Lithium carbonate as a treatment for various antipsychotics-induced leukopenia and neutropenia in a patient with schizophrenia: a case report

Gonca Aşut^{1*}, Erol Göka²

¹Department of Psychiatry, Başkent University Faculty of Medicine, Ankara, Turkey
²Department of Psychiatry, Bilkent City Hospital, University of Health Sciences, Ankara, Turkey

Abstract

Leukopenia and neutropenia are rare but serious adverse effects which can happen with psychopharmacological treatment. Although clozapine is the antipsychotic most likely to cause leukopenia and neutropenia, olanzapine, quetiapine, aripiprazole, risperidone and paliperidone were all reported to be associated with this side effects. When blood dyscrasias occur switching to another antipsychotic usually resolves the problem. But if this not works the adjuvant use of lithium carbonate or granulocyte colony-stimulating factor can be tried.

In this case, we report a 50-year-old, female, clozapine-naïve patient with schizophrenia who developed reversible leukopenia and neutropenia in response to three different antipsychotic (risperidone, amisulpride, paliperidone) medications. Initiating lithium carbonate treatment improved the observed leukopenia and neutropenia. This treatment did not influence psychotic symptoms.

There is no doubt that many different drugs used in psychiatry can cause leukopenia and neutropenia. Although these events are rare, they represent serious and life-threatening hematological side effects. On the basis of our case report it may be important to be consider that the WBC and neutrophil counts should be monitored regularly while using antipsychotics other than clozapine.

Key words: Leukopenia, Neutropenia, Antipsychotics, lithium carbonate

Introduction

Risperidone is an antagonist of the serotonin 5-HT_{2A}, dopamine D₂, α₁-adrenergic and α₂-adrenergic, histamine H₁ receptors and it also has a low affinity for muscarinic cholinergic receptors. Paliperidone (9-hydroxyrisperidone) is the primary active metabolite of risperidone. Amisulpride enhances dopaminergic neurotransmission by blocking presynaptic dopamine D₂/D₃ autoreceptors at low doses. At higher doses, it antagonises postsynaptic dopamine D₂ and D₃ receptors.

Leukopenia is a decrease in the number of white blood cells and is often due to neutropenia. Neutropenia can be defined as a neutrophil count of < 1.50 × 10⁹/L. The pathophysiology of medication-induced neutropenia might be related to toxic effects or immune reactions in the bone marrow. It usually occurs after taking medications for 7 to 14 days, the severity of neutropenia is associated with duration of exposure and the dosage of medication.

Antipsychotics are known to be associated with a risk of neutropenia, especially clozapine. Although newer atypical antipsychotics have been developed with the view of being safer alternatives to clozapine, neutropenia has also been reported with other second generation antipsychotics such as olanzapine, quetiapine, risperidone, paliperidone, ziprasidone, and aripiprazole. There are two well-known treatment strategies: switching to another antipsychotic and the adjuvant use of lithium carbonate or granulocyte colony-stimulating factor.

Herein, we report a case of drug-induced leukopenia and neutropenia associated with 3 different antipsychotics (risperidone, amisulpride and paliperidone) in a clozapine-naïve patient.

Case Report

50-year-old female was admitted to our inpatient unit with 3-months history of auditory hallucinations, persecutory delusions, aggressive behaviour and 2-weeks history of selective mutism. She had been diagnosed with schizophrenia for 10 years and had taken no medication for the last 3 months. On admission, the laboratory tests were within the normal ranges. Risperidone 2mg/day treatment was initiated and the dose was increased to 6mg/day on the 7th day of treatment. After 5 days of treatment her hallucinations disappeared gradually, although her delusions were continued. Therefore, the dose of risperidone was increased to 6mg/day. 10 days after initiation of the risperidone treatment routine laboratory tests showed strong decrease in her WBC and absolute neutrophil count; WBC decreased to 2800/μl and neutrophils to 1200/μl. The result of Hematology consultation suggested that her leukopenia and neutropenia might be associated with the antipsychotic medication.

Risperidone was stopped as a possible cause. We did not substitute risperidone with another antipsychotic drug. WBC counts gradually increased from the second day on. 5 days after the cessation of risperidone treatment her hallucinations, agitation and mutism recurred. On 7th day her WBC count was 4400/μl and neutrophil count was 1800/μl. Escitalopram 5mg/day and Amisulpride 200mg/day treatments were initiated and the amisulpride dose was increased to 600mg/day on the 7th day of treatment. On the 5th day of amisulpride treatment her hallucinations and aggressive behavior subsided again and WBC and neutrophil counts were within reference ranges. Two weeks after the medication, WBC and neutrophil counts dropped again to 2900/μl and 1400/μl, respectively. Therefore, we ceased amisulpride and escitalopram treatments and followed the patient without any medication. 4 days after the cessation of amisulpride treatment her hallucinations recurred. On 5th day, her WBC count was 4600/μl and neutrophil count was 1700/μl, paliperidone treatment was initiated. On the 3th day of paliperidone treatment WBC and neutrophil counts decreased again to 2800/μl and 1400/μl. Lithium carbonate 300mg/day was added. At five days after lithium carbonate administration, the WBC and neutrophil counts had returned within the normal ranges (WBC count of 5200/μl and neutrophil count of 2800/μl). After 2 months, the patient was discharged from the hospital, blood counts remained stable and was no longer experiencing hallucinations and delusions.

Discussion

Granulocytopenia seldom occurs with antipsychotic treatment, mostly with clozapine or olanzapine, and switching to another antipsychotic usually resolves the problem. When granulocytopenia occurs, risperidone is considered to be a safe alternative.

The mechanism for drug-induced neutropenia has been studied extensively in regard to clozapine. The exact mechanism is unknown. A recent report showed that inactivated clozapine may itself exert toxic effects. Since risperidone and aripiprazole have different chemical structures compared to clozapine, olanzapine, and quetiapine, it appears that other mechanisms are involved.

In this case, there was no history of leukopenia and/or neutropenia, no other potentially haematotoxic drugs were taken concurrently, and the patient's blood counts were normal before initiating each different antipsychotic. No other cause of neutropenia was identified.

This case implies that clinicians should be aware of the risk of leucopenia and neutropenia due to atypical antipsychotics other than clozapine. We propose that the WBC and neutrophil counts should also be monitored carefully during treatment period with atypical antipsychotics other than clozapine.

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