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Postoperative Analgesic Efficacy of Tramadol and Diclofenac Sodium in Goats

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ABSTRACT

Postoperative analgesic effects of tramadol and diclofenac in goats presented for diaphyseal femoral fracture management were compared. Eight adult goats aged 10 to 24 months (16 ± 5.2 months) were used. The first group of 4 goats received 3 mg/kg of tramadol intramuscularly (IM), and 2.5 mg/kg of diclofenac sodium was administered to the second group of 4 goats before induction of anesthesia IM. Mechanical pain scores, clinico-physiological and red and white blood cell counts were evaluated over a period of twelve hours post drug administration. The study groups were not revealed to the postoperative pain assessors until the end of the study. There was no significant difference in the rectal temperature values and the analgesiometer readings between the tramadol and diclofenac groups ($p < 0.05$). The variations in the pulse rate, respiratory rate, red and white blood cell counts between the groups fluctuated within the normal physiological limits. It was therefore concluded that preoperative intramuscular administration of tramadol at 3 mg/kg provided similar effective postoperative analgesia with diclofenac at 2.5 mg/kg IM following femoral diaphyseal fracture management in goats.

Keywords: Analgesia; Diclofenac; Fracture Goats; Tramadol

INTRODUCTION

Postsurgical pain is considered beneficial to animals because body activities are slowed thereby preventing more injury to the surgical site (Hellyer *et al.*, 2007). Recognition of pain in human is a subjective experience, but its nature in animals can be challenging since many animals have evolved to hide signs of illnesses and pain (Souza *et al.*, 2008). Hence, the perception of pain is thought to be minimal and insignificant, and consequently neglected in ruminants (Hellyer *et al.*, 2007). Improper management of post-operative pain can result to chronic pain, cardiorespiratory depression (Mastrocinque and Fantoni, 2003) and delayed wound healing (Lascelles *et al.*, 1999; Buvanendran *et al.*, 2003). In addition, pain following surgical procedure such as fracture reduction-fixation, suppresses the immune system of a patient and must be properly managed (Pollock *et al.*, 1991). Fractures involving femoral diaphysis are frequently reported in goats that are left to scavenge for food in the environment. This system of management predisposes them to automobile accident or being hurled with hard objects, resulting into fractures (Witmer, 2016). Therefore, preemptive analgesia to prevent central and peripheral sensitization caused by incisional and inflammatory injuries is essential for effective

postoperative pain management (Katz *et al.*, 1992; Kissin, 2000). Both opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) are the most frequently used drugs for the management of postoperative pain (Lee, 2011). Nonsteroidal anti-inflammatory drugs have been successfully used in veterinary practice for the management of postoperative pain.

Diclofenac sodium is among the frequently use NSAIDs in veterinary practice (Booth, 2001; Lascelles and Mair, 2001), its harmful side effects such as the gastrointestinal discomfort, cardiopulmonary depression (Elghazali *et al.*, 2008) and inhibition of antibody production (Bancos *et al.*, 2009) limits its use. Most opioid have been shown to be effective analgesics in the clinical setting in dogs (Waterman and Kalthum, 1989), albeit with a short duration of action. Opioids also produced a reversible behavioral (KuKanich *et al.*, 2008) and physiological (Wagner, 2002) side effects such as respiratory depression and constipation. Tramadol is an analgesic with a dual mechanism of action where it is found to bind to the μ_1 -opioid receptor (Kukanich and Papich, 2004; Guedes *et al.*, 2005) as well as inhibit the monaminergic pathway (McMillan *et al.*, 2008). Due to this reason, tramadol is also referred to as an "atypical opioid" (McMillan *et al.*, 2008). The aim of the study was to compare the postoperative analgesic effects of tramadol and diclofenac in goats following femoral fracture reduction-fixation.

