



Successful treatment of paliperidone palmitate induced akathisia with mirtazapine: A case report

Paliperidon palmitat enjeksiyonu sonrası gelişen akatizinin mirtazapinle başarılı tedavisi: Bir olgu sunumu

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Abstract

Paliperidone palmitate is a long-acting injectable preparation and is indicated in acute and maintenance treatment of schizophrenia. Akathisia is an extrapyramidal symptom characterized by inner restlessness and the need to keep moving. Although β -blockers, benzodiazepines and anticholinergics have been used in the treatment of antipsychotic-induced akathisia, mirtazapine is also effective in the treatment of antipsychotic-induced akathisia. However, our search of literature did not reveal any cases of use mirtazapine in the treatment of akathisia associated with the use of long-acting antipsychotics. In this case, we used each treatment line to be used in the treatment of akathisia; however, the patient could be stabilized only by mirtazapine.

Keywords: Schizophrenia, Paliperidone palmitate, Akathisia, Mirtazapine, Antipsychotic.

Öz.

Paliperidon palmitat uzun etkili enjekte edilebilir bir preparattır ve şizofreninin akut ve idame tedavisinde endikedir. Akatizi, iç huzursuzluk ve hareket etmeye devam etme gereksinimi ile karakterize ekstrapiramidal bir semptomdur. Antipsikotikle indüklenen akatizi tedavisinde β -blokerler, benzodiazepinler ve antikolinergikler kullanılmasına rağmen, mirtazapinin de etkili olduğu gösterilmiştir. Ancak, literatür taramamızda, uzun etkili antipsikotiklerin kullanımıyla ilişkili akatizi tedavisinde mirtazapin kullanımıyla ilgili bir olguya rastlanmamıştır. Bu olgu rutin akatizi tedavisiyle fayda görmeyip, sadece mirtazapinden yarar görmüştür.

Anahtar kelimeler: Şizofreni, Paliperidon palmitat, Akatizi, Mirtazapin, Antipsikotik

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Introduction

Schizophrenia is a severe, relapsing psychiatric disorder requiring long-term treatment with antipsychotic medications and the treatment process can be challenging at times. Paliperidone palmitate is a long-acting injectable preparation and is indicated in acute and maintenance treatment of schizophrenia and is administered as monthly intramuscular injections (1). On the other hand, long-term injections may lead to several movement disorders including extrapyramidal symptoms and tardive dyskinesia (2). Akathisia is an extrapyramidal symptom characterized by inner restlessness and the need to keep moving.

There are reports indicating that mirtazapine, a 5HT 2A and 5HT 2C blocker is also effective in the treatment of antipsychotic-induced akathisia (3-5). However, our search of literature did not reveal any cases of use mirtazapine in the treatment of akathisia associated with the use of long-acting antipsychotics.

In this paper, we will mention the treatment of a patient with schizophrenia who developed akathisia after paliperidone palmitate injection.

Case Report

An 18 year-old male patient, A.C., who presented with "inability to stay still and restlessness", was seen in the outpatient clinic in company with his mother. The patient had experienced several symptoms for the last one year including introversion, poor self-care, talking to himself, continuously looking at the mirror, run away from home and he had mostly preferred to stay at his room. His family had brought him to another health center since he had stopped eating one week ago. Paliperidone palmitate was injected to the patient intramuscularly (into the deltoid muscle) at a dose of 150 mg, however he developed a variety of symptoms several hours later including inability to stay still, restlessness, hypersalivation, rigidity and torticollis. In the mental health assessment of the patient, he appeared his stated age, he was showing signs of self-neglect, and his cooperation was limited and he was anxious. He was fully oriented to space, time and person. No sensory processing disorder was detected. Thought content was impoverished but he had no hallucinations. His thoughts begin and continue as goal-oriented and he frequently showed deviations from the subject matter and purpose. Connotations were disorganized. Attention was impaired. He had no insights and showed psychomotor agitation. The medical history of patients was otherwise unremarkable. His family history was unremarkable. The patient was admitted to the ward. Laboratory tests including a complete blood count and blood biochemistry, electrocardiogram, electroencephalogram, neuroimaging studies and neurological examination

were within normal limits. According to DSM-5, the patient was diagnosed with schizophrenia, drug-induced acute akathisia, acute dystonia and Parkinsonism. Clinical symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS). The patient's PANSS scores: positive scale 13, negative scale 37, and general psychopathology scale 61. His initial Clinical Global Impression-Severity of Illness (CGI-SI) score was 6. Barnes Akathisia Scale (BAS) (6) score was 14. He was started on biperiden at a dose of 6 mg daily, propranolol at a dose of 60 mg daily and clonazepam at a dose of 6 mg daily. The signs of dystonia resolved in the second day of therapy however symptoms of akathisia persisted and lorazepam was added to the treatment on the seventh day of the treatment at a dose of 7.5 mg daily, in addition, bornaprine HCl was also added to the therapy at a dose of 12 mg daily, as Parkinsonian symptoms (rigidity, bradykinesia and parkinsonian posture) were intensified. By the 11th day, Parkinsonian signs were resolved, however akathisia symptoms were not adequately improved, therefore clonazepam was discontinued and mirtazapine (in the evening) was added to the therapy at a dose of 15 mg daily. Akathisia symptoms were completely resolved and the patient slept well that night when he was started on mirtazapine. However, the next day the symptoms recurred before the midday and another mirtazapine dose (morning dose) was added to the treatment. In the 13th day of the treatment, the BAS score was 0. He scored 3 on the CGI-GI and achieved a PANSS scale total score of 62 (The patient's PANSS scores: positive scale 9, negative scale 22, and general psychopathology scale 31). In the 20th day of hospitalization, upon the recurrence of the symptom of laughing at himself and aggravation of the social isolation (The patient's PANSS scores: positive scale 11, negative scale 29, and general psychopathology scale 43) olanzapine was added to the therapy at a daily dose of 10 mg. However the addition of olanzapine to the treatment further increased the severity of akathisia symptoms. Therefore, considering the propensity of the patient to develop extrapyramidal symptoms, olanzapine was switched to clozapine. Clozapine was started at a dose of 25 mg daily and gradually increased up to 400 mg daily, within 2 months. No further aggravation was observed in the akathisia symptoms for the next two months, after the initiation of clozapine therapy. Mirtazapine was discontinued in the second day of the clozapine treatment and akathisia symptoms did not recur. The patient has a PANSS scale total score of 30 in the follow up visit, 1 month after the discontinuation of mirtazapine (The patient's PANSS scores: positive scale 7, negative scale 7, and general psychopathology scale 16); he scored 2 on the CGI-GI and 0 on the BAS.

