Effects of antipsychotic treatment on haematological parameters of psychotic patients in tertiary care hospital of India

Nutanbala N. Goswami¹*, Jignesh Gondliya², Alpeshpuri P. Goswami³

¹³Associate Professor, ²Senior Resident, ¹Dept. of Pharmacology, ²³Dept. of Pathology, Government Medical college, Bhavnagar, Gujarat, India

*Corresponding Author: Nutanbala N. Goswami
Email: dralpeshgosai79@gmail.com

Abstract
Introduction/Aim of study: Use of some antipsychotic agents results in haematological changes like leukopenia, neutropenia, thrombocytopenia, anaemia, Leukocytosis, thrombocytosis which may present a major problem for the management of psychotic patients.

Material and Methods: Twenty four patients on therapy with antipsychotic drugs for a minimum period of three months were recruited for study for haematological changes at tertiary care Hospital of India. The study was conducted between March and August, 2019.

Results: Out of 24 cases, 1 patient developed neutropenia (4.16%), and 01 patient developed anaemia (4.16%) within 3 month of treatment without any haematological disease.

Conclusion: The significant reduction in blood cell count observed associated with antipsychotic agents especially neutropenia. An appropriate monitoring strategy should be used for clozapine and other antipsychotic drug to minimize the adverse drug reaction and early shift of treatment.

Keywords: Antipsychotic drugs, Haematological parameters, Neutropenia.

Introduction
Psychotic disorders are described as a serious mental disorder and characterized by defective contact with reality often with hallucination or delusions. Psychosis which is also described as a syndrome of mental illness typified by radical changes in personality, impaired functioning, and a distorted sense of objective reality has been linked with various causative factors ranging from biological to psychological. There is usually a strong genetic link and in addition, psychosocial factors including smoking have been implicated. Antipsychotic agents may be broadly divided into two generation by their chemical classes. The phenothiazines are of the first generation and include chlorpromazine, prochlorperazines, mesoridazine, and thioridazine. These drugs are essentially similar in their mechanism of action and adverse effects. The Butyrophenones are haloperidol and Droperidol which primarily used in control of Tourette’s syndrome. Second generation are of the dibenzazepine derivatives and the benzisodioxil group. The dibenzazepine derivatives are Clozapine, olanzapine and quetiapine have been effective in controlling psychotic symptoms that have not been responsive to other drugs. The benzisodioxil group is composed of risperidone and ziprasidone which are useful for controlling bipolar mood disorder and as second-line treatment for schizophrenia respectively. Studies show that use antipsychotic agents results in haematological changes like leukopenia, neutropenia, thrombocytopenia, anaemia, Leukocytosis, thrombocytosis which may present a major problem for the management of resistant psychotic patients who do not respond to both conventional and novel antipsychotics. The significant reduction in neutrophil count (absolute) shows agranulocytosis associated with antipsychotic agents especially involves the polymorphonuclear neutrophils not due to direct effect of the disease itself. Clozapine, referred to as the gold standard for the treatment of schizophrenia, is the most underutilized medication; i.e., it is prescribed in only a proportion of eligible patients. Hematological side effect of agranulocytosis: a deficiency of neutrophils
Table 1: Haematological finding in patient on antipsychotic drug therapy for minimum 3 months (n=24)

| Hematological finding     | 1st generation antipsychotic (6) | 2nd generation antipsychotic (10) | Combination of 1st and 2nd (8) | Total |
|---------------------------|----------------------------------|-----------------------------------|-------------------------------|-------|
| Neutropenia               | 00                               | 01                                | 00                            | 01    |
| Thrombocytopenia          | 00                               | 00                                | 00                            | 00    |
| Thrombocytopenia with     | 00                               | 00                                | 01                            | 01    |
| Neutropenia               |                                   |                                   |                               |       |
| Anemia                    | 00                               | 00                                | 00                            | 00    |
| Pancytopenia              | 00                               | 00                                | 00                            | 00    |

that renders the person vulnerable to infections. The cumulative prevalence of agranulocytosis and neutropenia in those taking clozapine is approximately 0.9 and 3.8%, respectively, and the peak incidence is one month after exposure to clozapine treatment.\textsuperscript{8,9} The causes of clozapine-induced agranulocytosis and neutropenia remain unclear although a genetic contribution has been established.\textsuperscript{10,11}

**Materials and Methods**

Patient visited Sir T hospital; Bhavnagar, Gujarat psychiatry department and taking anti-psychotic therapy of either generation for at least three months were included. We have collected and analysed data of haematological findings of these patient. Total 24 cases were included during 6 month of time period from March to August of 2019 excluding other organic cause. Normal total WBC count, absolute neutrophil count, platelet count, haemoglobin, RBC count are 4500-1000/µl, 1500-7000/µl, 1.5-4.0 lac/µl, 12-17gm/dl, 4.5-6 million/µl respectively and abnormal count were taken into consideration. Five part hematology auto-analyzer with microscopic examination were used for haematological parameter.

**Results**

Total 24 patients were subjected to antipsychotic treatment during six month duration and patient had normal blood parameter on starting of new drug. Shift to new drug with normal blood count was considered as new.

Out of observed cases, 1 patient developed neutropenia (4.16%), and 01 patient developed anaemia (4.16%) within 3 month of treatment. Chlopramazine, haloperidol, fluphenazine were used first generation and Clozapine, risperidone, ziprasidone, quetiapine were used second generation antipsychotic. Out of 8 patient taking clozapine 01(12.5%) case of neutropenia observed. Out of 07 patient taking clozapine and risperidone combination, 1(14.3%) developed neutropenia and 1(14.3%) with thrombocytopenia.

**Discussion**

The reported incidence of clozapine-induced agranulocytosis varies between 1% to 2%.\textsuperscript{12,13} The observed mortality rate ranges between 0.1 and 0.3 per thousand, and the case-fatality rate is between 2.2 and 4.2 per thousand.\textsuperscript{14} The significant reduction in neutrophil count (absolute) shows agranulocytosis associated with antipsychotic agents especially involves the polymorphonuclear neutrophils. Inuwa et al.\textsuperscript{15} (2004), reported significant left shift in neutrophil population of patients after treatment with antipsychotic drugs concluding that agranulocytosis results basically from the medication and not the disease itself. Marnelli A Bautista-Quach et al\textsuperscript{16} reported a case of Pancytopenia associated with clonazepam.

This study reveals that the antipsychotic drugs could have adverse effect on haematological parameter. Hence, a careful assessment of haematological parameters before and during neuroleptic drug treatment could serve as an important means for monitoring various changes associated with the drug intake. An appropriate monitoring strategy should be used for clozapine and other antipsychotic drug to minimize the adverse drug reaction and early shift of treatment.
Conclusion
The significant reduction in blood cell count associated with antipsychotic agents especially the polymorphonuclear neutrophils. We recommend patients taking clonazepam to be monitored with regular complete blood count to check for clinically significant pancytopenia or thrombocytopenia. Further prospective research is necessary to evaluate clozapine therapy during management of schizophrenia.

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Conflicts of Interest
There are no conflicts of interest.

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