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Haemorrhological and Haemostatic Changes in Patients on Antipsychotic Chemotherapy: Benin City, Edo State Experience

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Abstract

Changes in haemorrhological and haemostatic mechanism of blood may result during or after treatment with antipsychotic drugs. This present study is aimed at assessing the haemorrhological and haemostatic changes that may occur in antipsychotic chemotherapy in Benin City. A total of 70 samples comprising of 35 participants on antipsychotic chemotherapy as test subject (21 males and 14 females) with mean age of 40.5 ± 5.0 years and 35 apparently healthy participants (20 males and 15 females) with mean age of 25.5 ± 1.5 years as controls. The test participants were randomly selected from patients undergoing psychotic chemotherapy for more than a month at the Federal Neuro – Psychiatric Hospital, Benin City. While the controls were mainly student from the University of Benin. Platelet counts were manually counted using 1% ammonium oxalate solution, prothrombin time, (PT) prothrombin time test with kaolin (PTTK) were performed using commercially available Diagen reagent kits, erythrocyte sedimentation rate (ESR) was performed by the Westergreen method. Plasma and whole blood viscosity were done by method described by Reid and Ugwu, while fibrinogen concentration was done by the Ingram dry clot weight method. Result showed that fibrinogen and WBV increased in test when compared to controls, while ESR and PV reduced in test when compared to controls ($p=0.154$, $p=0.057$, $p=0.909$ and $p=0.804$ respectively). Prothrombin Time (PT) and PTTK increased significantly in test when compared to controls ($p<0.05$ and $p=0.001$ respectively) while platelet counts reduced in test when compared to controls ($p=0.456$). This study shows that antipsychotic chemotherapy increases blood rheology and causes increase in PT and PTTK levels in individuals.

Keywords: Haemorrhology, Haemostasis, Psychosis

Introduction

Antipsychotic agents can be grouped as a class of drugs used in the management of various psychotic disorders. They are primarily composed of tranquilizers (Ford-Martin, 2004). These antipsychotics are classified into typical first-generation antipsychotics which include the phenothiazines, butyrophenones, thioxanthenes and the atypical second-generation antipsychotics which include clozapine, risperidone and quetiapine (De Leon *et al.*, 2004). Studies reveal that the use of these drugs can result in some haematological abnormalities in the body (Patterson and Jennings, 1993), which may present a major problem in the management of resistant psychotic patients who do not respond to both conventional and novel antipsychotics.

Psychotic disorders exert various effects on the quality of life of the affected individuals with corresponding diversified side effects from the drugs used in management. An assessment of haemorrhological and haemostatic parameters such as fibrinogen concentrations, prothrombin time, and partial thromboplastin time with kaolin, whole blood and plasma viscosities is a significant diagnostic and prognostic tool which may be used to infer physiological and pathological changes in these patients. These



changes can be linked to increase in blood flow circulation and abnormal bleeding. This aim of this study was to investigate the effects of antipsychotic chemotherapy on blood rheology and haemostatic activities.

Materials and Methods

Patient Selection

This was a case study of participants attending the Federal Neuro – Psychiatric Hospital, Uselu, Benin City. Inclusion criteria included age (≥ 18 years), use of antipsychotic chemotherapy for over one month and willingness to offer a verbal informed consent to participate in the study. The following patients who did not meet the inclusion criteria (< 18 years, non-use of antipsychotic chemotherapy, use of antipsychotic chemotherapy for less than one month and refusal to offer verbal informed consent to participate in the study) were excluded from this study.

Sample Collection

Venous blood was collected from each of the participants into EDTA anticoagulant and sodium citrate containers. They were well mixed and taken to the laboratory within 1 hour of collection for analysis. Also, ethical approval was obtained from the Ethics and Research Committee of the Federal Neuro – Psychiatric Hospital, Uselu Benin City.

Sample Analysis

Fibrinogen concentration was measured by the clot weight method (Ingram, 1961). Whole blood and plasma viscosities were measured by method describes by Reid and Ugwu (1987).

Platelet count was done by method described by standard method (Dacie and Lewis, 2001). While the PT and PTTK were measured using commercially available Diagen PT and PTTK reagents (Diagen Diagnostics, UK). The ESR was measured using the Western-green method.

Statistical Analysis

Data obtained were analyzed using the IBM statistical software SPSS version 20. The mean, standard deviation, probability value (p-value) and level of significance were gotten using the independent sample t –test, while the one-way analysis of variance (ANOVA) was used to analyze the variation in the mean values of the various age groups. Statistical significance was set at $p \leq 0.05$.

Results

Table 1 shows the haemorrhological parameters investigated. Fibrinogen concentration and WBV increased in test when compared to control, while the ESR and PV reduced in test when compared to controls ($p=0.158, 0.057, 0.909$ and 0.804) respectively. The ESR, RPV and RWBV were reduced in females when compared to male. The difference was however not statistically significant ($p=0.100, 0.084$ and 0.370) respectively as shown in table 2. There was no statistically significant difference in the fibrinogen concentration based on gender. Prothrombin time and partial thromboplastin time with kaolin were significantly increased in test subjects when compared to the controls ($p < 0.05$ and 0.001) respectively as shown in table 3. Table 4, shows the various parameters investigated in relation to gender.

