

RESEARCH ARTICLE

RISPERIDONE INDUCED LEUCOPENIA AND NEUTROPENIA: A CASE REPORT AND BRIEF REVIEW OF LITERATURE

M. Berghalout, A. Ait Idar, H. Guennouni, K.El Ouazzani, I. Adali and F. Manoudi Department of Psychiatry, IBN NAFIS Hospital, Mohammed VI University Hospita Marrakech, Morocco.

1	2	5 /	1 /	2	1	/

Manuscript Info	Abstract				
<i>Manuscript History</i> Received: 19 December 2020 Final Accepted: 22 January 2021 Published: February 2021	Hematological abnormalities are frequently encountered during treatment with antipsychotic drugs. Most of these are mild and of no clinical significance, but in a small minority of patients, hazardous, potentially life-threatening hematological effects, including leucopenia, neutropenia, agranulocytosis, thrombocytopenia, anaemia , leucocytosis, thrombocytosis, eosinophilia and altered platelet function. (1). Clozapine is associated with several well-known abnormalities of blood cell count (2), but some case reports associate novel antipsychotics, such as risperidone with leucopenia and agranulocytosis (3). This report describes a case of leucopenia under treatment with Oral Risperidone , suggesting the necessity of early recognition of leucopenia in order to prevent occurrence of potentially life-threatening agranulocytosis. (1).				
	Copy Right, IJAR, 2021., All rights reserved.				

· · · · · · · · · · · ·

Introduction:-

Antipsychotic drugs effectively control psychotic symptoms, but may cause important side effects, significantly increasing morbidity and mortality [4]. Hematologic abnormalities are frequent and may be life-threatening in some patients. Agranulocytosis is the major threat of clozapine treatment and prompts periodic white blood cell (WBC) count monitoring [4].

Most of the literature on haematological adverse effects (mostly leucopaenia, neutropaenia and thrombocytopaenia) has been well documented with regard to clozapine. However, there is also evidence (though limited) for the haematological adverse effects of other second generation antipsychotics like risperidone oral as well as in depot long acting preparations, quetiapine and olanzapine [5].

Godleski and Sernyak reported agranulocytosis after addition of risperidone to clozapine. One patient developed leukopenia after taking both risperidone and aripiprazole. One patient with serious medical comorbidities and simultaneous co-treatment developed blood dyscrasia after introduction of risperidone [6]. We describe a case of leukopenia/neutropenia occurring during treatment with Risperidone.

Case :

Mr. K, 21 years old, operated at the age of 13 for a pituitary adenoma, never followed in psychiatry, hospitalized for a chronic dissociative psychosis of chronic evolution for 4 year, revealed by delusional persecution syndrome, with psychomotor agitation. The patient was put on Risperidone as standard treatment f his psychosis . At admission , his routine laboratory tests showed no abnormalities. WBC count and neutrophils were normals .

Corresponding Author:- M. Berghalout A. Ait Idar Address:- Department of Psychiatry ,IBN NAFIS Hospital, Mohammed VI University Hospita Marrakech, Morocco. The patient received 2 mg/day of Risperidone , for the first days, increasing it to 6 mg/day in the second week . the biological control assessment revealed a decrease in white blood cell, with leukopenia at 3170 μ L, and neutropenia at 1690 μ L.

As Riperidone increased to 9 mg per day, the blood test continued to show an objective decrease in white blood cell, with leukocytes at $2810 \,\mu$ L, and neutrophils at $1090 \,\mu$ L.

Mr. K's physical examination is normal, he does not have any signs or symptoms of infection, and additional lab tests are negative.

The dose of Risperiodne was reduced to 6 mg per day becausewe considered it as a possible cause of leukopenia. The check-up showed an improvement in the white line: leukocytes at 4430 μ L, and neutrophils at 2170 μ L. The number of white blood cells which increases after the reduction of risperidone is very suggestive that this agent caused Mr. K's leukopenia / neutropenia.

Discussion:-

Leucopenia is a low white blood cell count (WCC). When it occurs in association with psychotropic medication it is often due to neutropenia. Neutropenia can be defined as a neutrophil count of <1.5 /mm3.

As neutrophils make up the majority of circulating leucocytes, neutropenia is suggested by a WCC of <3.0 /mm3 [1].

Agranulocytosis literally means an absence of circulating granular leucocytes (neutrophils, basophils and eosinophils). In practice it is defined as a neutrophil count <0.5 /mm3, and is suggested by a WCC of <1.0 /mm3 [1].

To an extent these definitions are arbitrary and hence may differ slightly between centres/studies. In many cases the red cells and platelets are unaffected in neutropenia and, therefore, haematocrit and platelet counts are often normal.

Neutropenia and agranulocytosis are the most important drug-related blood dyscrasias clinically since, as compared to other blood dyscrasias, they are relatively common. Furthermore, agranulocytosis can be very serious and requires urgent management [1].

Agranulocytosis is rare, except with clozapine, but is the most common andmost serious (less than 0.1%) hematologic side effect of the antipsychotics[7]. Low-potency antipsychotics have a higher frequency of agranulocytosis than high-potency ones. Clozapine causes agranulocytosis in 0.8% of patients,) and phenothiazines (chlorpromazine agranulocytosis risk approximately 0.13%)[1].

