

SOME HAEMATOLOGICAL CHANGES ASSOCIATED WITH CONSTANT RATE INFUSION OF KETOPROFEN AND KETOPROFEN-TRAMADOL COMBINATION IN DOGS UNDERGOING LAPAROTOMY

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Abstract

This study evaluated the effects of constant rate infusion (CRI) of ketoprofen and ketoprofen-tramadol combination on hematology of dogs undergoing laparotomy. Nine female Nigerian mongrels were randomly assigned to three groups of 3 dogs each. The groupings and their specific treatments were: group 1 – treated with normal saline placebo; group 2 – treated with 1.0mg/kg/hr ketoprofen and group 3 – treated with a combination of tramadol and ketoprofen at 0.5mg/kg/hr each. The dogs were all anaesthetized with 25mg/kg ketamine hydrochloride after premedication with 2.0mg/kg xylazine hydrochloride, and given their specific treatments as stated above. Ventral midline laparotomy was performed on all the dogs. A dose of 4mg/kg ketoprofen was given subcutaneously for 3 days post-surgery (Ps) to all the groups. Parameters assessed include packed cell volume (PCV), hemoglobin concentration (Hb) and total white blood cell count (TWBC). These parameters were assayed on days 1, 3 and 7 post-surgery (Ps) following standard procedures. Results showed that the mean PCV and Hb did not differ significantly ($p > 0.05$) between all the dog groups all through the seven days Ps. However, dogs in groups 2 and 3 had significantly higher ($p < 0.05$) TWBC than the group 1 dogs (control) on Ps day 1, but the TWBC of the all groups did not significantly vary on Ps days 3 and 7. It was concluded that CRI of ketoprofen and ketoprofen-tramadol combination led to no significant short-term negative effects on the PCV, Hb and TWBC of dogs undergoing laparotomy.

Key words: constant rate infusion, dogs, haematology, ketoprofen, tramadol.

Introduction

Pain is an unpleasant sensory or emotional experience most commonly associated with actual or potential tissue damage (Hellyer et al., 2007). Unrelieved pain is associated with numerous side effects; therefore, its containment is important for the functionality of a patient. Drugs presently used for the management of pain and inflammatory conditions include the opioids, non-steroidal anti-inflammatory drugs, steroidal anti-inflammatory drugs and local anaesthetics (Eze et al., 2004; Hansen, 2005). The side effects associated with the use of single analgesics have resulted in the combined use of two or more types of analgesics, termed multimodal analgesics.

Ketoprofen is a non-steroidal anti-inflammatory drug used to relieve short-term post-operative pain, inflammation, and swelling after spaying, neutering, and other procedures (Fox and Johnston, 1997) while tramadol is a centrally acting opioid analgesic used to treat postoperative and chronic pain in humans and animals (Wagner et al., 2002).

Changes in haematological parameters had been used as indicators of cellular damage, as the blood is the major transporter of substances in the body (Schalm et al., 1975; Ihedioha, 2004). There is no information in available literature on the effects of constant rate infusion (CRI) of ketoprofen and ketoprofen-tramadol combination on the

haematology of dogs undergoing laparotomy, hence the study. The objective of this present study was therefore to evaluate some of the hematological changes associated with constant rate infusion of ketoprofen and ketoprofen-tramadol combination in dogs undergoing laparotomy.

Materials and Methods

Nine female Nigerian mongrels were used for the study. They were randomly assigned to three groups of 3 dogs each. The groupings and their specific treatments were: group 1-treated with normal saline placebo; group 2 – treated with 1.0mg/kg/hr ketoprofen and group 3 – treated with a combination of tramadol and ketoprofen at 0.5mg/kg/hr each. The dogs were all anaesthetized with 25mg/kg ketamine hydrochloride after premedication with 2.0mg/kg xylazine hydrochloride, and given their specific treatments as stated above. Dogs in group 2 received a loading dose of 5mg/kg ketoprofen while group 3 dogs received 2.5mg/kg each of ketoprofen and tramadol before the infusions. Infusions were administered from 30 minutes before surgery till 45 minutes post surgery. Ventral midline laparotomy was performed on all the dogs. Ketoprofen (4 mg/kg) was given subcutaneously for 3 days post-surgery (Ps) to dogs in all the groups.

Haematological parameters evaluated include packed cell volume (PCV), hemoglobin concentration (Hb) and total white blood cell count (TWBC). The PCV was determined by the microhaematocrit method while TWBC was done following the haemocytometer method (Schalm et al., 1975). The Hb concentration was determined by the cyanomethaemoglobin method (Kachmar, 1970). These parameters were assayed on days 1, 3 and 7 post-surgery (Ps).

