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Cent. Eur. J. Med. • 6(5) • 2011 • 662-664
DOI: 10.2478/s11536-011-0055-8

Central European Journal of **Medicine**

Withdrawal related adverse effects of antipsychotic medication in a patient with first-episode schizophrenia

Case Report

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Received 27 September 2010; Accepted 2 May 2011

Abstract: Withdrawal-emergent adverse effects of antipsychotics are an infrequently identified condition which can appear during antipsychotic dose reduction and medication change. In this paper, we present the case of severe extrapyramidal symptoms after a dose reduction of risperidone is presented. A patient, 23 years of age, was admitted to a health care facility due to an unexpected change in his behavior, with paranoid delusions, incoherent thinking, and significant anxiety. An initial risperidone treatment was soon changed to zuclopenhixol. Subsequently, severe extrapyramidal symptoms appeared, after which the medication was switched back to resperidone. Following this treatment, the patient left the health care facility and stopped the medication of his own volition. Psychotic symptoms and massive extrapyramidal symptoms again occurred. These symptoms subsided only slowly during a subsequent treatment with olanzapine.

The development of adverse neurological effects together with a worsening of productive psychotic symptomatology may be explained by withdrawal of antipsychotic medication. These symptoms are often attributed to new medications, which are prematurely discontinued after the appearance of an adverse effect, but which are potentially beneficial to a patient, provided that enough time for a spontaneous subsidence of withdrawal-emergent effects is given. Any change in antipsychotic treatment should be carefully considered and thoroughly planned.

Keywords: *Schizophrenia • Antipsychotics • Withdrawal-related adverse effects*

1. Introduction

Withdrawal-emergent adverse effects represent a significant barrier to a successful medication change during routine treatment. It is important to be aware of the potential development of adverse effects during discontinuation of antipsychotic drugs.

An extrapyramidal syndrome (EPS) which follows a discontinuation of antipsychotic drugs can be associated with a supersensitive (rebound) psychosis [1]. One of the first cases of EPS related to a decreased dose of risperidone, was reported in 1996 [2] and other cases quickly followed, ranging from dyskinesias, similar to the tardive dyskinesias [3,4], to potentially fatal dyskinesia of the respiratory muscles [5].

2. Presentation of the case

The presented case relates to a 23 years old patient without any previous psychiatric history. The patient history included neither head injury with loss of consciousness nor any paroxysmal conditions; 4 years prior admission he was examined for hyperthyroidism, however, thyroid gland function was found to be normal. School attendance started with a one-year delay. Despite the delay, the patient went through school with excellent grades and graduated from university with a degree in computer technology. Before admission to hospital he had been working as a computer technician. In the family history there was a single case of psychiatric hospitalization involving his mother's sibling with the diagnosis of an acute psychotic disorder. In the winter of 2008 the patient was admitted to a department of psychiatry due to a sudden change in his behavior, which included para-

noid delusions, incoherent speech, insomnia, tension, and anxiety persisting for several days. Upon admission, the patient did not show any signs of somatic disease nor was he taking any medications. However, he reported recent use of LSD, cannabis, and psilocybin. The toxicological examination of urine and examinations carried out to exclude somatic causes of symptoms (examination of fundus oculi, biochemical screening) were negative, therefore an acute schizophreniform psychotic disorder according to ICD-10 criteria was operationally diagnosed, and treatment with risperidone (4-6 mg daily), methotrimeprazine (75-175 mg daily) and promethazine (100-175 mg daily) begun. After 6 days of treatment, psychotic symptoms further increased and it was decided to change the patient's medication: risperidone was discontinued completely and, a dose of 100 mg of zuclopenthixol acetate was administered three times by injection with 48-hour intervals between administrations. After the third dose (12th day after admission) paranoid delusions and anxiety subsided but massive adverse effects in the form of acute dystonia, followed by hypokinesia, hypomimia, and tremor occurred. As a response, biperiden (2-4 mg daily) and, again, peroral risperidone (4 mg daily) were introduced. However, during following 6 days, hypokinesia and tremor grew more severe and anxiety together with psychotic symptoms began to appear again in a form of paranoid and hypochondric delusions, which were not previously seen. EPS (repeated dystonia, hypokinesia and tremor) and psychotic symptomatology reached a peak and became more severe than the original symptomatology 18-days after initial admission when the patient left the health care facility and discontinued the therapy completely for two days. When the patient returned, olanzapine (10 mg daily) was initiated and amantadine (100 mg daily) and clonazepam (1,5 mg daily) were used as adjuvant medication. Over the next 10 days, all of the adverse extrapyramidal effects declined, and after increasing the olanzapine dose to 15 mg daily, an improvement of psychotic symptoms appeared.

3. Discussion and conclusion

Spontaneous movements related to dose reduction of antipsychotics, in patients who are not diagnosed with tardive dyskinesia, are termed withdrawal dyskinesia [2]. Literature reports cases of dyskinesia appearing during the process of risperidone dose reductions [2,4]. In the present case, the increased manifestation of EPS symptoms occurred several days after the discontinuation of risperidone or zuclopenthixol. There were two peaks of EPS. The first one could be ascribed to zuclopenthixol injection, however the possibility that these symptoms could have been caused by risperidone withdrawal cannot be overlooked. The withdrawal-related effects may be mixed with adverse effects of a newly introduced antipsychotic. This should be always taken into account if adverse effects of the treatment occur shortly after discontinuation of one medication and the introduction of a new antipsychotic agent [6]. The second peak of EPS worsening appeared after discontinuation of all antipsychotics and was combined with the rapid deterioration in a psychotic symptomatology with a slightly different symptom profile and higher severity of psychotic symptoms. Patients who suffer from withdrawal-emergent EPS may also be more likely to manifest other withdrawal-related effects such as increased plasma prolactin levels [7] and so-called supersensitive psychosis [8]. According to one of the theories explaining the development of withdrawal dyskinesia, the blockade of dopamine receptors, induced by antipsychotic agents, results in up-regulation of receptors. When treatment with dopamine antagonists is discontinued, or the dose is reduced, the patient may be prone to an increased sensitivity to endogenous dopamine – supersensitive psychosis [8] and withdrawal EPS [9]. The growing number of cases of supersensitivity psychosis after clozapine withdrawal suggest that others mechanisms, namely the supersensitivity of cholinergic, serotonergic and GABAergic system or their interaction can be the cause as well [10].

Adverse effects related to the discontinuation of antipsychotics may appear rapidly and show a tendency toward spontaneous subsidence. The adverse effects which arise during a medication change are often ascribed to the newly administered drug and may lead to a premature discontinuation of a new drug, which might otherwise be helpful to the patient [1]. Therefore the possibility of withdrawal-emergent extrapyramidal symptoms should be kept in mind; any changes in antipsychotic medication should be carefully considered and potential change of medication should be thoroughly planned.

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