Granulocytopenia seldom occurs with antipsychotic treatment. It emerges mostly with clozapine or olanzapine, and switching to another antipsychotic usually resolves the problem . When blood dyscrasias occur, risperidone is considered to be a safe alternative [8]. Nevertheless, there have been several reports of risperidone-associated leukopenia [8].

Among the antipsychotics drugs, risperidone tends to have a lowerrisk of hematotoxicity. King et al. reviewed the antipsychotic-related hematological side effects and reported in the UK monitoring system between 1963 and 1996. They concluded that among 16 antipsychotics agents, clozapine and remoxipride have the highest risk of inhibiting hemopoietic production related to the aliphatic phenothiazine derivatives, and that no evidence of increased risk is noted with high-potency drugssuch as haloperidol, pimozide, sulpiride, or risperidone [9].

Furthermore, Mahmood et al. Suggested that risperidone may be considered as an alternative when blood dyscrasias occur with the first generation classic antipsychotics drugs [10].. Two cases were reported to develop neutropenia and thrombocytopenia with the use of phenothiazine and butyrophenone, but the hematological condition was improved after the antipsychotic drug was switched to risperidone [11].

Eight possible cases of risperidone-induced leukopenia and neutropenia have been noted in a literature review. But the causal relationship betweenrisperidone and blood dyscrasias is debatable in seven cases, because five of them

had a previous history of other antipsychotic-induced leukopenia or were under concomitant clozapine treatment [11].

The sixth case was a 90-year-old man who developed leukopenia, neutropenia and pneumonia after a six-month treatment with risperidone 2 mg/day [11].

The seventh case was a 24-year-old female schizophrenic patient who developed leucopenia after a nine-day risperidone treatment (2-6 mg/day), but she suffered from infl uenza B virus infection at the same time. Therefore, the causality of a virus infection cannot be excluded[9].

Only the last case had a higher possibility of causality. In another report, an African adolescent was found to develop leukopenia 10 days after receivingrisperidone therapy (4 mg/day), and leukopenia was found again with rechallenge of risperidone at 2 mg/day [11].

Despite blood dyscrasias being possible with atypical antipsychotics, there is no sound clinical evidence to support a clear pathophysiological relationship. While the effect on hematopoiesis is reported to occur through intermediate nitrenium metabolites for clozapine and olanzapine, andpossibly quetiapine [4], there is no such mechanism demonstrated for risperidone. Toxic metabolites were also proposed for risperidone, but the general mechanism appears to differ from the mechanism of olanzapine [4]. We need more studies to address this issue.

Conclusion:-

This case report suggest the necessity of follow up of WBC count in the patients taking antipsychotics, tablets or injectable, in order to recognize leucopenia and prevent occurrence of potentially life-threatening agranulocytosis. Aripiprazole might be a useful alternative when another antipsychotic causes leukopenia and neutropenia. In addition to regularly monitoring the blood cell count during antipsychotic treatment, the neutrophil and platelet counts should be monitored [12].

Bibliographie:-

A. [1] Hall RL, Smith AG, Edwards JG.

B. Haematological safety of antipsychotic drugs. Expert Opin Drug Saf 2003;2(4):395-9.

[2] Robert J. Flanagan and Louisa Dun.

- Haematological toxicity of drugs used in psychiatry . Human Psychopharmacology, 01 Jan 2008, 23 Suppl 1:27-41.
- C. [3] Sluys M, Guzelcan Y, Casteelen G, de Haan L. Risperidone-induced leucopenia and neutropenia: a case report. Eur Psychiatry 2004;19(2):117.

[4] Giovanni Manfredi¹, Andrea Solfanelli, Giorgia Dimitri, Ilaria Cuomo, Gabriele Sani, Giorgio D Kotzalidis, Paolo Girardi.

Risperidone-induced leukopenia: a case report and brief review of literature . 10.1016/j.genhosppsych.2012.03.009 [5] Yogender Kumar Malik¹, Swapnajeet Sahoo¹, Ajit Avasthi Olanzapine-induced leucopaenia and thrombocytopaenia in an elderly patient: a case report and review of the evidence . 10.1136/gpsych-2018-000013. [6] Godleski LS, Sernyak MJ. Agranulocytosis after addition of

risperidone to clozapine treatment. Am J Psychiatry 1996;153:735-6.

[7] Rajagopal S. Clozapine, agranulocytosis, and benign ethnic neutropenia. Postgrad Med J 2005;81:545-6.

[8] Mahmood T, Silverstone T, Spittle B. Risperidone appears safe in

patients with antipsychotic-induced blood dyscrasias. Int Clin

Psychopharmacol 1996;11:53-4.

[9] King DJ, Wager E: Haematological safety of antipsychotic

drugs. J Psychopharmacol 1998; 12: 283-8.

[10]Mahmood T, Silverstone T, Spittle B.

Risperidone appears safe in patients with antipsychotic-induced blood dyscrasias. Int Clin Psychopharmacol 1996; 11: 53-4.

[11] Chih-Yuan Hung, M.D.1, Ya-Mei Bai, M.D., Ph.D.

Risperidone-induced Leukopenia and Neutropenia.

Taiwanese Journal of Psychiatry (Taipei) Vol. 25 No. 2 2011

[12] Kairav Shah, MD, MPH, and Muhammad Rizvi, MD.

Bicytopenia: Adverse effect of risperidone . Current Psychiatry. 2014 April;13(4):E1.