Data collected were subjected to one way analysis of variance (ANOVA) using SPSS statistical package version 16. The least significant difference method was used to separate the means at post hoc. Probability values of less than 0.05 were considered significant.

Results and Discussion

There were no significant variations ($p > 0.05$) between the mean PCV and Hb of all the dog groups all through the 7 days of evaluation (Tables 1 and 2). However, on day 1 post-surgery, the TWBC of dogs in groups 2 and 3 were significantly ($p < 0.05$) higher than that of the group 1 dogs (normal saline placebo control), while on days 3 and 7 post-surgery there were no significant ($p > 0.05$) variations between the groups in their TWBC counts (Table 3).

The finding in this present study that treatment with ketoprofen alone and ketoprofen + tramadol combination did not lead to any significant effect on PCV and Hb is in agreement with the reports of Singh et al. (2009) and Paresh et al. (2012) who investigated the haematological effects of short-term repeated administration of ketoprofen alone intravenously in calves, and that of Akhtardanesh et al. (2014) who evaluated the effects of short term administration of tramadol alone on haematology of dogs. It is therefore noteworthy in this study that a combination of both drugs did not significantly affect PCV and Hb. The significantly higher TWBC counts recorded in both groups 2 and 3 at post-surgery day 1 in this present study is however in contrast with earlier reports by Singh et al. (2009) and Paresh et al. (2012), but it is in agreement with the reports of Tsai & Won (2001) and Mohammed et al (2014) on rats given tramadol. It is thought that the significantly higher TWBC recorded in this present study on day 1 post-surgery may be part of the normal leukocytic defensive reaction to introduction of foreign chemical agents (Coles, 1986; Ihedioha, 2004), since it gradually reverted to not being significantly different from the control on days 3 and 7 post-

surgery.

Conclusion

Based on the results of the study, it was concluded that administration of ketoprofen and ketoprofen + tramadol combination as used in dogs did not lead to any significant effects on their PCV and Hb all through the 7 days of evaluation post-surgery, but there was an immediate significant elevation of the TWBC count on day 1 post-surgery in the dog groups given ketoprofen and ketoprofen + tramadol combination which reverted to normal on days 3 and 7 post-surgery.

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Table 1: The packed cell volume of dog groups given constant rate infusion of ketoprofen alone and ketoprofen-tramadol combination compared with an untreated (normal saline placebo) control.

Post-surgery time (days)	Group 1 (normal saline placebo)	Group 2 (ketoprofen only)	Group 3 (ketoprofen + tramadol)
Day 0 (baseline)	31.33±2.23	28.00±2.31	32.00±1.53
Day 1	28.68±2.59	32.00±1.16	33.68±6.36
Day 3	26.00±1.59	32.68±2.33	27.33±4.06
Day 7	31.33±1.73	30.68±3.28	28.33±2.03

No significant variations between the means of the groups ($p > 0.05$)

Table 2: The haemoglobin concentration (Hb) of dog groups given constant rate infusion of ketoprofen alone and ketoprofen-tramadol combination compared with an untreated (normal saline placebo) control.

Post-surgery time (days)	Group 1 (normal saline placebo)	Group 2 (ketoprofen only)	Group 3 (ketoprofen + tramadol)
Day 0 (baseline)	12.51±0.78	10.33±0.49	10.67±0.29
Day 1	12.09±0.38	10.67±2.14	11.90±1.11
Day 3	11.83±0.80	10.90±1.33	09.87 ±1.49
Day 7	12.81±1.07	11.23±0.90	10.23±3.75

No significant variations between the means of the groups ($p > 0.05$)

Table 3: The total white blood cell count (TWBC) of dog groups given constant rate infusion of ketoprofen alone and ketoprofen-tramadol combination compared with an untreated (normal saline placebo) control.

Post-surgery time (days)	Group 1 (normal saline placebo)	Group 2 (ketoprofen only)	Group 3 (ketoprofen + tramadol)
Day 0 (baseline)	12.17±2.23	14.20±0.35	13.83±6.00
Day 1	15.68±2.32 ^a	28.03±5.44 ^b	44.00±3.69 ^c
Day 3	12.03±1.44	15.67±4.99	21.27±9.14
Day 7	10.52±1.60	14.18±1.75	12.53±3.64

^{abc} Different alphabetical superscripts in a row indicate significant difference between the means of the groups ($p < 0.05$).