

EFFECT OF ANTIDEPRESSANT TREATMENT ON HAEMATOLOGICAL PARAMETERS OF DEPRESSIVE DISORDERED PATIENTS IN A NIGERIAN TEACHING HOSPITAL

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ABSTRACT

Background: The effect of antidepressant, a major pharmacological agent of treating depressive disorders, on the hematological parameters of depressive disordered patients was studied.

Materials & Methods: Forty patients (male and female) at the mental health clinic, Ladoke Akintola University of Technology Teaching Hospital, Osogbo and forty apparently healthy individuals served as controls. Haematological parameters were estimated using SYSMEX KX-2IN blood auto-analyzer, erythrocytes sedimentation rates using Westergreen method.

Results: show that there is a statistically significant ($p < 0.05$) elevation in the erythrocytes sedimentation rates of the depressive disordered patients than in the control group. Statistically significant decrease was observed in hematological parameters such as haematocrit, hemoglobin, red blood cells count, platelets count and total white blood cell count in depressed patients on treatment with antidepressants, e.g Amitriptyline, Imipramine, etc. However, there is no statistically significant difference ($p > 0.05$) in the mean corpuscular volume (MCV) and mean cell haemoglobin (MCH) of both the patients under treatment for depression and control subjects.

Conclusion: Therefore, a good monitoring of the haematological parameters of depressive disordered patients before and during antidepressant's administration could serve as a reliable means of observing changes resulting from the use of antidepressant drugs.

KEYWORDS: Antidepressants, Depressive Disorder, Hematological Parameters

INTRODUCTION

Major depression is a chronic illness with a high prevalence and is a major component of disease burden. Depressive disorders were the second leading cause of years lived with disability in 2010 in Canada, the United States and globally (Whiteford HA, Degenhardt L, Rehm J, et al, 2013). The lifetime prevalence of depression ranges between 10 and 21% in population (Noble, 2005). According to the precipitation of the World Health Organization (WHO), depression is estimated to become the second leading cause of dysfunction by the year 2020. By 2020, depression would be the leading

cause of burden of disease in developing countries (Murray and Lopez, 1997; Ozdmir and Rezaki, 2007).

In the 19th century, depression was seen as an inherited weakness of temperament. In the first half of the 20th century, Freud linked the development of depression to guilt and conflict. John Cheever, the author and a modern sufferer of depressive disorder, wrote of conflict and experiences with his parents as influencing his development of depression (Cassano *et al.*, 2002).

Antidepressants are drugs that relieve the symptoms of depression. They were first developed in the 1950s and have been used regularly since then (Westbrook *et al.*, 2010). Antidepressants primarily work on brain chemicals called neurotransmitters, especially serotonin and norepinephrine. Other antidepressants work on the neurotransmitter dopamine. Scientists have found that these particular chemicals are involved in regulating mood, but they are unsure of the exact ways that they work (Cassano *et al.*, 2002). The newest generation antidepressants are called selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs). Tricyclic antidepressants are the old generation antidepressants, they are powerful, but their use today are reducing because of their potential side effects especially on the heart. Monoamine oxidase inhibitors (MAOIs) are the oldest class of antidepressant medications. Its use nowadays are very low because of a reaction called cheese reaction.

Hematological parameters involve the estimation of all blood cells and its constituents. These parameters include red blood cell (RBC) count which determines the total number of red blood cells (RBCs) in the body, the test helps to diagnose anemia and other red cell abnormalities and it is expressed in $10^9/L$ (Goldman *et al.*, 2012); Haemoglobin estimation which determines the haemoglobin concentration of the body expressed in g/dl (McCance *et al.*, 1994); The hematocrit or packed cell volume (PCV) which is the proportion, by volume, of the blood that consists of red blood cells expressed in percentage (%); Erythrocyte sedimentation rate (ESR), also called a sedimentation rate or Westergren ESR, is the rate at which red blood cells sediment in a period of 1 hour. It is a non-specific measure of inflammation, measured and reported in mm/hr; The mean cell volume (MCV), is a measure of the average red blood cell size that is reported as part of a standard complete blood count expressed in femtoliters (fL) (Akanni *et al.*, 2011); The mean cell hemoglobin (MCH) is the average mass of hemoglobin per red blood cell in a sample of blood and it is expressed in picograms (MedlinePlus Medical Encyclopedia, 2009.). The normal value for MCHC is about 32 to 36 g/dl. (MedlinePlus Encyclopedia *RBC indices*); Red blood cell distribution width (RDW) calculates the varying sizes of red blood cell (RBC) volume in a blood sample, it is expressed in percentage (%) (Choladda *et al.*, 2012). The objective of this study is to show the effects of antidepressant treatment on the haematological parameters of depressive disordered patients.

MATERIALS AND METHODS

Subject Selection

A total of eighty subjects comprising of forty patients (male and female) with depressive disorders in the psychiatric clinic of the LAUTECH Teaching Hospital, Osogbo and forty apparently healthy subjects as control were recruited for the study.

Sample Collection

Five milliliters of venous blood was collected from each subject, dispensed into EDTA anticoagulant specimen bottles and carefully mixed.

METHOD

Differential white Cell Count

Leishman staining technique was used according to Dacie and Lewis, 2006). This was prepared by diluting 0.6 g of Leishman powder in 600 ml of absolute methylalcohol and then filtered.

A thin blood film was made and allowed to air dry. It was flooded with neat Leishman stain for 2 minutes and diluted with buffered distilled water at pH 6.8 to stain for 10 minutes. The slide was rinsed with the buffered water and allowed to air dry. The stained slide was then examined microscopically using oil immersion objective (x100). One hundred consecutive white blood cells were counted in all, indicating various types of leukocytes encountered and recorded.

