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# Effects of Pyrethroid Insecticide Exposure on Haematological and Haemostatic Profiles in Rats

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**Abstract:** High malaria burden has led to the increase use of insecticides in the tropics and subtropics. This study thus aimed at assessing the haematological effects and associated haemostatic alteration of pyrethroid insecticide exposure using experimental animal model. Rats of comparable ages and weights were randomized into four groups (A-D). Rats in groups B, C and D were exposed to pyrethroid insecticide by inhalation for 1, 2 and 3 min daily respectively for three weeks. Rats in group A (control) were not exposed. Haematological and haemostatic variables were comparable in all groups (<0.05). Results from the study show that minimal exposure to pyrethroids is safe.

**Key words:** Pyrethroid, insecticide, red cell, white cells, haemostasis

## INTRODUCTION

Heavy burden of malaria infection in the tropics and subtropics with resultant high cases of death, especially in Africa (WHO, 1992; Smyth, 1994; Akhigbe *et al*., 2011) has led to increased prophylactic measures to curb the disease spread. Such measures include the use of insecticides. A common active chemical in insecticides are pyrethroids, derivatives of pyrethrins, natural substances obtained from the flowers of *Pyrethrum* species (Luty *et al*., 2000). It has been considered unharmful because most vertebrates have necessary enzymes required for rapid metabolism. Synthetic pyrethroid insecticides are now used as substitutes for pest control (Jayakumar *et al*., 2008; Sangha *et al*., 2011), thus accounting for over 30% of insecticide used globally (Shukla *et al*., 2002).

Though there is a common perception of users about the safety of this group of insecticide, studies have reported its toxic effects (Inayat *et al*., 2007; Kamal *et al*., 2007; Sangha *et al*., 2011). Cypermethrin, a pyrethroid has been documented to cause clinical signs such as increased urination, licking of legs, jerky movements, ataxia, incoordination, staggering gait, dizziness, altered blood biochemistry, hepatoxicity (Yavasoglu *et al*., 2006; Saxena and Saxena, 2010), haematoxicity (Sayim *et al*., 2005; Kamal *et al*., 2007) and neurotoxicity (Sayim *et al*., 2005).

Although, there are a lot of studies in the scientific open literature that documented the toxicity of cypermethrin, no study has reported the toxic effect of a formulated insecticide containing two or more pyrethroids (as commonly used in Nigeria and other African countries). This study hence assessed the haematoxicity of a pyrethroid-formulated insecticide.

## MATERIALS AND METHODS

**Laboratory animals:** Sprague dawley rats weighing between 170 and 190g were procured and bred in the Animal Holding Unit of the Department of Physiology, Ladoke Akintola University of Technology, LAUTECH Ogbomoso, Nigeria. They were kept maintained under standard conditions with a 12 h day/light cycle and fed with standard chow and water ad libitum. They were allowed to acclimatize for two weeks before the commencement of the experiment (Eghoghosoa *et al*., 2011).

**Treatment:** Rats were randomized into four groups (A-D). Rats in groups B, C and D were exposed to 30 mg $m^{-3}$ pyrethroid insecticide, containing 0.02%/w/w imiprothrin, 0.03%/w/w d-phenothrin and 0.10%/w/w D-transallethrin, (®Mortein-Reckitt Benckiser, Nigeria) by inhalation for 1, 2 and 3 min daily respectively for three weeks. Rats in group A (control) were not exposed.

All animals received humane care in compliance with the institution's guideline and criteria for humane care as outlined in the NIH Guide for the Care and Use of Laboratory Animals (NIH publication No. 85 -23 revised 1985: US Department of Health, Education and Welfare, Bethesda, Maryland, USA).

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**Collection of blood sample:** After the experimental protocol, the blood samples were collected by cardiac puncture into appropriate specimen bottles.

**Determination of haematological indices:** Evaluation of haematological parameters was carried out as described in previous studies (Dacie and Lewis, 1991; Joshi *et al*., 2002; Akhigbe *et al*., 2008a; Saka *et al*., 2011).

**Statistical analysis:** Analyses of data were done using the SPSS software (SPSS Inc, Chicago, USA). Data are mean of 5 replicates ± SEM. Comparisons were made using one-way analysis of variance (ANOVA) and unpaired t-test. Values of $p<0.05$ were regarded statistically significant (Akhigbe *et al*., 2008b).

## RESULTS

Table 1 and 2 show the changes in red cell count and its indices. RBC, PCV and Hb were higher in the test groups when compared with the control rats but these values were however marginal and statistically insignificant ($p>0.05$). Similarly, red cell indices were insignificantly higher in the test groups ($p>0.05$).

Though, there were no significant differences in all groups ($p>0.05$), the test groups showed higher values of TWBC and DWBC, except lymphocytes which were lower in the test groups when compared with the control (Table 3).

Platelets and bleeding time were also insignificantly reduced in test groups when compared with the control ($p>0.05$), however, clotting time was insignificantly higher in the test groups (Table 4).

Although, there were insignificant alterations in the haematological and haemostatic indices in the test groups in comparison with the control, these changes were not duration-dependent.