MATERIALS AND METHODS

Eight client-owned goats undergoing femoral diaphyseal fracture reduction-fixation at the Veterinary Teaching Hospital of Usmanu Danfodiyo University Sokoto, Nigeria were used for the study after obtaining verbal consent. Ages of the goats ranged from 10 to 24 months with a (mean±SD) of 16±5.2 months. The body weight of the goats ranged from 12 kg to 17.5 kg with a (mean±SD) of 14.1±1.8 kg. All animals were clinically evaluated and were classified according to the American Society of Anesthesiologists scale (ASA 1 to 5). Only goats within ASA 1 to ASA 3 scales were included in the study (Ortega and Cruz, 2011). In addition, goats with open fracture were not included in the study. They were denied feed for 12 hours and water for 2 hours before the surgery. The goats were randomly divided into two groups of four animals each. Group I was treated with tramadol (Tramadol[®], Ozone Laboratories Group, Romania) at 3 mg/kg intramuscularly (IM) and group II received diclofenac sodium (Fitking Diclofena[®] inj, Jiangsu Huayang Pharmaceutical Co., Ltd. Siyang County Jiangsu, China) at 2.5 mg/kg IM before induction of anesthesia. A ketamine-xylazine combination (ketamine 5 mg/kg and xylazine 0.1mg/kg) was administered intravenously to achieve general anaesthesia, and normal saline (0.9% NaCl) (Braun Medical, Romania) was infused IV (10 mL/kg/h) throughout the surgical procedure. Pulse rate, respiratory rate and rectal temperature, red and white blood cell changes were the physiologic parameters used as indicators of acute pain (Buhari *et al.*, 2012; Tesfaye *et al.*, 2017). Above parameters were taken before drug administration (0 hr) and hourly for 12 hours post-fracture reduction. Similarly, mechanical pain threshold was evaluated using analgesimeter (PainTest[™] FPX 25 Algometer, Wagner Instruments, Greenwich, USA) for post-surgical analgesia (Reid *et al.*, 2007). The device has been described as a reliable measure of pain in muscle, joints, tendons, and ligaments for experimental use in animal and humans (Moak *et al.*, 2010; Buhagiar *et al.*, 2011). The FPX 25 acts as a mechanical stimulus by applying increasing pressure until a response is noted proves the benefits of applied medication (Haussler *et al.*, 2007). The analgesimeter FPX 25, used for pain threshold testing, is appropriate for determining the minimum pressure that triggers pain at the point of interest (Polianskis *et al.*, 2002). The device was applied at four different areas 2 cm away from the site of incision (cranially, caudally, proximally, and distally). Maximum reading was set at 15N to avoid trauma to the area. The assessment was conducted before drug administration (0 hr) and hourly for 12 hours post-fracture reduction.

Statistical Analyses

Data were recorded as mean ± SD. A Kolmogorov–Smirnov-test was performed to assess normality of the variables. The data were analyzed using repeated measure of ANOVA. Significant differences ($p < 0.05$) were further assessed by using Least Significant Difference (LSD) post hoc test (IBM SPSS software, ver. 16 for Windows; IBM, New York, USA). A P value < 0.05 was considered statistically significant.

RESULTS

There was no significant difference ($p < 0.05$) between the groups treated with tramadol and diclofenac with regard to the rectal temperature and the analgesimeter pain thresholds in goats (Figures 1 and 2).

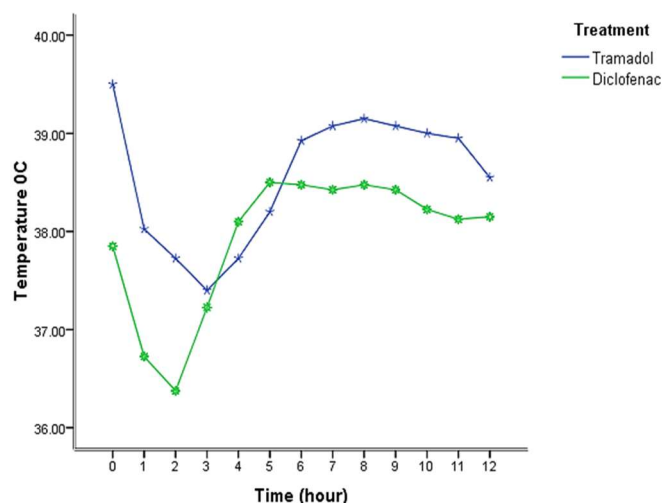


Figure 1: Comparison of rectal temperature reading (means ± SD) between goats receiving tramadol (3 mg/kg BW, IM) and goats receiving diclofenac sodium (2.5 mg/kg IM) preoperatively, $n = 4$ in each group. There was no significant difference between the groups at $p > 0.05$.