Table 1: Haemorrhheological changes in Psychiatric Patients on Antipsychotic Chemotherapy

Parameters	Group	N	Mean ± Std. Deviation	P-value	Level of significance Investigated
PCV (%)	Control	35	44.6 ± 7.1	0.003	S
	Test	35	40.1 ± 4.7		
ESR (mm/h)	Control	35	9.0 ± 11.1	0.909	NS
	Test	35	8.7 ± 9.6		
Rpv (Mpal.S)	Control	35	2.56 ± 1.62	0.804	NS
	Test	35	2.47 ± 1.05		
Rwbv (Mpal.S)	Control	35	4.63 ± 0.99	0.057	NS
	Test	35	5.13 ± 1.16		
Fibrinogen (G/L)	Control	35	3.06 ± 0.58	0.154	NS
	Test	35	3.31 ± 0.84		

S= Significant NS= Not-significant

PCV = Packed Cell Volume, ESR = Erythrocyte Sedimentation Rate,

RPV = Relative Plasma Viscosity, RWBV = Relative Whole Blood Viscosity.

**Table 2: Differences in Haemorheological parameter based on the gender of Psychiatric patients**

Parameter Investigated	Gender	N	Mean \pm Std. Deviation	P- value	Level of sig.
PCV (%)	Female	14	36.0 \pm 4.3	0.000*	S
	Male	21	42.8 \pm 2.6		
ESR (mm/h)	Female	14	5.4 \pm 3.7	0.100	NS
	Male	21	10.9 \pm 11.7		
RPV (mpal/s)	Female	14	2.13 \pm 0.75	0.084	NS
	Male	21	2.70 \pm 1.17		
RWBV (mpal/s)	Female	14	4.91 \pm 1.01	0.370	NS
	Male	21	5.27 \pm 1.25		
FIBRINOGEN (g/l))	Female	14	3.3 \pm 0.8	0.941	NS
	Male	21	3.3 \pm 0.9		

S= Significant NS= Not-significant

Table 3: Haemostatic changes in Psychiatric patients on Antipsychotic Chemotherapy

Parameters measured	Group	Number of samples (n)	Mean ± Std. Deviation	P value	Level of significance
PT (secs)	Control	35	13.7 ± 1.6	0.000*	S
	Test	35	16.4 ± 2.5		
PTTK (secs)	Control	35	35.8 ± 8.0	0.001*	S
	Test	35	43.2 ± 9.4		
INR	Control	35	1.03 ± 0.09	0.000*	S
	Test	35	1.26 ± 0.25		
PLATELET (x10 ⁹ /L)	Control	35	179 ± 57	0.456	NS
	Test	35	190 ± 67		

S= Significant NS= Not-significant



Table 4: Effect of Gender on Haemostatic parameters in Psychiatric Patients on Antipsychotic Chemotherapy

Parameter measured	Gender	Number of samples (n)	Mean \pm Std. Deviation	P-value	Level of significance
PT (secs)	Female	14	16.1 \pm 1.7	0.589	p>0.05 NS
	Male	21	16.6 \pm 3.0		
PTTK (secs)	Female	14	39.9 \pm 7.4	0.071	p>0.05 NS
	Male	21	45.4 \pm 10.1		
INR	Female	14	1.24 \pm 0.17	0.655	p>0.05 NS
	Male	21	1.28 \pm 0.30		
PLATELET ($\times 10^9/L$)	Female	14	214 \pm 59	0.074	p>0.05 NS
	Male	21	174 \pm 68		

S= Significant NS= Not-significant

Discussion

The lack of iron and its role in erythropoiesis is well documented in the management of psychosis (Saunders *et al.*, 2001). Absence of enthusiasm, irritability, lethargy, lack of concentration, hypoactivity, increased anxiety and decreased cognition and attention are the symptoms associated with reduced iron metabolism (Inuwa *et al.*, 2004). In this study, it was observed that the relative plasma viscosity reduced in tests when compared to controls, while relative whole blood viscosity increased in test when compared to controls. This may be attributed to the antipsychotic therapy which reduces metabolic activities in an individual thereby reducing erythropoietic activities. In this study, it was observed that the patients were confined either in the wards or restricted areas with little or no space for physical activity. Some were observed to spend more hours at a particular position mostly on their beds. Fibrinogen an acute phase protein was observed to increase in test when compared to controls.

This may be attributed to increase in total iron binding capacity caused by reduced iron metabolism in individuals on antipsychotic therapy (Eegunranti *et al.*, 2016). This study also indicates increase in ESR, RPV and RWBV in males when compared to females. This may not be directly connected to the antipsychotic therapy but may be related to exposure to hard drugs. This is because males are more exposed to hard drugs like cocaine and marijuana more than the females.

Haemostatic disorders have been shown to be caused by the use of certain drugs and chemicals in the management of certain diseases and disorders (Bain *et al.*, 2012). This study showed a significant increase in the mean prothrombin time (PT) of the test subject when compared to the controls ($p=0.000$). The increase may be attributed to the anticoagulant properties in some antipsychotic drugs such as the chlorpromazine (Afolabi *et al.*, 2014; Osinbowale *et al.*, 2010). A prolonged PTTK was also observed among the test groups when

compared to the controls ($p = 0.001$). The prolongation could be attributed to the haemostatic effects of antipsychotic drugs through mechanisms such as impairment of liver function where most procoagulant proteins are synthesized (Mohammed *et al.*, 2011). There was no statistically significant correlation between the PT and PTTK of test subjects which suggests that the changes in these parameters are independent. This means that the prolongation in PTTK may be as a result of defect in the intrinsic coagulation pathway, while that of the PT is from the extrinsic pathway (Bain *et al.*, 2012). This implies that the prolongation in PT and PTTK is not connected with the concentration of fibrinogen and or prothrombin which are both factors in the common coagulation pathway (Greer *et al.*, 2013).

Conclusion

We therefore conclude that antipsychotic chemotherapy increases blood rheology due to inactivity caused by these drugs and it increases PT and PTTK levels. We recommend the inclusion of clotting profile analysis during these treatments to monitor those who may be at risk of abnormal bleeding.

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Conflict of Interest

We declare that there are no conflicts of interest

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