Journal of Animal and Veterinary Advances 10 (7): 922-927, 2011
ISSN: 1680-5593

Postoperative Analgesic Effects of Carprofen Following Osteotomy and Laparotomy in Dogs

Muharrem Erol and Celal Izci
Department of Surgery, Faculty of Veterinary Medicine,
University of Selcuk, 42079 Kampus, Konya, Turkey

Abstract: This study investigated the effects of postoperative pain following soft and hard tissue operations in dogs on Adrenocorticotrophic Hormone (ACTH) levels, dopamine levels, haemocoel values and blood gases. It also evaluated the results of the applied treatments. The study was carried out in 4 groups each comprising 6 dogs. Dogs in the 1st and 3rd groups underwent laparotomy and those in the 2nd and 4th groups underwent osteotomy. Carprofen (4.4 mg kg^{-1}) (Rimadyl, Pfizer) was administered subcutaneously as an analgesic to the dogs in the 1st and 2nd groups following the operation. Venous blood samples were collected from the animals before the operation and in the subsequent hours to determine the ACTH and dopamine levels. In the postoperative period, ACTH and dopamine levels were significantly higher in the groups that underwent osteotomy than in the groups that underwent laparotomy ($p<0.05$). Statistically significant decreases were observed in the groups that received analgesia after the 2nd h ($p<0.05$). In this study, effective postoperative analgesia is required after both soft and hard tissue operations. Furthermore, effective and rapid implementation of the process is important for postoperative animal welfare and rapid return to normal physiological functions.

Key words: Postoperative pain, carprofen, osteotomy, laparotomy, dogs, venous

INTRODUCTION

The International association for the study of pain defines pain as an unpleasant sensory and emotional experience associated with real or potential tissue damage (Horstman *et al*., 2004; Johnson *et al*., 1993). Pain causes suffering and contributes to complications such as increased stress response, prolonged recovery and increased morbidity. Many metabolic alterations are known to occur as a result of pain.

The most important changes are the increasing levels of the stress hormones noradrenaline, adrenaline, cortisol and Adrenocorticotrophic Hormone (ACTH). All animals undergoing surgical procedures require pain relief after surgery to overcome the deleterious physiological effects of postoperative pain and to address humane and ethical concerns (Lascelles *et al*., 1994).

There are many different methods and drugs available for postoperative analgesia; Non-steroidal Anti-Inflammatory Drugs (NSAIDs) are clinically the most widely used. The analgesic effect of NSAIDs is lower than that of narcotic analgesics. However, they are preferred because they do not lead to drug addiction or have an anaesthetic effect on their application. Their indirect analgesic effects are caused by their direct antiinflammatory effects around the region of tissue damage. NSAIDs are estimated to reduce or eliminate inflammation or to hinder the local sensitivity of nerve endings (Dahl and Kehlet, 1991; Lobetti and Joubert, 2000; Schecter *et al*., 2002). In addition, these drugs have significant central analgesic effects. The analgesic effects of NSAIDs are attributed to their inhibition of cyclooxygenase enzymes which catalyse the formation of prostaglandins and some other prostanoids (thromboxane and prostacyclin) from arachidonic acid (Deneuche *et al*., 2004; Dzikiti *et al*., 2006; Martin *et al*., 2006; Zhu *et al*., 2003). Carprofen is an NSAID of the carbazole group and is a propionic acid derivative. It is especially highly effective in controlling the pain caused by degenerative joint diseases and is also quite effective in eliminating postoperative soft tissue and orthopaedic pain (Fox and Johnston, 1997; Grisneaux *et al*., 2003; Laredo *et al*., 2004; Slingsby *et al*., 2006).

This study aimed to determine, the effects of carprofen used in soft and hard tissue operations on serum ACTH levels, dopamine levels, haemocoel values and blood gases.