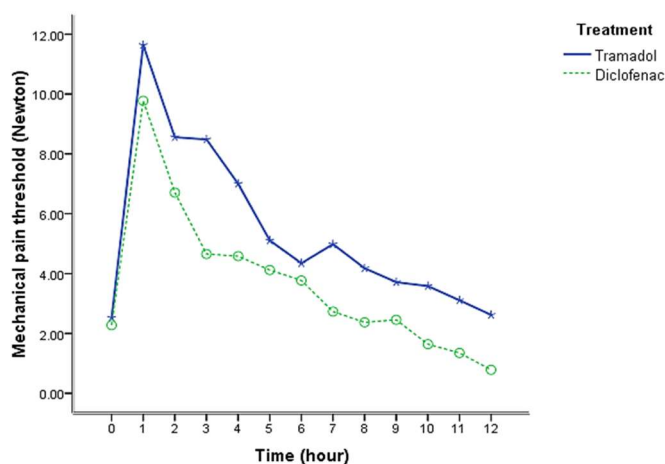


Figure 2: Comparison of analgesimeter pain threshold value (means ± SD) between goats receiving tramadol (3 mg/kg BW, IM) and the goats receiving diclofenac sodium (2.5 mg/kg IM) preoperatively, $n = 4$ in each group. There was no significant difference between groups at $p > 0.05$.

In addition, both groups treated with tramadol and diclofenac had a significant decrease in pain perception few hours post administration of the drugs. The differences in analgesimeter readings were widely variable in both groups over time. The tramadol and diclofenac sodium groups had an initial increase in the pain threshold of 12N and 11N at the first hour after surgery respectively ($p > 0.05$). Gradually, the threshold level decreases over the period of 12 hours (Figure 2). When their clinical and haematological parameters were evaluated, there were statistically significant

differences in the values of the pulse rates (Figure 3), respiratory rates (Figure 4), red blood cell (Figure 5) and white blood cell (Figure 6) counts between the groups.

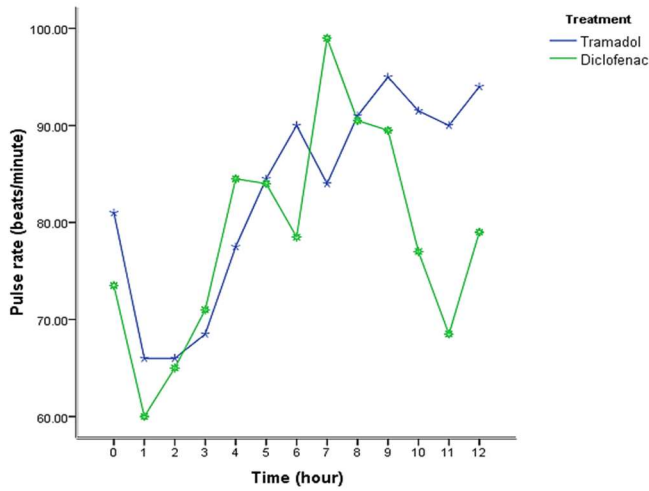


Figure 3: Comparison of pulse rates value (means \pm SD) between goats receiving tramadol (3 mg/kg BW, IM) and goats receiving diclofenac sodium (2.5 mg/kg IM) preoperatively, n = 4 in each group. There were significant differences between the groups at 6th, 7th, 9th, 10th, 11th and 12th hours post drug administration ($p < 0.05$).

