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CASE REPORT

Paliperidone Palmitate-Induced Delirium in an Adolescent with Schizophrenia

Case report

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الهذيان الناجم عن عقار الباليبريدون بالمتيت عند مراهق مصاب بالفصام

تقرير حالة

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ABSTRACT: Schizophrenia is a serious long-term mental disorder which usually presents in adolescence or early adulthood. However, poor adherence to oral antipsychotics can lead to relapse and rehospitalisation. We report an adolescent male with schizophrenia who was referred to the South London & Maudsley National Health Service Foundation Trust, London, UK, in 2015 due to worsening psychotic symptoms. Following poor compliance with oral medications, a four-week regimen of paliperidone palmitate long-acting injections was initiated, with an initial positive response. However, 10 days after the second dose, the patient developed severe acute-onset delirium with fluctuating levels of consciousness. Paliperidone palmitate was discontinued and the patient instead underwent a course of zuclopenthixol decanoate long-acting injections with a favourable outcome.

Keywords: Adolescent Psychiatry; Schizophrenia; Antipsychotic Agents; Delirium; Paliperidone Palmitate; Zuclopenthixol; Case Report; United Kingdom.

الملخص: مرض الفصام هو اضطراب نفسي خطير على المدى الطويل وعادة ما يظهر المرض خلال فترة المراهقة أو مرحلة البلوغ المبكر. ويعتبر ضعف الالتزام في تناول الأدوية عن طريق الفم من أسباب أنتكاسة المريض وسببا لإعادة تنويم المرضى. نعرض هنا تقرير لحالة مراهق ذكر مصاب بالفصام تم تحويلة إلى مؤسسة جنوب لندن ومودسلي للخدما ت الصحية الوطنية، لندن، المملكة المتحدة عام 2015 بسبب تفاقم أعراض ذهانية نتيجة سوء الالتزام في تناول الادوية عن طريق الفم، بدأت خطة الأربع أسابيع باستخدام حقن الباليبريدون بالمتيت طويلة المفعول مع استجابة إيجابية أولية. ومع ذلك، بعد 10 أيام من الجرعة الثانية أصيب المريض بأعراض حادة وشديدة من الهذيان مع تقلبات في مستوى الوعي. تم إيقاف أستخدام الباليبريدون بالمتيت واستبداله بحقن عقار الزكلوبينثكسول طويل المفعول والتي ترتبت علية نتائج إيجابية.

الكلمات المفتاحية: الطب النفسي للمراهقين؛ الفصام؛ مضادات الذهان؛ الهذيان؛ عقار الباليبريدون بالمتيت؛ عقار الزكلوبينثكسول؛ تقرير حالة؛ المملكة المتحدة.

Schizophrenia is a serious mental disorder characterised by the distortion of thought, perception and affect.[1] Overall, the disease has a massive global burden, with a lifetime prevalence of four cases per 1,000 individuals.[2,3] In younger patients, extra care needs to be taken when prescribing antipsychotic medications, since such individuals are at higher risk of developing side-effects.[4] In general, second-generation antipsychotics (SGAs) are the first line of treatment for children and adolescents, whereas first-generation antipsychotics (FGAs) should be avoided due to the high risk of extrapyramidal side-effects.[5] Nevertheless, adherence to oral antipsychotic medications remains an ongoing challenge among patients with schizophrenia; the administration of medication in the form of a long-acting injection (LAI) can help overcome this issue, thus reducing the chance of relapse and rehospitalisation.[6]

Case Report

A 16-year-old Caucasian male patient was referred by his general practitioner to the Child & Adolescent Mental Health Services of the South London & Maudsley National Health Service Foundation Trust, London, UK, in 2015, following the worsening of existing psychotic symptoms. The patient had a one-year history of low mood, anxiety, paranoia and social isolation. These symptoms initially presented solely in the context of cannabis use; however, the patient had stopped smoking cannabis when he noticed that this worsened his distress. Psychiatrically, he exhibited all the hallmarks of paranoid ideation. He believed that his room was being monitored and described auditory command hallucinations in which voices would tell him to get dressed in the middle of the night and go outside to walk in the park, as well as

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making derogatory remarks about him. The command hallucinations overpowered his usual distress of leaving his house, but did not tell him to harm himself or others. He also described elements of thought interference—i.e. thoughts being taken from and put into his head—and worried that his thoughts were being broadcast to others.

The patient had a strong family history of mental disorders, with a history of depression in his mother and two half-siblings who suffered from psychotic illness. Regarding his personal history, he had achieved normal developmental milestones and attended primary school; however, he had been excluded from secondary school following repeated altercations with his teachers. He had no friends and led a reclusive lifestyle. His social functioning had deteriorated significantly over the last year and even more drastically in the weeks prior to his referral. He reported feelings of low mood, anxiety, anhedonia and difficulty falling asleep.

