



## Haematological Changes Following Intramuscular and Per-Rectal Diclofenac Sodium Administration in Dogs undergoing Orchiectomy

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### ABSTRACT

A total of 30 Nigerian indigenous male dogs aged 1-2 years ( $1.65 \pm 0.47$ ) and 11-15kg ( $13.4 \pm 1.27$ ) body weight were used for the study. They were randomly allocated into 6 groups of 5 dogs each. Groups A1, B1 and C1 for intramuscular at 2mg/kg, 3mg/kg and 4mg/kg respectively and Groups A2, B2 and C2 for per-rectal at 2mg/kg, 3mg/kg and 4mg/kg. Haematological values of Packed cell volume (PCV), haemoglobin (Hb), Red blood cell (RBC), White blood cell (WBC) and Differential leucocyte counts (DLC) of Lymphocyte (LYM), Neutrophils (NEU), Monocyte (MON) and Eosinophils (EOS) were determined. Statistical Package for Social Sciences Software Version 22.0 (SPSS Inc. Chicago. Illinois). General Linear Model (GLM) using repeated measures Analysis of Variance (RM-ANOVA), to compare the mean of different groups at a 95% confidence interval and a 5% level of significance was used. The PCV, Hb and Rbc values of the dogs castrated were within normal range when compared with specie corresponding values. The PCV value was lowest  $38.6 \pm 1.9$  at 2nd hour 2mg/kg for per rectum and highest of  $44.1 \pm 1.9$  at the 9th hour for per rectum at 4mg/kg dose. The Hb value was lowest at  $12.9 \pm 0.5$  at 1st hour for per rectum at 4mg/kg dose and the highest of  $15.3 \pm 0.8$  at 0 hour for intramuscular at 2mg/kg. The Rbc value was lowest at  $4.0 \pm 1.5$  at 4th hour, 2mg/kg for per rectum and the highest of  $6.6 \pm 0.3$  at 7th hour, 2mg/kg. The Total leucocyte count (TLC) values of WBC and DLC also recorded significant differences. There was significant difference ( $P < 0.05$ ) between routes but values remain within normal range of values. This finding shows that the use of Diclofenac as a short term analgesic caused no significant changes on the haematocrit values of dogs when used after castration. This finding has also indicated that short-term use of diclofenac through the per rectum route may be safe and had no deleterious effect on haematological value of Nigerian indigenous male dogs

**Key words:** Dogs, diclofenac sodium, haematology, intramuscular, per-rectal, orchiectomy

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## INTRODUCTION

Orchiectomy also known as castration is a common elective surgical procedure in veterinary practice [1]. It is associated with haemorrhage and pain because of skin incision, exteriorization of the testis and clamping of spermatic cords [1,2]. Some studies have investigated haematological values in dogs undergoing surgical procedures [1,2]. There are steroidal and non-steroidal anti-inflammatory drugs used in managing postoperative pain [3]. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most prescribed drugs in human and veterinary medicine [4], they provide anti-inflammatory, antipyretic, analgesic, antispasmodic, and anticoagulant effects and of all the NSAIDs, diclofenac sodium is widely available drug. It is used for the symptomatic treatment and management of inflammation, fever and or pain associated with disease or injury of domestic livestock [5]. Diclofenac has long been approved as safe and effective for the treatment of acute and chronic pain through some variety of routes. The inhibition of cyclooxygenase (COX) by the NSAID (diclofenac) allows it to be highly effective in decreasing pain and inflammation [6]. Intravenous, intramuscular, oral, suppository, transdermal patch, and gel forms of diclofenac are available in markets for human and veterinary use [7, 8]. It was reported by [9] that diclofenac amongst the NSAIDs is the most widely available veterinary drug [10,11]. This study aims to investigate the haematological changes following intramuscular and per- rectal diclofenac sodium administration in dogs undergoing orchiectomy as it is among the most common surgical procedures performed in veterinary practice by small animal practitioners [12, 13].

