CASE REPORT

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Neutropenia in a schizophrenia patient following combined lurasidone and paliperidone therapy: a case report

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Abstract

Purpose: Lurasidon is a relatively new, second-generation antipsychotic drug with an interesting receptor profile. It is considered to be safe and has a low risk of side effects. It is a substance with a multi-receptor mechanism of action: it mainly blocks dopaminergic D_2 and serotonergic 5-HT_2A receptors. According to the Summary of Product Characteristics, the adverse reaction of neutropenia was too rare to enable the estimation of its frequency.

Case description: A case of 39-year-old patient is presented in the article, diagnosed with paranoid schizophrenia, who developed neutropenia as a result of treatment with lurasidone. After the discontinuation of lurasidone and recommended supplementation, the blood test results gradually improved and finally reached the normal range.

Comment: This case report shows the need for regular monitoring of blood cell parameters in patients treated with second-generation antipsychotics, as there is a risk of neutrocytopenia or even agranulocitosis.

Key words: paranoid schizophrenia, neutropenia, lurasidone.

PURPOSE

Lurasidone is a relatively new, second-generation antipsychotic with an interesting receptor profile. The drug is effective in reducing positive symptoms of schizophrenia, but it also has a positive effect on negative symptoms and cognitive functions. It is a substance with a multi-receptor mechanism of action; it mainly blocks dopaminergic D_2 and serotonergic 5-HT_2A, 5-HT_6, 5-HT_7 receptors. The blockade of D_2 and 5-HT_2A receptors is responsible for the properties of the atypical antipsychotic drug.The antagonism of the 5-HT_7 receptor and partial agonism of the 5-HT_1A receptor confers the property of the antidepressant effect [1].

At the same time, it shows low affinity to α1 and α2A adrenergic receptors as well as to histamine and cholinergic receptors, which reduces the range of possible side effects, such as orthostatic hypotension, memory disorders or excessive weight gain [2]. The most common side effects occurring in about 5% of patients include somnolence, akathisia, nausea, and drug-induced parkinsonism. According to the Summary of the Product Characteristics, the adverse reaction of neutropenia was too rare to enable the estimation of its frequency [3].

This article describes a case of neutropenia most likely related to the patient's treatment with lurasidone, with a normalization of blood test results after the discontinuation of the drug. The aim of the article is to draw attention to the risk associated with the use of second-generation antipsychotics and the occurrence of blood count abnormalities, especially neutropenia.

CASE DESCRIPTION

A 39-year-old female patient, with an 18-year history of psychiatric treatment, was hospitalized eight times due to psychiatric reasons. In 2014, she was diagnosed with paranoid schizophrenia. Her last hospitalization took place in 2021. The patient had leukopenia before, which was confirmed by medical history – according to the 2014 documentation available, the level of leukocytes in the blood count was below the norm: 3.20×10^3/μl (norm: 4×10^3/μl to 10×10^3/μl). This could be related to infections, cer-

tain medications, or vitamin deficiencies. We are unable to ascertain the precise cause without a complete medical history, however, we can exclude both cancer and autoimmune diseases based on the available information. In December 2020, the patient was admitted to a psychiatric ward from the emergency department, where she was consulted following actively aggressive behavior directed towards her mother. On admission, the patient was conscious, with full orientation. Her train of thought was increased, with slides from the thematic line. Bizarre religious delusions and persecutory delusions were presented in her speech. She denied hallucinations, suicidal thoughts or intentions. In the physical examination, visible atrophy of adipose and subcutaneous tissue and hair follicles on the forearms were present. Upon admission to the inpatient unit, the patient's BMI was 17.31. The emergency medical team that intervened at the patients home reported extreme neglect of the dwelling, with no food fit for consumption. Most likely due to psychotic reasons, she significantly reduced her food intake.

During the hospitalization, it was necessary to use a nasogastric probe due to a habitual refusal to eat. It was also decided to include paliperidone, in the monthly intramuscular injections, due to the lack of compliance on the part of the patient. As a result of the medical treatment, the patient gained 4 kg, and her BMI on the day of discharge was 18.8. However, no improvement in the white blood cell count was observed; in fact, a slight decrease from a value of 3.67×10^3/µl to 3.4×10^3/µl was noted.

