

Effects of Antipsychotic Chemotherapy on Haematological Parameters of Psychotic Patients in Lautech Teaching Hospital, Osogbo, Nigeria

¹E.O. Akanni, ²A.A. Raji, ³B.A. Eegunranti, ¹E.O. Bamisaye and ¹O. Sodipe

¹Haematology Division, Department of Biomedical Science, Ladoke Akintola, University of Technology, College of Health Sciences, P.M.B. 4400, Osogbo, Nigeria

²Department of Haematology and Blood Transfusion, College of Health, Sciences, Ladoke Akintola University of Technology, P.M.B. 4400, Osogbo, Nigeria

³Department of Psychiatry, Ladoke Akintola University of Technology, College of Health Sciences, P.M.B. 4400, Osogbo, Nigeria

Abstract: The possible effects of antipsychotic agents on haematological parameters of psychotic patients placed on combination therapy were studied. This is in view of some toxicological events on haematopoietic cells and haematimetric parameters usually accompany administration of some chemotherapeutic drugs. Sixty (60) individuals consisting of thirty two in-patients (male and female) receiving treatment at the Mental Health Ward, Ladoke Akintola University of Technology Teaching Hospital Osogbo and twenty eight apparently healthy individuals who served as controls were involved. Haematological parameters were estimated in all the samples using Sysmex KX-21N auto-analyzer with Erythrocyte Sedimentation Rate (ESR) estimated by Westergren method. Ion selective electrode method was used in estimating the lithium level of the samples. Results show that there is an elevated erythrocyte sedimentation rate in the psychotic patients than in the control group which is statistically significant ($p < 0.05$). There is no significant difference ($p > 0.05$) in the packed cell volume, haemoglobin concentration, white blood cell concentration and platelet levels between the patients and the controls. However, there is a statistically significant increase ($p < 0.05$) in the mean cell volume, mean cell haemoglobin and mean cell haemoglobin concentration in the psychotic patients as compared with the controls. There is also no statistically significant difference ($p > 0.05$) in the lithium level between the psychotic patients and the control. This study reveals that the antipsychotic drugs could have increased the plasma protein content in the patients as a result of inflammation or possible agranulocytosis. 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.

Key words: Antipsychotic drugs, erythrocyte sedimentation rate, haematological parameters, psychosis

INTRODUCTION

Psychotic disorders are described as a serious mental disorder and characterized by defective contact with reality often with hallucination or delusions (Beers and Robert, 2002). 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 (e.g., abnormality in the brain structure and brain chemistry), to psychological (mental or emotional). There is usually a strong genetic link and in addition, psychosocial factors including smoking have been implicated (Beers and Robert, 2002). Antipsychotic agents constitute a class of drugs used to treat psychotic disorders as well as other mental and

emotional conditions which are primarily composed of major tranquilizers (Ford-Martin, 2004). Antipsychotic agents may be divided by their chemical classes. The phenothiazines are the oldest group, and include chlorpromazine (Thorazine), mesoridazine (Serentil), prochlorperazines (Compazine), and thioridazine (Mellaril). These drugs are essentially similar in their mechanism of action and adverse effects. They may also be used as anti-emetics. The Butyrophenones are haloperidol (Haldol) and Droperidol which are primarily useful in control of Tourette's syndrome (De Leon *et al.*, 2004). The diphenylbutylpiperidines are pimozone (Orap) and Fluspirilene.

On the other hand, the dibenzazepine derivatives, Clozapine (Clozaril), loxapine (Loxatane), olanzapine (Zyprexa) and quetiapine (Seroquel) have been effective

in controlling psychotic symptoms that have not been responsive to other classes of drugs. The benzisoxindol group is composed of risperidone (Risperdal) and ziprasidone (Geodon) which are useful for controlling bipolar mood disorder and as second-line treatment for schizophrenia respectively. In addition to these drugs, the classes of agents used in psychiatry includes lithium carbonate (Eskalith, Lithonate), used for the control of bipolar mood disorder, and thiothixene (Navane), which is used in the treatment of psychosis (De Leon *et al.*, 2004).