## MATERIALS AND METHODS

A total of 30 Nigerian indigenous male dogs aged 1-2 years ( $1.65 \pm 0.47$ ) and 11-15kg ( $13.4 \pm 1.27$ ) body weight were used for the study. The dogs were sourced from Sokoto and its environs. They were kept at the kennel of the Faculty of Veterinary Medicine Usmanu Danfodio University Sokoto. They were conditioned for two weeks after which they were clinically examined and judged to be apparently healthy. The study was ethically approved by the Faculty Animal Research and Ethics Committee, Faculty of Veterinary Medicine, Usmanu Danfodiyo University, Sokoto. The animals were randomly allocated into 6 groups of 5 dogs each. Groups A1, B1 and C1 for intramuscular administration of diclofenac at 2mg/kg, 3mg/kg and 4mg/kg respectively while Groups A2, B2 and C2 for per-rectal at 2mg/kg, 3mg/kg and 4mg/kg. The dogs were prepared for surgery but allowed access to water until 2 hours prior to induction of anaesthesia. Dogs in groups A1, B1 and C1 received diclofenac sodium (Nouvasant pharmhealth limited, Nanjing Jiangsu, China) 2mg/kg, 3mg/kg and 4mg/kg respectively intramuscularly while those in groups A2, B2 and C2 received diclofenac sodium (Nouvasant pharm health limited, Nanjing Jiangsu, China) 2mg/kg, 3mg/kg and 4mg/kg respectively by depositing the aqueous solution in the rectum. A 20- gauge 1 ¼ inch sterile catheter was placed and secured in a cephalic vein. A 2ml venous blood sample was collected from each dog before drug administration (0 hour), to form the baseline data. Each dog was pre-medicated with atropine sulphate (Pauco Pharmaceutical Industry Nigeria Limited) 0.04mg/kg IM and Acepromazine maleate (Kyron Prescriptions, Benrose, South Africa) 0.05mg/kg IM. Anaesthesia was induced with Ketamine hydrochloride (Jawa Pharmaceuticals, India

Pvt. Limited) 10 mg/kg IV. Thereafter, orchiectomy was performed according to the method described by [14]. Blood samples (2ml) were collected from the cephalic vein and emptied into Ethylene diamine tetraacetic acid (EDTA) bottles using sterile needle and syringe hourly up to the 9th hour after recovery from anaesthesia. Packed cell volume (PCV), haemoglobin concentration (Hb), red blood cell (RBC) and white blood cell (WBC) counts were determined using a method described by [15]. Differential leucocyte counts (DLC) were also determined from Giemsa stained slides.

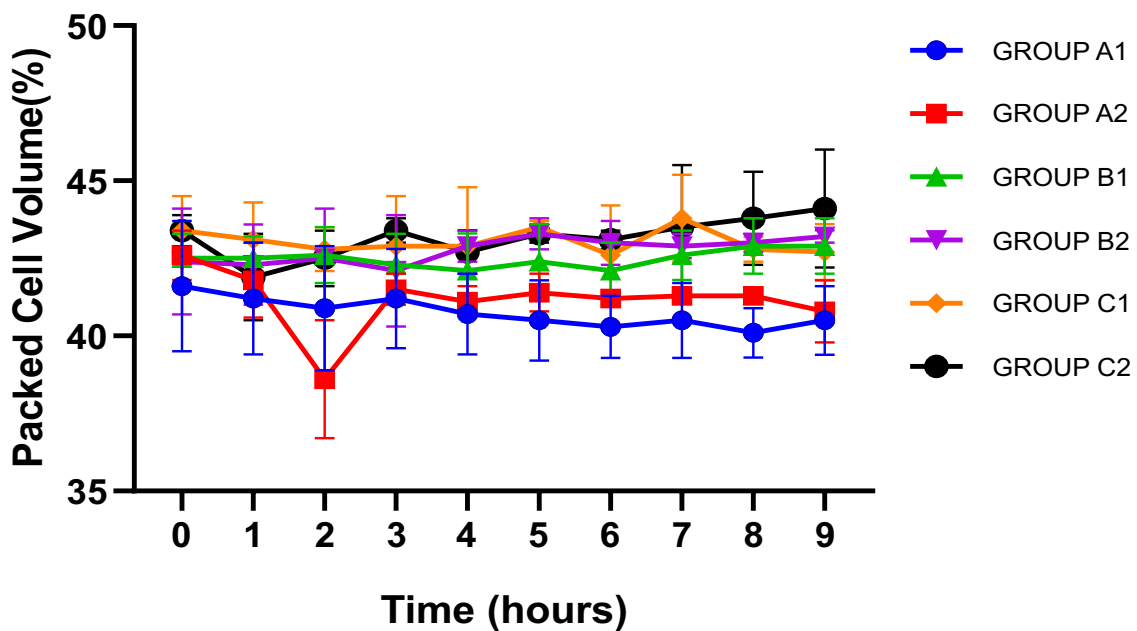
**Statistical Analysis**

Data was first tabulated in Microsoft excel Spreadsheet 2016 and exported into the Statistical Package for Social Sciences Software Version 22.0 (SPSS Inc. Chicago.