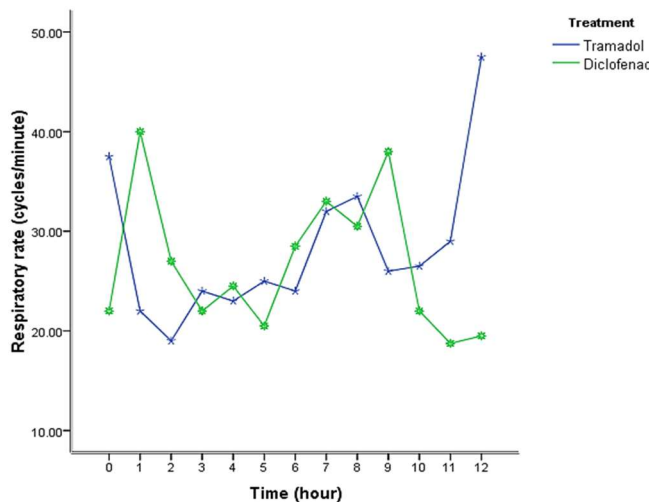


Figure 4: Comparison of respiratory rate values (means \pm SD) between goats receiving tramadol (3 mg/kg BW, IM) and goats receiving diclofenac sodium (2.5 mg/kg IM) preoperatively, n = 4 in each group. There were significant differences between the groups at first two hours and at 9th, 11th and 12th hours post drug administration ($p < 0.05$).

DISCUSSION

Over three decades, the veterinary profession has witnessed a significant revolution in analgesic administration. Currently, several choices in different drugs for postoperative pain management are made available (Bateman *et al.*, 2008). For a better and practical choice of analgesic drug, randomized blinded evaluation to compare different analgesic agents is essential. In general, NSAIDs are considered suitable analgesics for postoperative pain management in small animals, alone or in combination with opioids (Morgaz *et al.*, 2013). Diclofenac provided a smooth and good analgesic effect during this study. Abu-Seida

(2012) reported an excellent analgesic effect using diclofenac in dogs undergoing ovariohysterectomy. Diclofenac was used to treat experimentally produced myositis in goats (Aktaruzzaman *et al.*, 2008) and its significant effect on blood cell count subsided 72 hours post drug administration (Ahmad *et al.*, 2013).

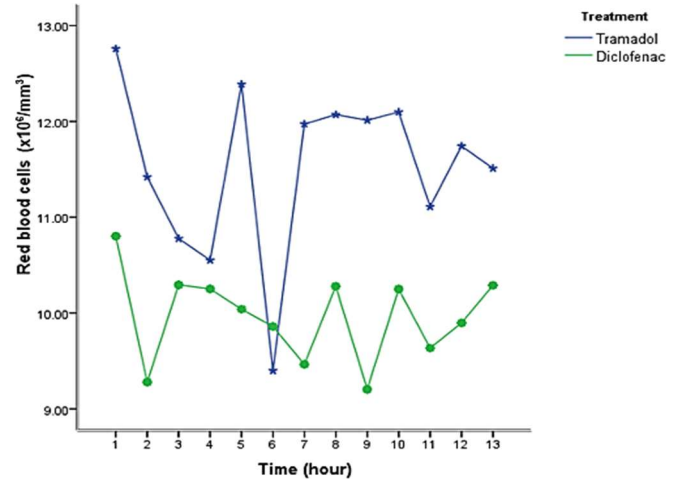


Figure 5: Comparison of red blood cell counts (means \pm SD) between goats receiving tramadol (3 mg/kg BW, IM) and goats receiving diclofenac sodium (2.5 mg/kg IM) preoperatively, n = 4 in each group. The red blood cell counts significantly differ between the groups except at the 5th hour post drug administration ($p < 0.05$).

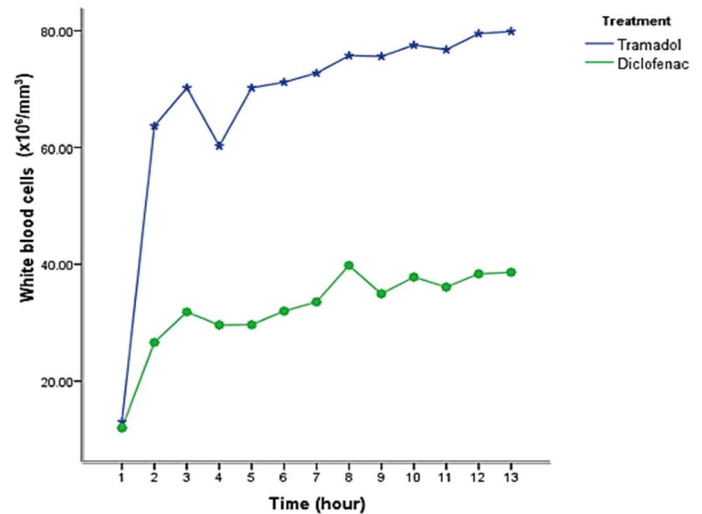


Figure 6: Comparison of white blood cell counts (means \pm SD) between goats receiving tramadol (3 mg/kg BW, IM) and goats receiving diclofenac sodium (2.5 mg/kg IM) preoperatively, n = 4 in each group. There was significant increase in the white blood cell counts in the group treated with tramadol ($p < 0.05$).