Studies reveal that the use of certain antipsychotic agents results in haematological dyscrasias amongst which are leukopaenia, neutropaenia, thrombocytopenia, anaemia, Leukocytosis, thrombocytosis (Patterson and Jennings, 1993) which may present a major problem for the management of resistant psychotic patients who do not respond to both conventional and novel antipsychotics (Varsh *et al.*, 2004). Lithium, used in the treatment of manic-depressive disorder, is a common cause of drug induced, nephrogenic diabetes insipidus, and thiazide diuretics have been found to be helpful in treating it. Serum lithium levels must be carefully monitored in this situation, since diuretics may reduce renal clearance of lithium and raise plasma lithium levels into the toxic range. However, lithium alone is rarely successful in treating schizophrenia, adding it to an antipsychotic may salvage an otherwise treatment-resistant patient (Williams *et al.*, 2001). Leukocytosis is always present during lithium treatment, probably reflecting a direct effect on leukopoiesis rather than mobilization from the marginal pool. This "adverse effect" has now become a therapeutic effect in patients with low leukocyte counts (Williams *et al.*, 2001).

Haematological indices refer to various parameters found in the human blood which are evaluated with the aid of a Complete Blood Count (CBC). CBC is a series of test employed to evaluate the composition and concentration of the cellular components of blood. It consists of the following tests: red blood cell count, total and differential white blood cell count, platelets count and Red blood cell indices (Saunders *et al.*, 2001). They provide important clinical data ranging from: states of infections, malignancies and immune derangements, hence, they have come to occupy critical roles in the diagnosis, prognosis and management of various diseases and disorders. Erythrocyte Sedimentation Rate (ESR) measures the speed of sedimentation of red cell in plasma over a period of 1hour base on the shift in albumin/globin ratio. It is used in diagnosis of systemic diseases and to monitor patient's response to therapy (Thompson and Proctor, 1999).

Psychotic disorders exert various effect on the quality of life of the affected patients with corresponding diversified side effects from the antipsychotic agents employed for treatment, an evaluation and assessment of

haematological parameters such as packed cell volume, full blood count and erythrocyte sedimentation rate as a potentially significant diagnostic and prognostic tool in this study may be used to infer physiological and pathological changes in the patients on such drugs which may be of importance in prevention or modification of their individual effects for maximum benefits of the drugs. This study is therefore aimed at investigating the effects of the antipsychotic agents used in treatment of psychotic conditions in the study population on haematological parameters of the patients such as agranulocytosis and granulocytopenia and others with a view to monitoring the selection and cytotoxicity levels of the drugs for the effective patients' management.

MATERIALS AND METHODS

Subjects selection: Thirty-two patients (male and female) on combination therapy with some antipsychotic drugs for a minimum period of four weeks were recruited for this study from the Psychiatry ward of Ladoke Akintola University of Technology Teaching Hospital Osogbo and twenty-eight apparently healthy individuals served as controls. The study was conducted between December 2009 and April, 2010. The antipsychotic drugs involved in the combination therapy administered on patients include: haloperidol, benzhexol, trifloxacin, trifluoperazine (TFP), fluphenazine, amitriptyline, carbamazepine and risperidone.

Sample collection: About 6.0 mL of venous blood was collected from each subject. The blood was appropriately dispensed into EDTA specimen bottles for the estimation of haematological parameters, citrate bottle for the estimation of erythrocyte sedimentation rate and into a plain tube for serum extraction, which was separated and stored frozen at -20°C until analysed for Lithium estimation.

Analytical procedure: Sysmex KX-21N auto-analyzer was used for the estimation of haematological parameters: red blood cell count, packed cell volume, platelet count, platelet count, the total and differential white blood cell count, and generation of haematological indices. Westergren's and Ion Selective methods were used for Erythrocyte Sedimentation Rate and lithium estimation respectively. The parameters were estimated using the Haematology / Blood Transfusion and Chemical Pathology Departments Laboratories facility of the Ladoke Akintola University of Technology Teaching Hospital, Osogbo, Nigeria.