Illinois) for further analysis. Haematological parameters (PCV, Hb, RBC, WBC, Lymphocyte, Neutrophil, Monocyte and Eosinophil counts) of dogs were analyzed in a General Linear Model (GLM) using repeated measures Analysis of Variance (RM-ANOVA), to compare the mean of different groups at a 95% confidence interval and a 5% level of significance.

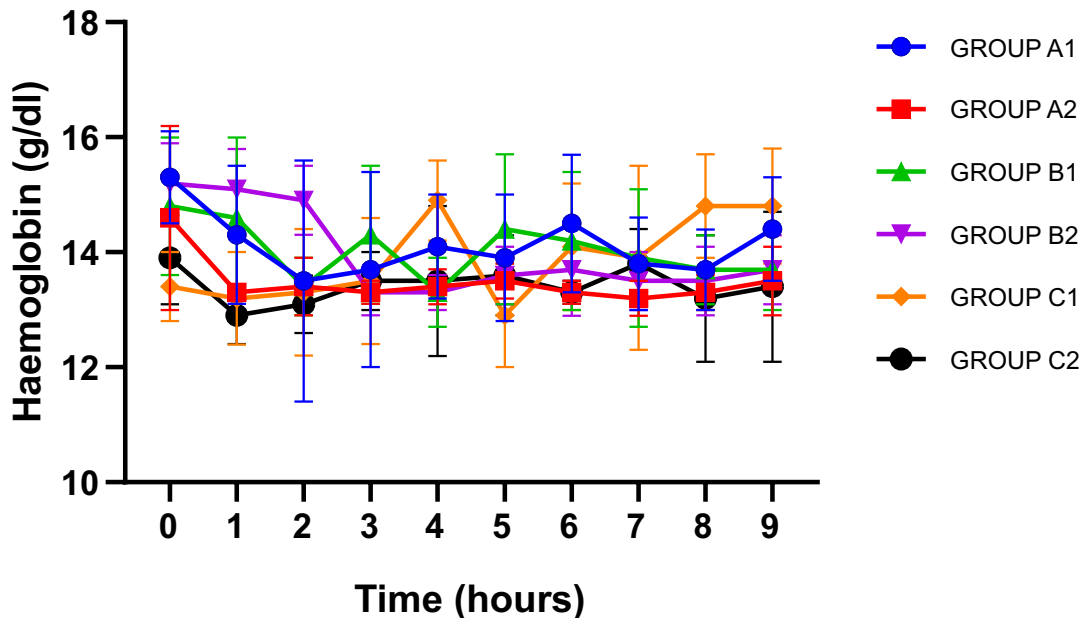
**RESULTS AND DISCUSSION**

**Changes in PCV:** The lowest PCV values of the experimental dogs is  $38.6 \pm 1.9$  at the 2nd hour per rectum for 2mg/kg dose. The highest value is  $44.1 \pm 1.9$  at the 9th hour per rectum at 4mg/kg dose. There were significant differences ( $P < 0.05$ ) both increase and decrease over time. All of the values recorded were within normal range (Figure 1).