Corresponding Author: Muharrem Erol, Department of Surgery, Faculty of Veterinary Medicine, University of Selcuk, 42079 Kampus, Konya, Turkey

MATERIALS AND METHODS

The study included 24 healthy dogs aged 1-7 years. This study was approved by the ethical board of the faculty of Veterinary Medicine of the University of Selcuk, Konya, Turkey (Approval no. 2004/9). About 4 groups, each comprising 6 dogs were included in the study. About 2 groups (G1 and G3) were subjected to laparotomy while osteotomy was performed in the other 2 groups (G2 and G4).

Induction was performed for animals in all groups through intravenous administration of 20 mg kg^{-1} of 5% sodium pentothal (Abbot laboratories). Animals were intubated following the induction. Anaesthesia was continued with 2% isoflurane. Animals to receive laparotomy were fixed on the operation table in the lateral supine position and a median line of 10 cm was established.

Medial laparotomy was performed through this region. Animals to undergo osteotomy were laid down with the right foreleg raised. The os radius of the left foreleg was accessed by creating a longitudinal skin incision of 5-7 cm in the medial antebrachium at the level of the spatium interosseum antebrachii. The radius was incised with a 2 mm Gigli wire inserted through this gap.

The incision was constantly wetted with physiologic serum (0.9% NaCl) to prevent demolition by heat created by the friction between the Gigli wire and bone. Following the incision process, the os radius was left in its present position. The operation wound was appropriately closed as for routine procedures and a support bandage was applied to the limbs.

When the animals in G1 and G2 came out of anaesthesia, 4.4 mg kg^{-1} of carprofen (Rimadyl, Pfizer) was used as an analgesic at the same time on each of the following 4 days. For the dogs in other 2 control groups (G3 and G4), 0.9% physiologic serum in an amount equal to that of carprofen and corresponding to live weight was injected subcutaneously at the same times as was carprofen.

Animals given carprofen were clinically followed up during the treatment in terms of side effects. Venous blood samples were collected from all animals for the measurement of stress hormones before and after the operation upon awakening from anaesthesia and at the subsequent 1st, 2nd, 4th, 6th, 8th, 24th, 48th, 72nd, 96th, 120th, 144th and 168th h. The blood samples were then placed into tubes with K^{3+} EDTA and the plasma contents were extracted. Concentrated plasma samples were stored in Eppendorf tubes in a refrigerator at -20°C. Plasma dopamine concentrations were determined by a High-performance Liquid Chromatography (HPLC) system (Chromsystems, Gilson, Inc., Germany) and plasma ACTH concentrations were determined by Enzyme-linked Immunosorbent Assay (ELISA, ELx800 and ELx50; BioTek, Germany). Blood gas (GEM Premier PAK) and haemocell (Medonic CA 530 Thor) values of the collected blood samples were also determined.

Statistical analysis: Minitab release 12.1 packet software was used for statistical analysis of the data obtained in the study. The Wilcoxon t test was used for inter-group differences based on median values while the Kruskal-Wallis and Mann-Whitney U tests were employed for intra-group differences.

RESULTS AND DISCUSSION

Statistically significant increases in the inter-group dopamine plasma concentrations were detected in G2 at the 1st and 2nd postoperative hours ($p<0.05$). Increases were observed in G4 at the 2nd, 4th, 6th and 8th h (Table 1).The dopamine levels were higher in G2 at the 1st and 2nd postoperative hours while they were higher in G3 and G4 following the 4th h (Fig. 1). Statistically significant increases were observed in inter-group plasma ACTH levels ($p<0.05$).

These increases lasted in G1 and G2 until the 1st and 2nd postoperative hours while they continued in G3 and G4 until the 8th h (Table 2). After the 2nd h, intra-group plasma ACTH values were lower in G1 and G2 than in G3 and G4 (Fig. 2). Statistically significant decreases were detected in the PCO_2 values of all groups at the 1st postoperative hour ($p<0.05$). No statistically significant differences were detected between the groups (Table 3). Postoperative increases were observed in the PO_2 values of all groups. These increases lasted until the 2nd

Table 1: Mean values of plasma dopamine levels in different groups (mean±standard deviation) (pg mL^{-1}) (n = 6)

