desired pharmacological effect of methylphenidate resides entirely in the d-threo isomer. The mechanism of action of methylphenidate is similar to other stimulants like cocaine and amphetamine. However, the complete mechanism of action is still not fully understood. Methylphenidate inhibits the reuptake of dopamine by binding to the dopamine transporter in the presynaptic cell membrane. In addition to the effect on dopamine, methylphenidate increases extracellular norepinephrine (8,9).

Methylphenidate is commonly used for attention-deficit/hyperactivity disorder (9). Some studies have suggested that psychostimulants, such as methylphenidate, might be effective in reversing or reducing antidepressant-associated sexual dysfunction (6,10). In the current case, methylphenidate was prescribed after the subject who was having erectile dysfunction induced by the long acting injectable paliperidone palmitate failed to respond to sildenafil. We propose that the main mechanism of action of methylphenidate, an

increase of the synaptic concentration of dopamine by blocking reuptake of dopamine at the synapse, may reverse the sexual side effects of paliperidone palmitate.

There are several precautions while using methylphenidate in patients with psychosis. Acute psychotic symptoms must be treated and controlled before methylphenidate treatment is considered. Psychotic symptoms, including visual and tactile hallucinations have been reported in patients given stimulant products, including methylphenidate. Chronic abuse of psychostimulants such as methylphenidate can lead to marked tolerance and psychological dependence with varying degrees of abnormal behavior. Close monitoring of the use of methylphenidate is required to reduce the risk of dependence (11). Lastly, methylphenidate should be used with caution in patients with epilepsy, as clinical experience has shown that it can cause an increase in seizure frequency in a small number of such patients (9).

In conclusion, clinicians should be aware of the possibility of emergent sexual dysfunction induced by the long acting injectable paliperidone palmitate. Erectile dysfunction among male subjects should be addressed early and methylphenidate could be used as a treatment option with proper precautions.

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