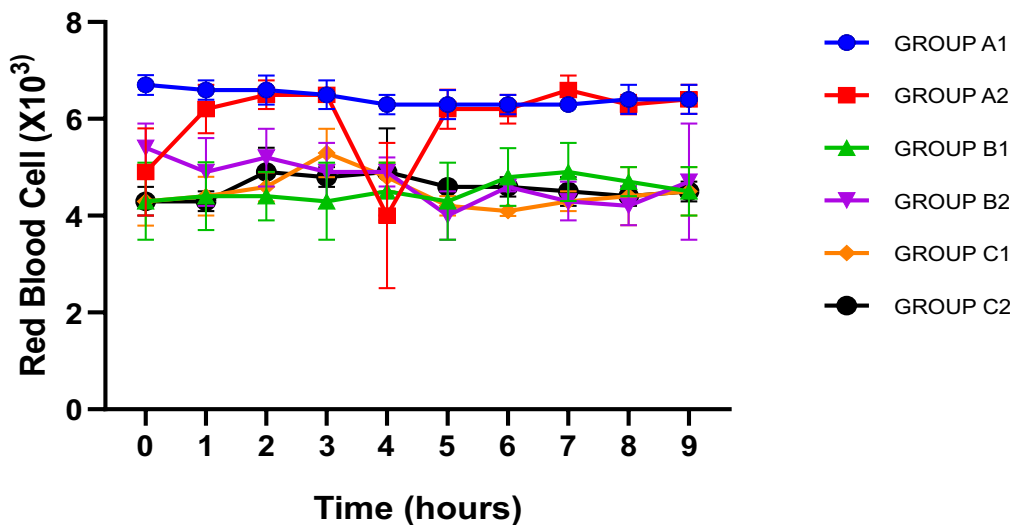
**Figure 1: Changes in mean Packed cell volume (PCV) of six groups of dogs treated with different doses of diclofenac sodium intramuscularly and per-rectal.**

**Changes in Hb:** The Hb values of the experimental dogs was lowest at  $12.9 \pm 0.5$  at 1st hour for per rectum at 4mg/kg dose and the highest of  $15.3 \pm 0.8$  at 0 hour for intramuscular at 2mg/kg. There were significant differences ( $P < 0.05$ ) both increase and decrease over time. All of the values recorded were within normal range (Figure 2).



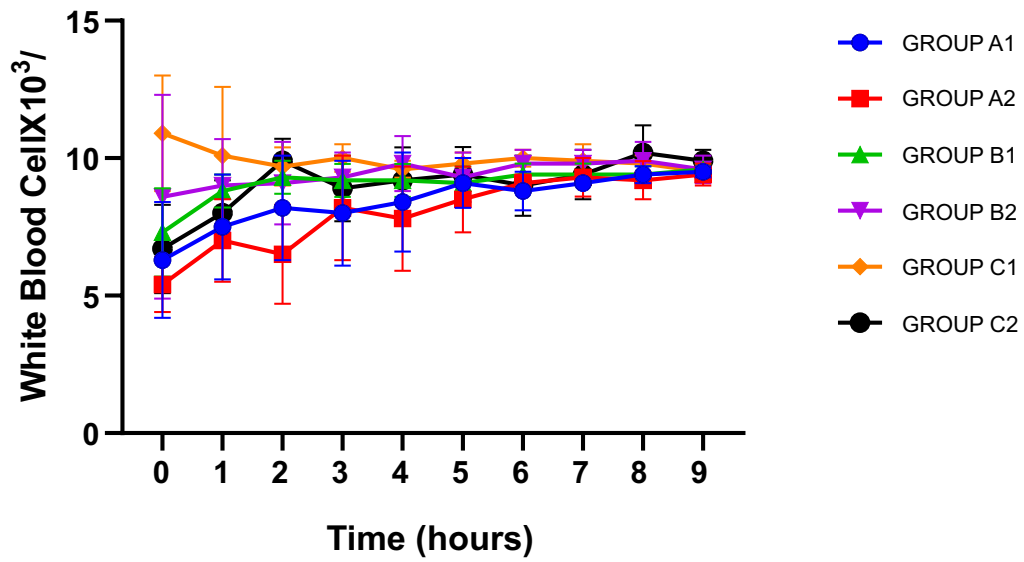
**Figure 2: Changes in mean Haemoglobin (Hb) of six groups of dogs treated with different doses of diclofenac sodium intramuscularly and per-rectal.**

**Changes in RBC:** The RBC values of the experimental dogs was lowest at  $4.0 \pm 1.5$  at 4th hour, 2mg/kg for per rectum and the highest of  $6.6 \pm 0.3$  at 7th hour for per rectum. There were significant differences ( $P < 0.05$ ) over time. All of the values recorded were within normal range (Figure 3).