Statistical analysis: ANOVA was used for the data analysis using SPSS version 16. 'p<0.05' denotes significant difference between treatments.

Table 1: The estimated haematological and biomedical parameters in the studied patient and control populations

Parameters	Tests (n = 32)	Control (n = 28)	p-value
WBC (10 ⁹ /L)	4.650±1.34	4.918±1.36	0.445
HCT (%)	38.131±4.86	36.982±4.36	0.342
RBC109L	4.5152±0.72	4.7964±0.60	0.106
HGB_gdL	12.1818±1.78	11.4036±1.65	0.102
MCV (fL)	83.928±6.80	79.214±4.00	0.002
MCH (pg)	26.963±1.95	24.575±1.81	0.000
MCHC (g/L)	320.22±19.49	308.86±16.02	0.018
PLT (10 ⁹ /L)	208.88±58.96	208.18±87.90	0.971
LYM (%)	47.081±13.13	46.582±6.65	0.856
Mxd (%)	8.575± 5.99	6.354±4.28	0.108
NEUT (%)	44.344±12.03	47.096±7.27	0.296
LYM (10 ⁹ /L)	2.122±0.71	2.096±0.62	0.884
MXD (10 ⁹ /L)	0.575±0.67	0.368±0.28	0.134
NEUT (10 ⁹ /L)	1.99±0.87	2.454±0.81	0.039
ESR (mm)	45.79±32.789	6.57±1.91	0.000
Li (mmol/L)	0.8438±0.96	0.8071±0.12	0.188

Data are given as Mean±SD; Comparison of the patient and control values was done using ANOVA method. p<0.05 denotes significant difference between the two groups

RESULTS

The results (mean±Standard deviation) of various haematological parameters and Lithium levels for the test and control subjects are as represented in the Table 1. The haematological parameters include Packed Cell Volume (PCV), Differential White Blood Cell Count (Neutrophils, Eosinophils, Lymphocyte, Basophil and Monocytes). Total white blood cell count, Red blood cell count, packed cell volume, Platelets count and Erythrocyte Sedimentation Rate (ESR). The result showed that there is significant increase (p<0.05) in the red cell indices such as Mean Cell Volume (MCV), Mean Cell Haemoglobin (MCH) and Mean Cell Haemoglobin Concentration (MCHC) in the test subjects. Moderate but not statistically significant increase was also observed in the Packed Cell Volume (PCV) and lymphocyte count as platelet count shows no statistical differences. White Blood Cell (WBC) count was slightly reduced in the test subjects which is inversely proportional to the significant increase (p<0.01) found in Erythrocyte sedimentation rate in the test subjects. It also shows there was no statistically significant difference (p>0.05) in the sample of the patients compared with the controls.

DISCUSSION

The result of this study showed that with the increased erythrocyte sedimentation rate observed amongst the test group when compared with the control, although not definitive (Table 1), there have been evidences of inflammatory processes mediated by the psychoactive drugs which is correlated by Seifert (1984) who observed an increased ESR in antipsychotic drug therapy. This may be as a result of changes in the physicochemical properties of the plasma which includes plasma colloids, increase in plasma fibrinogen and

relative variation in the plasma protein ratio marked by this significant increase in the sedimentation rates among the test subjects.

The significant increase (p<0.05) in the Mean Cell Volume (MCV), Mean Cell Haemoglobin (MCH) and Mean Cell Haemoglobin Concentration (MCHC) obtained in this study between the test and control subjects may be due to the increase in the level and activity of liver enzymes-Gamma glutamyl transferase and transaminases (ALT and AST) and ALP. These may reflect in the toxic effects of the drugs on the microsomal structures in the liver cells coupled with intrahepatic obstruction of bile flow by drugs such as chlorpromazine as established by Henderson and Moss (2001) who observed increased liver enzymes secondary to antipsychotic medication and may have minimal effect in the red cells resulting in the appearance of moderately large red cells characterized by the increased haematological indices observed in the test subjects. This result correlates positively with the findings of (Harold and Benjamin, 1985) whose observation confirms that increased level of liver enzymes secondary to hepatic stimulations result in increased haematological indices.

