Paliperidone-induced mania: a case report

Neşe B. Bal[1]
https://orcid.org/0000-0002-6445-9393

Meryem G. Teksin Bakir[1]
https://orcid.org/0000-0001-6080-2337

Ali Çayköylü[1]
https://orcid.org/0000-0003-1586-9334

Elvan Özalp[1]
https://orcid.org/ 0000-0001-9618-8148

Çağla Koçberber[1]
https://orcid.org/0000-0002-7549-4143

Bahriye E. Yilmazoğlu[1]
https://orcid.org/0000-0002-8209-3583

[1] *Psychiatry Clinic, T.C.S.B. Dr. Abdurrahman Yurtarslan Oncology Training and Research Hospital, Ankara, Turkey.*

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Introduction

Paliperidone is an atypical antipsychotic derived from 9-hydroxyrisperidone. Paliperidone shows antagonistic activity on dopamine D2, serotonin 5HT2A, and histamine H1 receptors as well as the alpha1 and alpha2 adrenergic receptors[1]. Paliperidone palmitate is an injectable form of paliperidone that has long-lasting potency and has been developed to improve treatment compliance in patients who have schizophrenia. Paliperidone shows high binding affinity to dopamine D2 and serotonin 5HT2A receptors. It also shows significant binding affinity to α_{2a} receptors. This leads to an increase in serotonin release, which may also induce antidepressant activity[2]. Although it seems to be paradoxical, manias that are associated with atypical antipsychotic drugs have been reported in the literature[3]. However, very little research has been published on paliperidone- and paliperidone palmitate-induced mania[1,4]. This report will discuss the case of a patient who was hospitalized with a diagnosis of schizophrenia and manic symptoms during paliperidone palmitate treatment.

Case report

A 27-year-old male was diagnosed with paranoid schizophrenia six years ago. His initial complaints were social and emotional withdrawal and referential, persecutory, and nihilistic delusions. Treatment with oral haloperidol 20 mg was started, but his psychotic symptoms did not improve so he was switched to olanzapine 15 mg/day. His symptoms improved with the olanzapine treatment. In the follow-up visits, the olanzapine dosage was reduced to 10 mg/day because of the metabolic side effects of olanzapine, and the patient was in remission for two years. However, his psychotic symptoms began to worsen due to poor treatment compliance with regard to taking the olanzapine. The patient was hospitalized, and the olanzapine dose was increased to 30 mg/day. His psychotic symptoms abated with this treatment regime, and he remained in remission while taking the olanzapine 30 mg/day until 2018. However, his psychotic symptoms worsened, once again due to poor medication compliance, and he was involuntarily hospitalized. Because of his reduced compliance to oral medication, long-acting paliperidone palmitate treatment was planned. Treatment with oral paliperidone 6 mg/day was started, and a paliperidone palmitate injection was scheduled for the 10th day of taking the oral paliperidone. Oral paliperidone treatment was stopped at the 15th day of the initial injection of paliperidone palmitate. The initial dose was set at 150 mg for the first treatment, increasing to 100 mg for the eighth, and staying on a maintenance dose of 100 mg for the first month. Because of the continuation of his symptoms after the maintenance dose of 100 mg, the next paliperidone palmitate injection was set at 150 mg, and oral paliperidone 6 mg/day was added to the treatment regime until the next injection. One week after he had been given this treatment, the patient started to experience decreased sleep requirements, logorrhoea, grandiosity, euphoria, and psychomotor agitation. His score on the Young Mania Rating Scale (YMRS) was 30. Clonazepam 3 mg/day was added to control the manic symptoms. Although the patient's mobility decreased and his sleep improved, he continued to experience grandiosity, and sodium valproate 500 mg was started and gradually increased to 1,500 mg/day. Three weeks after the addition of the sodium valproate (VPA: 117 mEq/lt), the patient's YMRS score had decreased to 26. The paliperidone palmitate injections and oral paliperidone were discontinued and replaced by clozapine. By the third week, the patient's manic symptoms had decreased with a dosage of clozapine 400 mg/per day (YMRS:16). The clozapine was gradually increased to 700 mg/day, and his last YMRS score before discharge from hospital was 6. After discharge, the patient was treated with clozapine 700 mg and sodium valproate 1,500 mg/day and did not show any reoccurrence of psychotic, manic, or hypomanic symptoms.

Discussion

Here we reported on the case of a patient who had a diagnosis of schizophrenia and developed manic symptoms after being treated with paliperidone palmitate. Although the patient had been taking antipsychotic medication for six years, no manic symptoms had been found during this time. The emergence of manic symptoms after paliperidone palmitate treatment with no other combination medication suggests causality: that the patient's manic symptoms were due to the paliperidone palmitate treatment. There have been reports of cases of mania with atypical antipsychotics such as risperidone, aripiprazole, and quetiapine[3]. However, reports of mania cases that were induced by paliperidone are limited[1,4,5].

Address for correspondence: Meryem G. Teksin Bakir. Psychiatry Clinic, T.C.S.B. Dr. Abdurrahman Yurtarslan Oncology Training and Research Hospital. Mehmet Akif Ersoy Mh. 13. Cadde No: 56, Yenimahalle, 06200, Ankara, Turkey. Telephone: +90-312-4340990/6410. Fax: +90-312-4324915. E-mail: gulteksin@gmail.com

Paliperidone, is a new atypical antipsychotic drug. Although risperidone has antimanic activity, it has also been reported to induce mania in some cases[4]. Atypical antipsychotic-induced mania has been reported as being associated with frontal dopamine release via the 5HT2A receptor blockade[3]. Paliperidone also has D2 and 5HT2A receptor blockade activity. In addition, paliperidone has significant α2A antagonistic activity, and this antagonism tends to increase the release of serotonin. This increase in serotonin is associated with the antidepressant activity of paliperidone[2,4] and it is believed that this serotonergic effect might contribute to the development of manic symptoms. After taking a single dose of paliperidone palmitate, which has long-lasting potency, the plasma level gradually increases and reaches T_{max} on the 13th day. The release of paliperidone palmitate into the plasma begins from the first day and continues for four months. Furthermore, paliperidone palmitate rapidly reaches therapeutic concentration in the first week following the administration of the two initial doses, and adding oral paliperidone is, therefore, not recommended due to the rapid therapeutic effect of paliperidone palmitate after the onset of this regimen[4]. Although the pharmacological properties and possible antidepressant efficacy of paliperidone may have caused symptoms of mania in our case, it is not possible to provide a full explanation of the relationship between paliperidone palmitate treatment and mania from our case report alone.

Nevertheless, this case suggests that patients with schizophrenia should be carefully monitored during the transition to paliperidone palmitate with long-lasting potency, to watch for the development of symptoms such as mania. Further studies are needed to clarify the mechanisms of this clinical condition.

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