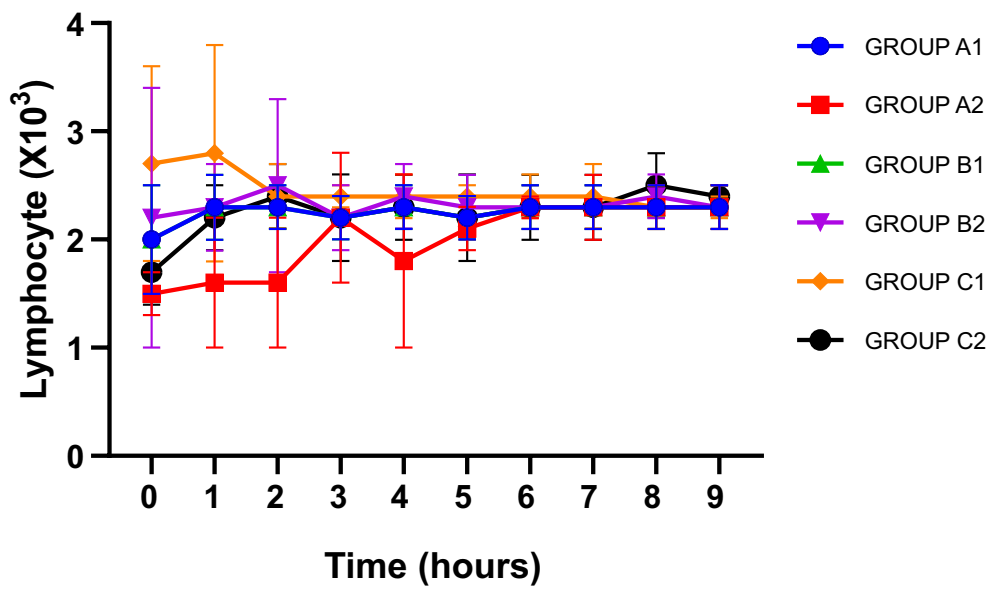
**Figure 3: Changes in mean Red blood cell (Rbc) of six groups of dogs treated with different doses of diclofenac sodium intramuscularly and per-rectal.**

**Changes in WBC:** The WBC values of the experimental dogs showed significant increase between the baseline and time points with highest increase at 9th hour  $9.5 \pm 0.2$  for intramuscular route at 2mg/kg. There were significant difference between groups with highest significant difference of  $10.9 \pm 2.1$  at 0 hour for intramuscular route at 4mg/kg dose. All of the values recorded were within normal range (Figure 4).



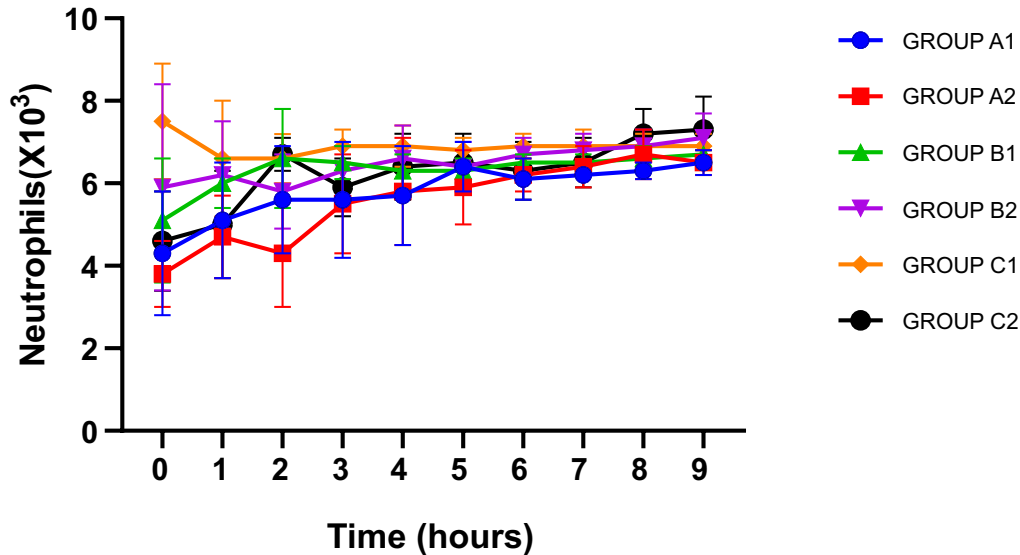
**Figure 4: Changes in mean White blood cell (WBC) of six groups of dogs treated with different doses of diclofenac sodium intramuscularly and per-rectal.**

**Changes in LYM:** The LYM values of the experimental dogs ranges from  $1.5 \pm 0.2$  to  $2.8 \pm 1.0$ . There were significant differences both increase and decrease over time for both the intramuscular and per-rectal route. All of the values recorded were within normal range (Figure 5).