Discussion

Paliperidone palmitate is the injectable form of long-acting, sustained-release, depot anti-psychotic paliperidone, an active metabolite of risperidone. As with other second-generation antipsychotics, paliperidone also acts as an antagonist of D2 receptors and serotonin 5HT2A receptors (7). This activity may lead adverse effects including weight gain, orthostatic hypotension and sedation (7).

Also, this drug may lead to movement disorders including extrapyramidal symptoms and tardive dyskinesia (2). Although the pathophysiology of antipsychotic-induced acute akathisia remains unknown, a potential mechanism associated with dopaminergic and serotonergic pathways has been suggested. B-blockers, benzodiazepines and anticholinergics have been recommended in the treatment of antipsychotic-induced akathisia. At therapeutic doses (30 to 90 mg daily), provides an antidepressant effect as a result of its strong antagonist activity of mirtazapine at presynaptic α -2 adrenergic receptors. Low-dose mirtazapine primarily antagonizes 5-HT_{2A} / 2C and H₁ postsynaptic receptors. In a study, it was suggested that antipsychotic-induced akathisia responded antagonistic effect of mirtazapine at 5HT_{2A} and 5HT_{2C} receptors (3). Even, it has been demonstrated that mirtazapine has been superior over propranolol and placebo in the treatment of antipsychotic-induced akathisia (3). In another randomized, double-blind, placebo or propranolol controlled study investigating the effects of mirtazapine in antipsychotic-induced akathisia, higher response rates were obtained with low-dose mirtazapine (15 mg daily) and propranolol (80 mg daily) in comparison to placebo, in patients with akathisia, while mirtazapine was better tolerated than propranolol (4). Furthermore, akathisia was three times less severe in patients who received mirtazapine compared to placebo. In another double-blind, placebo controlled study low-dose mirtazapine (15 mg daily) was found to be effective in neuroleptic-induced akathisia (5).

However, there are publications reporting that mirtazapine (≥ 15 mg/daily) may also cause akathisia (8-10). Our patient was refractory to a number of medication including propranolol, clonazepam and lorazepam but complete recovery occurred after treatment with mirtazapine.

In conclusion, the management of adverse effects associated with the medications used in the treatment of schizophrenia is as important as the treatment of schizophrenia. In this case, we used each treatment line to be used in the treatment of akathisia; however, the patient could be stabilized only by mirtazapine. Mirtazapine should be kept in mind as a potential alternative treatment of patients with akathisia, if β -blockers and anticholinergics cannot be used.

References

1. Kramer M, Litman R, Hough D, Lane R, Lim P, Liu Y, Eerdeken M. Paliperidone palmitate, a potential long-acting treatment for patients with schizophrenia. Results of a randomized, double-blind, placebo-controlled efficacy and safety study. *Intl J Neuro-psychopharm* 2010; 13: 635–47.
2. Taylor D. Psychopharmacology and adverse effects of antipsychotic long-acting injections: a review. *Br J Psychiatry Suppl*. 2009; 52: 13–9.
3. Hieber R, Dellenbaugh T, Nelson LA. Role of mirtazapine in the treatment of antipsychotic-induced akathisia. *Ann. Pharmacother* 2008; 42: 841–46.
4. Poyurovsky M, Pashinian A, Weizman R, Fuchs C, Weizman A. Low-dose mirtazapine: A new option in the treatment of antipsychotic-induced akathisia. A randomized, double-blind, placebo- and propranolol-controlled trial. *Biol Psychiatry* 2006; 59:1071–77.
5. Poyurovsky M, Epshtein S, Fuchs C, Schneidman M, Weizman R, Weizman A. Efficacy of low-dose mirtazapine in neuroleptic-induced akathisia: a double-blind randomized placebo-controlled pilot study. *J Clin Psychopharmacol* 2003; 23: 305–8.
6. Barnes TR. A rating scale for drug-induced akathisia. *Br J Psychiatry* 1989; 154: 672–6.
7. Shayegan DK, Stahl SM. Atypical antipsychotics: matching receptor profile to individual patient's clinical profile. *CNS Spectr* 2004; 9: 6–14.
8. Gulsun M, Doruk A. Mirtazapine-induced akathisia. *J Clin Psychopharmacol* 2008; 28 :467.
9. Ozyildirim I, Kosecioglu S. Mirtazapine induced tardive akathisia: a case report. *Eur Psychiatry* 2009; 24: 507.
10. Raveendranathan D, Swaminath GR. Mirtazapine Induced Akathisia: Understanding a Complex Mechanism. *Indian J Psychol Med* 2015; 37: 474.