After a month of hospitalization, the patient requested to be discharged, and she was discharged with the recommendation of monthly administration of intramuscular paliperidone and an indication to start treatment in a day ward of psychiatric rehabilitation. The last blood count analysis during the stay in the ward showed a reduced level of leukocytes – 3.40×10^3/µl, lymphocytes – 0.81×10^3/µl, the level of neutrocytes was in the lower limit standards – 2.03×10^3/µl. Other parameters in the laboratory tests were within the normal range.

In September 2021 the patient was admitted to the Psychiatric Rehabilitation Day Department. Upon admission, she was conscious, correctly oriented, and in a balanced mood. She denied having delusions, suicidal thoughts, or self-harm tendencies. During the interview, she mentioned that she had been experiencing periods of greater irritability, nervousness, and withdrawal from social contacts. She also reported sleeplessness. Since her last hospitalization, she received intramuscular paliperidone every thirty days, with the dose reduced from 100 mg to 75 mg at the Mental Health Clinic. In addition, she took lurasidone 37 mg twice daily due to incomplete remission of psychotic symptoms for several days. The patient weighed 49 kg and was 162 cm tall, but she denied following a strict diet, inducing vomiting, or purging. Since January 2021, she had not menstruated and reported elevated prolactin levels in a test she took on her own. Upon admission, the complete blood count revealed lowered levels of leukocytes (2.45×10^3/µl, norm: 4×10^3/µl to 10×10^3/µl) and neutrophils (1.04×10^3/µl, norm: 2.00-6.14 $\times 10^3$/µl). Due to these deviations, oral folic acid 15 mg, a complex of B vitamins once a day, and an internal medicine consultation were ordered. Upon the suggestion of the consulting internist, lurasidone was discontinued.The previously recommended supplementation was also maintained. A week later, an improvement was observed in the complete blood count – the level of leukocytes increased to 2.73×10^3/µl, and neutrophils to 1.6×10^3/µl. After the patient discontinued lurasidone, control blood tests were ordered on a regular basis, and a gradual improvement was observed (Table 1).

Additionally, her mood was balanced, and her weight increased from 49 kg to 56 kg, because the patient finally had no problems with her appetite which was associated with an overall improvement in her mental state. After discontinuing lurasidone, the leukocyte and neutrophil

Table 1. Results of laboratory tests performed regularly after discontinuation of lurasidone. At the end of November, a month and a half after discontinuation of the drug, normal ranges were reached

	23.09.2021	04.10.2021	14.10.2021	28.10.2021	10.11.2021	24.11.2021	08.12.2021
Leukocytes	2.45 × 10³/µl	2.73 × 10³/µl	2.39 × 10³/µl	2.66 × 10³/µl	2.79 × 10³/µl	4.09 × 10³/µl	4.03 × 10³/µl
Erythrocytes	4.26 × 10³/µl	4.31 × 10³/µl	4.48 × 10³/µl	4.06 × 10³/µl	4.08 × 10³/µl	4.39 × 10³/µl	4.22 × 10³/µl
Hemoglobin	12.90 g/dl	13.10 g/dl	13.80 g/dl	12.40 g/dl	12.50 g/dl	13.40 g/dl	13.10 g/dl
Hematocrit	37.40%	38.40%	39.40%	36.00%	36.60%	38.70%	38.10%
Thrombocytes	187 × 10³/µl	152 × 10³/µl	224 × 10³/µl	190 × 10³/µl	204 × 10³/µl	264 × 10³/µl	207 × 10³/µl
Neutrophils	1.04 × 10³/µl	1.60 × 10³/µl	1.24 × 10³/µl	1.53 × 10³/µl	1.78 × 10³/µl	2.72 × 10³/µl	2.62 × 10³/µl
Eosinophils	0.07 × 10³/µl	0.12 × 10³/µl	0.08 × 10³/µl	0.09 × 10³/µl	0.10 × 10³/µl	0.12 × 10³/µl	0.10 × 10³/µl
Basophils	0.02 × 10³/µl	0.02 × 10³/µl	0.01 × 10³/µl	0.01 × 10³/µl	0.02 × 10³/µl	0.02 × 10³/µl	0.01 × 10³/µl
Monocytes	0.27 × 10³/µl	0.29 × 10³/µl	0.34 × 10³/µl	0.29 × 10³/µl	0.24 × 10³/µl	0.39 × 10³/µl	0.38 × 10³/µl
Lymphocytes	1.05 × 10³/µl	0.70 × 10³/µl	0.72 × 10³/µl	0.73 × 10³/µl	0.64 × 10³/µl	0.83 × 10³/µl	0.92 × 10³/µl