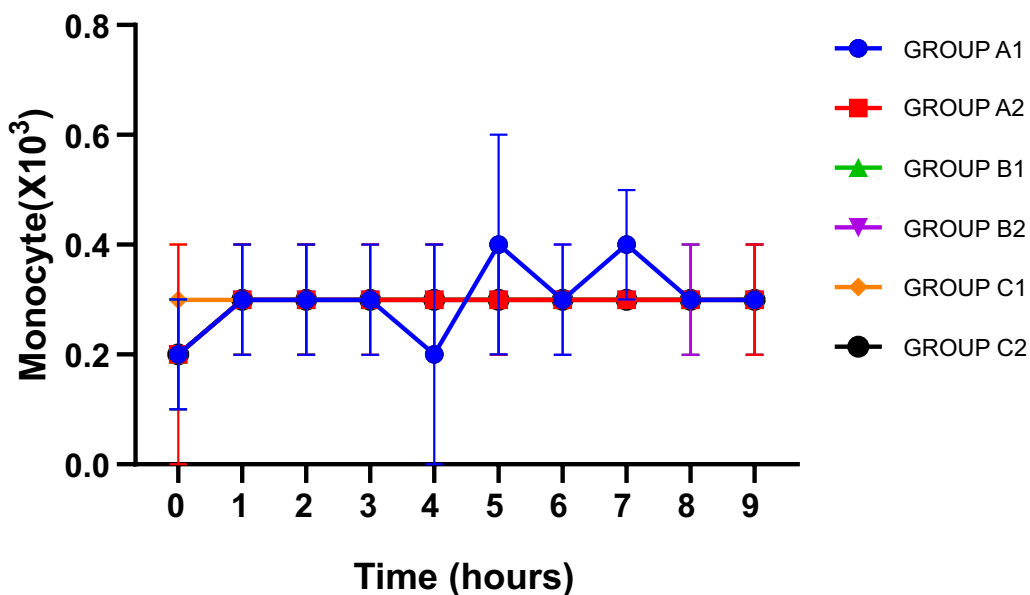
**Figure 5: Changes in mean White blood cell (WBC) of six groups of dogs treated with different doses of diclofenac sodium intramuscularly and per-rectal.**

**Changes in NEU:** The NEU values of the experimental dogs ranges from  $3.8 \pm 0.8$  to  $7.5 \pm 1.4$ . There were significant differences both increase and decrease over time for both the intramuscular and per-rectal route. All of the values recorded were within normal range (Figure 6).



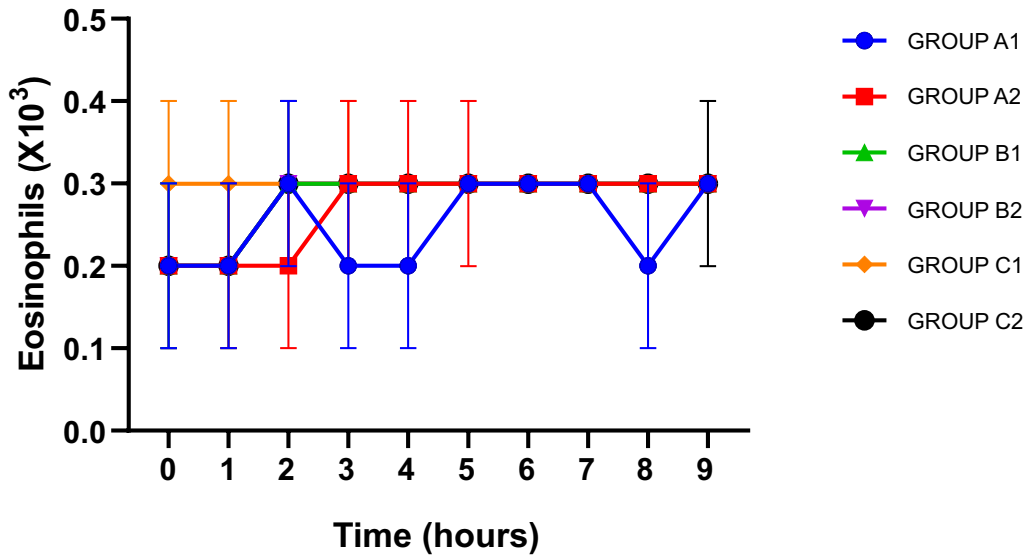
**Figure 6: Changes in mean Neutrophils (NEU) of six groups of dogs treated with different doses of diclofenac sodium intramuscularly and per-rectal.**

**Changes in MON:** The MON values of the experimental dogs ranges from  $0.2 \pm 0.1$  to  $0.4 \pm 0.1$ . There were significant differences both increase and decrease over time for both the intramuscular and per-rectal route. All of the values recorded were within normal range (Figure 7).