Time (h)	G1	G2	G3	G4
BO	35.25±4.49^{c}	35.20±12.78^{b}	23.75±3.30^{d}	29.40±6.41^{c}*
AO	36.15±3.54^{bc}*	35.45±10.55^{b}*	23.35±1.79^{d}	30.55±4.84^{c}*
1	35.50±3.95^{c}*	54.90±9.89^{a}*	27.70±2.18^{c}*	31.35±5.48^{c}*
2	37.00±5.45^{b}*	52.65±10.78^{a}*	34.00±2.91^{b}*	39.55±8.36^{a}*
4	39.40±4.54^{a}*	33.65±15.80^{b}	35.40±2.28^{b}*	37.70±3.00^{ab}*
6	39.45±4.15^{a}*	31.85±11.52^{c}	40.20±4.23^{a}*	39.60±10.23^{a}*
8	37.50±8.48^{b}*	36.15±12.85^{b}	41.10±5.71^{a}*	36.65±6.04^{b}*
24	34.15±5.54^{c}	27.20±11.61^{d}*	30.70±8.67^{bc}*	32.35±7.40^{c}*
48	33.45±3.15^{c}	27.10±18.74^{d}*	22.20±7.19^{d}	28.70±5.45^{c}*
72	32.35±7.95^{cd}	26.00±8.97^{d}*	22.50±5.84^{d}	27.70±9.50^{c}*
96	32.40±3.25^{cd}	33.00±7.05^{c}*	22.40±2.58^{d}	22.40±2.58^{d}*
120	31.70±4.54^{d}	35.30±8.03^{b}*	23.05±3.37^{d}	23.05±3.37^{d}*
144	33.65±3.53^{cd}	33.50±7.42^{c}*	22.10±3.13^{d}	22.10±3.13^{d}*
168	31.05±3.55^{d}	33.30±8.76^{c}*	21.45±1.37^{d}	21.45±1.37^{d}*

$^{a-d}$The difference between mean values in a column with different superscripts is statistically significant ($p<0.05$). BO: Before the Operation; AO: After the Operation

Table 2: Mean values of plasma ACTH levels in different groups (mean±standard deviation) (pg mL^{-1}) (n = 6)

Time (h)	G1	G2	G3	G4
BO	35.10±1.44^{b}	35.20±1.45^{c}	35.90±1.52^{c}	35.55±1.44^{d}
AO	39.45±1.28^{b}	39.35±1.09^{c}	39.65±1.82^{c}	39.80±1.31^{d}
1	45.60±1.46^{a**}	47.10±1.41^{a**}	45.80±1.99^{b**}	47.35±1.83^{b**}
2	42.65±1.90^{a**}	42.65±3.17^{b**}	48.95±2.45^{ab**}	51.10±2.24^{a**}
4	35.50±1.37^{b}	37.05±1.98^{c}	49.10±2.70^{a**}	46.85±3.41^{b**}
6	34.50±0.75^{b}	35.20±1.70^{c}	51.30±1.72^{a**}	49.85±1.68^{a**}
8	34.65±1.03^{b}	37.05±0.63^{c}	50.80±2.17^{a**}	51.00±3.39^{a**}
24	35.45±1.06^{b}	36.50±0.52^{c}	36.00±1.43^{c}	39.70±2.60^{c**}
48	34.50±1.54^{b}	36.55±1.34^{c}	34.40±1.55^{c}	35.35±1.82^{d}
72	35.30±1.38^{b}	34.45±2.39^{c}	35.35±0.98^{c}	36.05±079^{d}
96	36.75±1.37^{b}	35.30±0.83^{c}	35.85±1.25^{c}	35.40±1.45^{d}
120	36.55±3.03^{b}	35.50±1.29^{c}	35.90±1.58^{c}	35.15±1.00^{d}
144	35.00±0.56^{b}	33.45±1.01^{c}	34.85±1.62^{c}	35.90±1.53^{d}
168	36.35±1.31^{b}	36.35±1.75^{c}	34.10±0.72^{c}	34.50±1.15^{d}