Table 1: Effect of pyrethroids exposure on red blood cell (RBC), packed cell volume (PCV), and haemoglobin (Hb) concentration in rats

| Values | Group A | Group B | Group C | Group D |
|---|---|---|---|---|
| RBC ($x10^{12}$/L) | 6.38±0.36 | 6.74±1.31 | 8.14±1.19 | 7.81±1.17 |
| PCV (%) | 31.15±0.85 | 33.85±5.55 | 41.60±5.23 | 37.80±3.6 |
| Hb (g $dL^{-1}$) | 10.95±0.15 | 12.25±2.25 | 14.50±2.21 | 14.40±1.61 |

Table 2: Effect of pyrethroids exposure on red cell indices

| Values | Group A | Group B | Group C | Group D |
|---|---|---|---|---|
| MCV (fl) | 48.85±2.05 | 50.50±2.26 | 51.10±1.74 | 48.47±2.19 |
| MCH (pg) | 17.25±1.25 | 18.20±0.20 | 17.80±0.29 | 18.50±1.05 |
| MCHC (%l g/100 mL) | 35.25±1.45 | 35.95±0.75 | 34.97±0.49 | 38.10±1.21 |

MCV: Mean corpuscular volume, MCH: Mean corpuscular haemoglobin, MCHC: Mean corpuscular haemoglobin concentration

Table 3: Effect of pyrethroids exposure on total and differential white blood cells

| Values | Group A | Group B | Group C | Group D |
|---|---|---|---|---|
| TWBC ($x10^9$/L) | 6.40±2.10 | 13.75±2.75 | 10.73±2.71 | 10.00±2.46 |
| Neutrophils (%) | 6.00±3.00 | 9.50±4.50 | 19.33±6.17 | 19.33±5.6 |
| Eosinophils (%) | 1.50±0.50 | 2.50±0.50 | 2.00±0.50 | 2.67±0.33 |
| Monocytes (%) | 6.00±1.00 | 6.00±2.00 | 7.67±1.86 | 9.00±0.58 |
| Lymphocytes (%) | 86.50±4.50 | 82.00±6.00 | 70.67±8.17 | 68.67±6.96 |

TWBC: Total white blood cells

Table 4: Effect of pyrethroids exposure on some haemostatic variables

| Values | Group A | Group B | Group C | Group D |
|---|---|---|---|---|
| Platelets ($x10^9$/L) | 613.50±0.26 | 249.50±0.02 | 508.30±0.03 | 421.30±0.07 |
| Bleeding time (min) | 2.48±0.03 | 1.50±0.50 | 1.27±1.04 | 2.33±1.02 |
| Clotting time (min) | 0.26±0.03 | 0.49±1.02 | 0.55±1.05 | 1.35±1.01 |

## DISCUSSION

Evaluation of haematological indices plays a vital role in assessing the toxicity of any exogenous compound in the system. Since the blood accounts for the greatest percentage of the total body fluid, it remains the commonest route of transport of food, drug and any foreign substance. Accumulation of a compound in excess or lower than normal level of a compound in the blood is usually a pointer to a clinico-pathological condition. The toxic effect of a compound is usually seen as excess or deficit of one or more serum markers; an enzyme, a hormone or any endogenous compound. In assessing haematoxicity, increase or decrease in blood variables indicates excess or suppression of blood cells production respectively or an imbalance between blood cells production and destruction. Such analysis is relevant to risk evaluation as the changes in the haematological system have higher predictive value for human toxicity, when the data are translated from animal studies (Olson *et al*., 2000).

This study documents comparable values of RBC and related indices in pyrethroid-exposed and control rats. This conflicts with results from previous studies (Shakoori *et al*., 1988; Yousef *et al*., 2003; Kamal *et al*., 2007) that documented reduced RBC, PCV and Hb content. The disparity observed in this study in comparison with previous study could be due to the lower dose and minimal duration of exposure in the present study. The non-significant effect of pyrethroid insecticide as observed with the dose and duration of exposure in this study on RBC, PCV and Hb content suggests that the balance between RBCs production and degradation was unaltered. This could imply that the pyrethroids at the dose used do not stimulate erythropoietin release in the kidney which is the humoral regulator of RBC production (Polenakovic and Sikole, 1996; Sanchez-Elsner *et al*., 2004). Since RBC and Hb are very important in

transporting respiratory gases (De Gruchy, 1976), this observation also suggests that there was no changes in the oxygen-carrying capacity of the blood and the amount of oxygen delivered to the tissues following pyrethroids exposure. Furthermore, it shows that pyrethroids as used in the study do not induce anaemia, since these variables are anaemia markers. The calculated blood indices (MCV, MCH and MCHC) have a particular importance in anaemia diagnosis in most animals (Coles, 1986). They tell the particular type of anaemia based on the RBC size and relative Hb content. Results from this study thus imply that pyrethroids do not alter RBC size nor relative Hb content.

TWBC and DWBC counts were also comparable in all groups. This disagrees with results from previous study that reported immunotoxicity following pyrethroids exposure (Yavasoglu *et al*., 2006; Madsen *et al*., 1996). The variation seen in the present study could also be attributed to the dose and duration of exposure. The results from this study show that minimal exposure to pyrethroids does not have the potential to challenge the immune system nor increase vascular permeability.

Estimation of platelets counts, bleeding and clotting time is used in the assessment of haemostatis. Platelets are the blood cells involved in coagulation. Coagulation of blood requires that the platelets should be in sufficient size, number and function (Williams and Levine, 1982; Yakubu and Afolayan, 2009). Results from this study which shows similar platelet counts, bleeding and clotting time in exposed and control rats is at variance with previous study (Sayim *et al*., 2005) that reported a decrease in platelet count in rats exposed to pyrethroids. However, Sayim *et al*. (2005) documented a dose-dependent decrease in platelet counts which implies that observations in this study are dose-related. This suggests that at minimal exposure, pyrethroids do not have a stimulatory nor suppressive effect on thrombopoietin, the regulator of platelet production. It also shows that pyrethroids do not cause structural or functional damage to the platelets at minimal exposure.

## CONCLUSION

The results from the present study have shown that minimal exposure to pyrethroid insecticides does not pose toxicity on haematological variables and haemostatic function. It is thus recommended that adequate measures be taken to ensure minimal exposure to pyrethroids during domestic, veterinary, agricultural or industrial use.

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