**Figure 7: Changes in mean Monocyte (MON) of six groups of dogs treated with different doses of diclofenac sodium intramuscularly and per-rectal.**

**Changes in EOS:** The EOS values of the experimental dogs ranges from  $0.2 \pm 0.0$  to  $0.3 \pm 0.1$ . There were significant differences both increase and decrease over time for both the intramuscular and per-rectal route. All of the values recorded were within normal range (Figure 8).



**Figure 8: Changes in mean Eosinophil (EOS) of six groups of dogs treated with different doses of diclofenac sodium intramuscularly and per-rectal.**

The present study revealed that dogs administered diclofenac sodium at 2mg/kg showed decreased packed cell volume at eighth and ninth hour through intramuscular route and decreased PCV value at first hour for per-rectal route. There was significant difference ( $P < 0.0382$ ) in respect to routes with per-rectal having higher PCV value than intramuscular route. Administration of diclofenac sodium at 3mg/kg showed no significant difference ( $P > 0.05$ ) throughout the period of the study through both intramuscular and per-rectal routes. This is same for the administration at 4mg/kg through both routes but there was significant difference in respect to route of administration with per-rectal recording higher PCV than intramuscular route at the second, third and fifth hour. The result of the present study revealed that all the PCV, Hb and Rbc count values of the dogs castrated were within the normal range when compared with the corresponding values before the procedure. Although there was significant difference between the routes but the values remain within

the normal range of values. This finding shows that the use of diclofenac as a short term analgesic caused no significant changes on the haematocrit values of dogs when used for post-operative analgesia. This finding has also indicated that short-term administration of diclofenac may be safe and had no deleterious effect on haematological value of dogs. It is known that dog owners usually request for castration for their pets. The use of analgesic during the castration of dogs is to relief pain and to facilitate wound healing, since diclofenac is a non-steroidal anti-inflammatory. In addition, it was considered that surgery involves haemorrhage from the normal incision which may have some effect on PCV value. Changes in haematological parameters had been used as indicators of cellular damage, as the blood is the major transporter of substances in the body [16]. The findings of the present study are therefore consistent with the report of [2,16, 17, 18, 19, 20] who has also investigated the effects of some analgesic on the haematological

parameters of dogs that had undergone surgery and they reported no significant changes in haematology of dogs. The present study showed that the Total leucocyte count (TLC) that is the white blood cell (WBC) values and differential leucocyte count (DLC) of dogs given diclofenac as analgesic agent showed non-significant changes from the baseline value. This is similar to the report of [2] who also reported non-significant changes in TLC from control values following major and minor surgical interventions in dogs. Significant changes in TLC values are usually associated with the presence of pathogens or stressors, which might occur where there are post-operative complications [20]. The present study did not experience any such complication as a result of the castration conducted on the dogs. Even though, fluctuations in values were noted in the TLC in

the dogs during the period of records clerking. These fluctuations in values showed statistically significant difference between the different routes of administration and are all within the normal range when compared with the 0 hour. These findings are in accordance with the earlier findings of [2, 19, 20], who reported non-significant changes in TLC values after the use of ketoprofen and meloxicam in similar surgical procedure in dogs during their various studies.

### **Conclusion**

It was concluded that diclofenac sodium administered through both intramuscular and per-rectal routes in dogs undergoing orchietomy has no deleterious effect in haematological parameters, therefore safe for use in Nigeria indigenous breed of dogs.