Estimation of Haematological Parameters: Total white cell count, red blood cell count, haematocrit, Platelets, Haemoglobin, and other haematological indices. The methodology is by flow cytometry (direct current detection method), using cell pack and stromatolyser-WH solution (cell pack: 6.38 g/l of sodium chloride, 1.00 g/l of boric acid, 0.20 g/l of sodium tetraborate and 0.20 g/l of EDTA-2K, stromatolyser-WH: 8.5 g/l of organic quaternary ammonium salt, 0.6 g/l of sodium chloride). Fifty microlitres of the EDTA anticoagulated blood sample was aspirated by automated equipment SYSMEX KX-2IN auto-analyser which diluted the blood with cell pack in the white blood cell counting chamber and later detected the cell sizes as electric impulses (Hedwin *et al.*, 2006).

Erythrocyte Sedimentation Rate (ESR) using the standard Westergren Method (Dacie and Lewis, 2001)

Well mixed blood was added to sodium citrate anticoagulated dispette at the ratio of 9:1, mixed and drawn up to the zero mark on the Westergren tube. It was then left undisturbed for 1 hour. The height of the clear plasma above the upper limit of the column of sedimenting cells was read and recorded in mm in 1 hour.

Statistical Analysis

A paired t-test was used for the data analysis. $P < 0.05$ denotes a significant difference between groups.

RESULTS

The result for this study is represented in the Table 1. There is a statistically significant increase ($p < 0.05$) observed in the ESR of the depressed patients on treatment with tricyclic antidepressants e.g amitryptiline. On the other hand, statistically significant decrease was observed in hematological parameters such as packed cell volume (PCV), hemoglobin, red blood cells count, platelets count and total white blood cell count in depressed patients on treatment. However, there is no statistically significant difference ($p > 0.05$) in the mean corpuscular volume (MCV) and mean cell haemoglobin (MCH) of both the patients under treatment for depression and control subjects.

Differential with white blood cell count (Neutrophils, Eosinophils, Lymphocyte, Basophils and Monocytes).

Table 1: Shows the Mean \pm S.D of Haematological Parameters on Test and Control Subjects

Parameters	ESR(mm/hr)	RBC($10^9/l$)	HGB(g/dl)	HCT(%)	MCV(fl)	MCH(pg)	MCHC(g/l)	WBC($10^9/l$)	LYM(%)	NEUT(%)	LYM($10^9/l$)	MXD($10^9/l$)	NEUT($10^9/l$)
tests (n=40)	40.28 \pm 24.22	4.38 \pm 0.35	11.50 \pm 1.01	35.94 \pm 2.66	80.62 \pm 8.43	26.45 \pm 3.07	32.16 \pm 1.39	6.74 \pm 1.12	37.84 \pm 9.65	49.25 \pm 8.18	2.47 \pm 0.34	0.87 \pm 0.28	3.40 \pm 1.13
control (n=40)	7.13 \pm 0.24	5.20 \pm 0.30	14.28 \pm 0.38	43.73 \pm 0.75	80.88 \pm 2.47	35.07 \pm 2.50	35.07 \pm 2.50	4.55 \pm 0.35	49.92 \pm 2.05	37.70 \pm 0.70	2.16 \pm 0.04	0.62 \pm 0.04	1.72 \pm 0.04
t test	8.66	-11.32	-16.32	-17.79	-0.19	-0.05	-6.46	11.73	-7.74	8.9	5.62	5.7	9.8
p-value	0	0	0	0	0.852	0.963	0	0	0	0	0	0	0

Parameters	MXD(%)	NEUT(%)	LYM($10^9/l$)	MXD($10^9/l$)	NEUT($10^9/l$)	RDW-SD	RDW-CD	PDW	MPV(fl)	P-LCR(%)
tests (n=40)	12.91±3.74	49.25±8.18	2.47±0.34	0.87±0.28	3.40±1.13	44.29±3.69	14.74±1.92	13.21±1.69	10.04±0.66	26.60±4.92
Control(n=40)	13.92±1.82	37.70±0.70	2.16±0.04	0.62±0.04	1.72±0.04	40.65±1.85	13.36±0.47	14.70±0.52	11.45±0.43	34.55±1.32
t test	-1.63	8.9	5.62	5.7	9.4	5.6	4.4	-5.33	-11.32	-9.9
p-value	0.107	0	0	0	0	0	0	0	0	0

DISCUSSIONS

The result of this study showed that with the increased erythrocytes sedimentation rate observed amongst the test group when compared with the control, there have been evidences of inflammatory processes mediated by the antidepressants which may be as a result of the physiochemical properties of the plasma which includes plasma colloids, increase in plasma fibrinogen and relative variation in the plasma protein ratio marked.

An increase in the RDW relative to normal MCV values in the test patients may be due to osteomyelofibrosis which states that in situation of normal mean cell volume (MCV) coupled with a high red cell distribution width (RDW) then there is a confirmation of osteomyelofibrosis. However, these changes are mostly due to the drugs not the disease.

The significant change in the white blood cells is supported by the findings from studies conducted in the Department of Neurology, Würzburg, Germany (2004) which resulted from responses to the use of antidepressants such as Interferon- β -1a though resolved after some time.

CONCLUSIONS

This study showed that ESR is significantly raised in depressive disordered patients on antidepressant drugs. Hematological indices such as MCV and MCH remain the same while other haematological parameters are significantly raised. This may be due to the antidepressant used. Therefore a close monitoring of hematological parameters is essential in the use of antidepressant agents in order to avoid hematological complications.

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