Upon referral, the patient was initially prescribed oral olanzapine at a dosage of 10 mg once daily, which was titrated up to 20 mg per day. However, due to poor compliance with oral medications and the persistence of his psychotic symptoms, a regimen of olanzapine LAIs at a dose of 300 mg every two weeks was initiated. Although he demonstrated a reasonable response to the depot injections, these had to be discontinued due to the unavailability of a post-injection observation service and the lack of transport provision. Subsequently, the patient was prescribed oral risperidone for approximately two months, after which risperidone LAI was commenced. The dose of the depot injection was titrated to 50 mg every two weeks. The patient showed a moderate response to the treatment, although he was only partially compliant, often refusing injections and not attending his appointments every two weeks. As a result, the LAI treatment was also discontinued and the patient was again prescribed oral risperidone. This oral regimen was continued for approximately one month. The option of a monthly LAI formulation was then discussed with the patient and his caretaker. Eventually, a regimen of paliperidone palmitate LAIs every four weeks was agreed upon.

Based on his body mass index and medium build, the patient was prescribed off-label paliperidone palmitate LAIs, as per the manufacturer's instructions and the recommendations of the British National Formulary for adult patients, at an initial loading dose of 150 mg, followed by 100 mg on the 8th day.[7] Both the patient and his mother reported an initial positive response to the medication, with a marked reduction in distressing psychotic symptoms. However, 10 days after the second dose, the patient developed acute-onset altered *sensorium* and was admitted to the Accident & Emergency Department. Prior to this, the patient had been unable to sleep and reported unusual perceptual experiences such as hearing thunder and storms and smelling an unpleasant odour like burning tyres. He also suffered from fluctuating levels of consciousness, disordered speech with 'snort'-like breathing and flailing movements of the extremities.

Neurological impairment was minor, with a Glasgow Coma Scale score of 13–15. There were no frank convulsions and the patient was afebrile and did not report any headaches. He did not show any evidence of autonomic system imbalance and there was no rigidity or other features indicative of neuroleptic malignant syndrome. His C-reactive protein and serum creatine kinase levels were normal and a computed tomography scan of the brain, comprehensive metabolic panel, liver function tests, urinalysis and urine toxicology screening were unremarkable. A full blood count initially showed mildly raised leukocytes; however, when repeated the next day, all parameters were within normal ranges, with no signs indicative of a focal or systemic infection.

By the evening of the next day, the patient had regained consciousness and was found to be fully alert and awake. He could not recall any of the events of the previous day. He was subsequently discharged against medical advice and returned home to the care of his mother. Since the patient continued to experience both positive and negative schizophrenic symptoms, zuclopenthixol decanoate injections were prescribed at an initial test dose of 100 mg, before eventually being titrated to 200 mg monthly. After three months of treatment, there was a significant improvement in psychotic symptoms. At the time of the writing, the patient had not reported any serious side-effects and his activities of daily living had reverted to their premorbid status.

Discussion

The present case report describes an adolescent with schizophrenia who developed postinjection delirium/sedation syndrome (PDSS) following a regimen of paliperidone palmitate LAI. To the best of the authors' knowledge, few similar cases have been reported in the literature. Kokalj *et al.* reported a female schizophrenic patient who became delirious following an olanzapine LAI and a higher dose of paliperidone palmitate; as with the current case, the patient had a history of cannabis use.[8]

Paliperidone palmitate injections differ from other antipsychotic depot injections in that two loading

doses are required at the start of treatment, consisting of 150 mg on day one and 100 mg on day eight; these are then adjusted at monthly intervals according to the patient's response, with a recommended maintenance dose of 75 mg per month (range: 25–150 mg).[7] Although no long-acting antipsychotic injections are yet officially recommended for individuals under the age of 18 years, their use is not uncommon in patients with a history of poor medication adherence.[9]

Paliperidone palmitate is deemed an effective and acceptably tolerated antipsychotic in adolescents with psychotic spectrum disorders.[10] In a review of clinical trial databases, Alphs *et al.* found no cases of PDSS reported in completed trials of risperidone LAI, with only one PDSS case reported in a paliperidone palmitate LAI trial; however, the patient in this instance had been randomly allocated to the placebo treatment.[11] Nevertheless, manufacturers of paliperidone palmitate LAI have acknowledged that a confusional state is a possible, albeit rare, adverse reaction to the drug.[12] Although SGAs have been increasingly used as the first line of treatment for schizophrenia over the past decade, several studies have suggested there is limited or no advantage between the two classes of antipsychotics in terms of efficacy, with the only difference being the drug side-effect profile.[13,14] Similarly, despite their limited use, FGAs remain an option in the management of psychotic disorders among adolescents, as in the current case wherein the patient showed a good response and tolerability to zuclopenthixol decanoate.[15,16]

Conclusion

Schizophrenic patients and their caretakers should be made aware that PDSS is an uncommon side-effect of SGAs such as paliperidone palmitate. This case illustrates the importance of patient and family education regarding the potential side-effects of antipsychotic LAIs.

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