## REFERENCES

1. Adlin, C. A. (2011). Complications of ovariohysterectomy and orchiectomy in companion animals. *Veterinary Clinics of North America Small Animal Practice*, **41**, 1023–1039.
2. Fani, F. A., Mehesare, S. P., Pawshe, D. B., Khan, K. M., and Jadhav, D. (2008). Haematological and biochemical changes during epidural xylazine hydrochloride anaesthesia in dogs. *Veterinary World*, **1**(6), 175-177.
3. Lee, J., and Katayama, S. (1992). Nonsteroidal antiinflammatory drugs. Philadelphia.: WB Saunders Comp.
4. Ramesh, N., Honnegowda., N., Narayana, K., and Vijayasarathi, S. (2002). A study on toxicity of diclofenac in dogs. *Indian Veterinary Journal*, **79**, 4.
5. Oaks, J. L., Gilbert, M., Virani, M., Watson, R., Meteyer, C., Rideout, B., and Khan, A. A. (2004). Diclofenac Residues as the cause of vulture population decline in Pakistan, Letters to Nature. *Nature*, **427**, 4.
6. Mermelstein, F., Hamilton, D. A., Wright, C., Lacouture, P. G., and Ramaiya, A. (2013). Single-dose and multiple-dose pharmacokinetics and dose proportionality of intravenous and intramuscular HP $\beta$ CD-diclofenac (Dyloject) compared with other diclofenac formulations. *Pharmacotherapy*, **33**, 10.
7. Kaya, S., Bilgili, A., and Piriñçi, I. (2002). Nonsteroid antiinflammatuar drug, in *Pharmacology in Veterinary Medicine*, Ankara, Turkey.
8. Tras, B., and Elmas, M. (2012). Analgesic, antipyretic and anti-inflammatory drugs,” in *Veterinary Drug*, Konya, Turkey: Olgun-Celik Press.
9. Shultz, S. (2004). Diclofenac poisoning is widespread in declining vulture populations across the Indian subcontinent. Sorensen, E. and Acosta, D. Relative toxicities of several nonsteroidal anti-inflammatory in primary cultures of rat hepatocytes. *Journal of Toxicology and Environmental Health*, **16**, 16.
10. Ritter, J. K. (2000). Roles of glucuronidation and UDP glucuronosyl transferases in xenobiotic bio activation reactions. *Chemico-biological interactions*, **129**, 13.
11. Knights, K. M., Winner, L. K., Elliot, D. J., Bowalgaha, K., and Miners, J. O. (2009). Aldosterone glucuronidation by human liver and kidney microsomes and recombinant UDPglucuronosyltransferases: inhibition by NSAIDs. *British journal of clinical pharmacology*, **68**, 11.
12. Ajadi, T. A., and Oyeyemi, M. O. (2004). Comparison between Immunocastration and Surgical Castration in Dogs. *Proceedings of the Society of Theriogenology Annual Conference*.
13. Howe, L. M. (2015). Current Perspective on the Optimal Age to Spay/Castrate Dogs and Cats. *Dovepress*, **6**, 10.
14. Hedlund, C. S. (2007). *Surgery of the reproductive and genital systems*. (3rd ed.). St Louis: Mosby;.
15. Jain, N. (2000). *Schalm's Veterinary Haematology* (8th ed.). Philadelphia: Lea and Febiger.
16. Ihedioha, J. I., and Agina, O. A. (2013). Serum biochemistry profile of Nigerian horses (equus caballus, linnaeus 1758). *Animal Research International*, **10** (3), 1826-1833.
17. Fresno, L., Moll, J., Peñalba, B., Espada, Y., Andaluz, A., Prandi, D., and García, F. (2005). Effects of preoperative administration of meloxicam on whole blood platelet aggregation, buccal mucosal bleeding time, and haematological indices in dogs undergoing elective ovariohysterectomy. *The Veterinary Journal*, **170** (1), 138-140.
18. Akhtardanesh, B., Sharifi, H., Rasooli, R., and Aghazamani, M. (2014). Evaluation of haematological and biochemical changes

- after short term tramadol usage in healthy dogs. *Iranian Journal of Veterinary Medicine*, **8** (1), 41-45.
19. Fazio, E., Medica, P., Cravana, C., Pupillo, A., and Ferlazzo, A. (2015). Effects of ovariohysterectomy in dogs and cats on adrenocortical, haematological and behavioural parameters. *Acta Science Veterinarian*, **43**, 1339.
20. Ugwu, N., Eze, C., and Udegbonam, R. (2017). Evaluation of haematological and serum biochemical changes associated with constant rate infusion tramadol hydrochloride as an adjunct to ketoprofen in laparotomized and ovariohysterectomized dogs. *Comparative Clinical Pathology*, **26** (5), 1135-1140.
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