The significant reduction in neutrophil count (absolute) shows agranulocytosis associated with antipsychotic agents especially involves the polymorphonuclear neutrophils. The result is in line with the observation of Inuwa *et al.* (2004), who 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. The result showed no significant difference in lithium concentration between the test and the control subjects. This observation is supported by (Williams *et al.*, 2001) who recounts that the cation-lithium is excreted by the kidney, while its mechanism of synthesis in the body system in normal or in diseased

(psychotic) states is unclear but is assumed to be acquired through environmental sources. Routine lithium estimation in psychotic patients is suggested to be used for monitoring serum lithium concentration (Williams *et al.*, 2001) which may result in acute toxicity as serum concentrations greater than 1.0 mmol/L may be toxic.

Result from this work showed that ESR is raised significantly in psychotic patients on drugs such as chlorpromazine, risperidone, olanzapine, trifluoperazine and fluphenazine. The haematological indices such as MCV, MCH and MCHC are also raised and are statistically significant. These could be as a result of increased plasma proteins such as fibrinogen in the psychotic patients on the afore-mentioned drugs.

ACKNOWLEDGMENT

The authors appreciate the medical staff of the Psychiatry ward of Ladoke Akintola University of Technology Teaching Hospital Osogbo for their cooperation in samples collection and Medical Laboratory Scientists in the Haematology department of the same hospital for their technical assistance.

REFERENCES

- Beers, M.H. and B. Robert, 2002. Psychiatric Emergency. The Merck Manual of Diagnosis and Therapy. Section 15, Chap. 194, Merck Research Laboratories, Whitehouse Station, NJ.
- De Leon, A., N.C. Patel and M.L. Crismon. 2004. Aripiprazole: A comprehensive review of its pharmacology, clinical efficacy and tolerability. *Clin. Ther.*, 26: 649-666.
- Ford-Martin, P.A., 2004. Gale Encyclopedia of Medicine, The Gale Group Inc.
- Harold, I.K. and J.S. Benjamin, 1985. Drug Dependence. In: *Comprehensive Textbook of Psychiatry*. Williams and Wilkins, Baltimore, USA, 22: 1016-1020.
- Henderson, A.R. and W.D. Moss, 2001. Enzyme. In: *Tietz Fundamentals of Clinical Chemistry*. 5th Edn., WB Saunders Company, A. Harcourt Sciences, Company, 20: 352-389.
- Inuwa, I.M., Z. Zaidan and N. Viernes, 2004. White blood cell ultrastructure before and during antipsychotic therapy in schizophrenia. *J. Anat.*, 204(3): 227-238.
- Patterson, B.D. and J.L. Jennings, 1993. Spiking fever and profuse diarrhoea with clozapine treatment. *Am. J. Psychiatr.*, 150: 1126.
- Saunders, W.B., H. Prentice, E. Victoria and M.A. Dembranville, 2001. The complete blood count. *Best East Mediterranean Health J.*, 12(5): 627-652.
- Seifert, R.D., 1984. Therapeutic drug monitoring: Psychotropic drugs. *J. Pharm. Pract.*, 6: 403-416.
- Thompson, R.B. and S.J. Proctor, 1999. The Leucocytes Granulopoiesis. *The Granulocytes and Monocytes*. 5th Edn., Short Textbook of Haematology, pp: 26.
- Varsh, B., S. Abdus and M.M. Lubran, 2004. *An. Clin. Lab. Sci.*, 34: 131-137.
- Williams, Z.P. and E.H. Leo, 2001. Antipsychotic Agent and Lithium. In: Bertram, G.K. (Ed.), *Basic Clinical Pharmacology*. The McGraw-Hill Companies, Inc., New York, 29: 655-660.