Physiologic indicators of acute pain in animals include increased heart rate, increased blood pressure, peripheral vasoconstriction and cardiac dysrhythmias (Buhari *et al.*, 2012). In this study, other than the slight increase in pulse and respiratory rates observed among the goats treated with tramadol from eight hours after the drug administration pulse rates, respiratory rates, and rectal temperatures did not vary significantly between the groups. Similar observations were made following epidural administration of tramadol in dogs

undergoing stifle surgery (Guedes *et al.*, 2005). In horses that received epidural tramadol, good analgesia was achieved without significantly influencing the horses' behavioral and physiological parameters (Natalini and Robinson, 2000). Increase in the rectal temperature has been used as an indicator for postsurgical pain (Sanford *et al.*, 2006; Landa 2012) due to the stimulation of autonomic sympathetic system trigger the releases of adrenaline elevates body temperature (Koknaroglu and Akunal, 2013). Okafor *et al.* (2014) reported the decreasing effect of NSAIDs on rectal temperature. They inhibit neurotransmitter that mitigates the release of adrenocorticotrophic hormone from the hypothalamic pituitary system (Karanth *et al.*, 2000). The slight increase in these two parameters could be due to shorter half-life of tramadol compared to that of diclofenac (Brogden, *et al.*, 1980; McMillan *et al.*, 2008), hence tramadol may be administered every 12 hours (Lamont and Mathews, 2007) at dose rate of 4 mg/kg in goats (de Sousa *et al.*, 2008).

Increase in the number of white blood cells (WBC) observed in this study after tramadol administration was in agreement with what was reported earlier in rats (Aldiwan *et al.*, 2015). A decrease in WBC was also published in the rabbit after tramadol administration (Aldiwan *et al.*, 2015). Acute blood loss and surgical stress cause changes in both red and white blood cell counts (Hong, 2005). However, the variation in values of red blood cells and white blood cells between the groups fluctuated within the normal physiological limits and, therefore, has no clinical significance as far as the effects of the tramadol and diclofenac were concerned. Similar findings were also reported with epidural bupivacaine in goats and buffaloes (Singh *et al.*, 2007; Singh, 1999). Bupivacaine share similar mechanism of action with lignocaine albeit the longer duration of effect over lignocaine, but both of them offered similar analgesic effect (Devi and Singh 2018). Similarly, in the present study, both groups treated with diclofenac and tramadol had an effective postoperative analgesia. The mechanical pain threshold values suggested a more uniform analgesia to painful stimuli. The pain score did not significantly differ between the tramadol and diclofenac groups at any time (figure 2). Therefore, analgesic effects of the drugs are likely to be present for at least 10 hours after administration; tramadol and diclofenac have variable half-life of 3-6 hours and 10–24 hours respectively (Brogden, *et al.*, 1980; McMillan *et al.*, 2008). In another study by Brondani *et al.* (2009), tramadol provided similar analgesic effect with NSAIDs in cats undergoing ovariohysterectomy. These therefore, suggested comparable postoperative analgesia from both drugs.

Conclusion

Based on the study design, the data suggest that pre-treatment with tramadol (3 mg/kg IM) provided similar adequate postoperative analgesia as with diclofenac sodium (2.5 mg/kg IM) following femoral diaphyseal fracture reduction-fixation in goats. Further studies, however, will be needed for more detailed information on the quality of analgesia of both drugs in goats.

Conflict of Interest

The authors declare that they do not have any conflict of interest.

Author's Contribution

BS designed the research and supervised the project, AJ, BZM and AS were involved in blood sample collection and parameter evaluation, AN and BHA, served as assistant surgeons and anaesthesiologist, respectively; SMI participated in the statistical analysis, literature and manuscript review.

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