counts gradually normalized. Following three months of treatment, the patient was discharged with the following recommendations: to attend regular appointments at the Mental Health Clinic, to receive systematic monthly intramuscular injections of paliperidone, and to supplement with B vitamins and folic acid. Furthermore, monthly blood count checks were advised, and the patient was to be under the care of a hematology clinic.

COMMENT

Atypical antipsychotics, although associated with a much lower risk of causing extrapyramidal side effects and hyperprolactinemia, may cause abnormalities in blood count. Cases of agranulocytosis caused by taking clozapine are most often discussed in the literature. The exact pathomechanism of drug-induced neutropenia is unknown. Toxic damage to the bone marrow leading to inhibition of granulocyte production, autoimmune destruction of these cells, or a combination of these processes is postulated.

There is little literature on blood count abnormalities in patients taking lurasidone. Sood described the case of a patient with dose-dependent neutropenia induced by treatment with lurasidone. A 41-year-old African American man with a long history of treatment for schizophrenia had taken various antipsychotics (haloperidol, risperidone, aripiprazole, and ziprasidone) in the past. The man developed neutropenia after treatment with risperidone; therefore, risperidone was replaced with haloperidol, which the patient, despite the recommendations, had not used for several months. Due to the deterioration of his mental state, he was admitted to the hospital, where he received haloperidol in increasing doses twice a day. After some time, lurasidone was added in an increasing dose – from 20 to 120 mg. On the 37th day of lurasidone therapy, 8 days after increasing the dose to 120 mg, the blood count showed $1.4 \times 10^3/\mu l$; therefore, it was decided to reduce the dose to 80 mg, and six days later, the level of neutrophils improved to $1.6 \times 10^3/\mu l$ [4].

Rafi *et al*., reported a case of thrombocytopenia, most likely caused by lurasidone, in a 29-year-old man suffering from bipolar disorder. The patient, treated for 2.5 months with lurasidone 80 mg once daily, was hospitalized for 2 weeks with tremors, involuntary limb movements, vomiting, and a burning sensation in the stomach. Laboratory tests showed hyperprolactinemia and thrombocytopenia – the level of platelets was $37 \times 10^3/\mu l$. Due to symptoms and test results, the patient was discontinued from lurasidone, and after a week, an improvement was observed in control tests – the platelets increased to $183 \times 10^3/\mu l$, and the patient's clinical condition also improved [5]. Despite the fact that lurasidone is considered a very safe drug, in the literature you can find isolated descriptions of other, also non-hematological, side effects, e.g., the case of a 28-year-old patient who developed an oculogyric crisis after increasing the dose of the drug to 80 mg/d [6].

Both the case report presented in this article and the cases from the literature cited above show the need for regular monitoring of blood count parameters in patients treated with second-generation antipsychotics due to the risk of neutropenia, agranulocytosis, or thrombocytopenia, especially in patients predisposed to such disorders. Detection of abnormalities in the blood count in such patients should encourage regular repetition of tests and consideration of the relationship between pharmacotherapy and disturbed parameters. In case of an obvious correlation, if possible, the drug dose should be reduced or the drug should be changed to another, and blood count parameters should be monitored regularly.

Conflict of interest

Absent.

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