$^{a-d}$The difference between mean values in a column with different superscripts is statistically significant ($p<0.05$). BO: Before the Operation; AO: After the Operation

Table 3: Mean values of blood PCO_2 levels in different groups (mean±standard deviation) (mm Hg) (n = 6)

Time (h)	G1	G2	G3	G4
BO	30.20±4.83^{a}	31.35±5.72^{a}	33.70±1.57^{a}	35.85±6.21^{a}
AO	33.75±6.92^{a}	34.70±4.79^{a}	33.60±5.54^{a}	36.60±5.78^{a}
1	27.05±3.80^{b**}	28.90±1.89^{b**}	29.00±4.54^{b**}	32.00±1.49^{b**}
2	29.65±5.66^{a}	27.40±3.58^{b**}	26.55±6.30^{c**}	29.20±4.07^{bc**}
4	31.64±3.57^{a}	29.70±4.04^{a**}	30.45±2.85^{b**}	27.80±3.50^{c**}
6	29.65±3.19^{a}	29.15±1.17^{a**}	31.45±2.64^{ab**}	30.70±5.92^{b**}
8	29.60±4.49^{a}	29.25±4.28^{a**}	31.50±4.11^{ab}	34.30±3.28^{a}
24	34.60±5.46^{a}	31.30±2.37^{a}	33.90±1.42^{a}	34.75±1.23^{a}
48	33.25±3.00^{a}	29.95±4.56^{a}	34.20±2.61^{a}	35.05±3.40^{a}
72	32.20±2.16^{a}	34.10±1.67^{a}	34.95±3.14^{a}	36.45±5.15^{a}
96	34.35±1.08^{a}	31.30±2.37^{a}	34.00±1.47^{a}	34.75±4.68^{a}
120	29.95±4.06^{a}	29.95±4.56^{a}	34.50±1.94^{a}	33.05±2.92^{a}
144	32.25±5.14^{a}	34.15±1.67^{a}	35.15±3.18^{a}	34.60±15.6^{a}
168	30.75±4.68^{a}	34.25±1.87^{a}	34.90±3.42^{a}	36.25±5.14^{a}

$^{a-c}$The difference between mean values in a column with different superscripts is statistically significant ($p<0.05$). BO: Before the Operation; AO: After the Operation

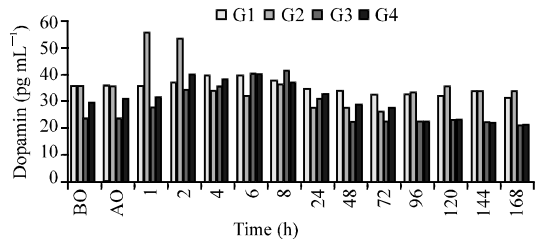

Fig. 1: Hourly changes in intra-group dopamine plasma concentrations

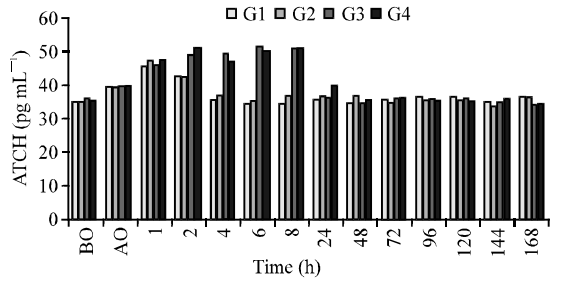

Fig. 2: Hourly changes in intra-group ACTH plasma concentrations

Table 4: Mean values of blood PO_2 levels in different groups (mean±standard deviation) (mm Hg) (n = 6)

Time (h)	G1	G2	G3	G4
BO	42.90±8.080^{b}	48.50±18.40^{b}	39.30±6.170^{b}	44.00±5.690^{c}
AO	41.15±7.310^{b}	45.00±13.34^{b}	41.55±17.78^{b}	44.50±23.86^{c}
1	45.80±5.460^{a*}	62.35±4.010^{a*}	53.10±15.53^{a*}	54.90±15.88^{a*}
2	46.25±11.42^{a*}	54.00±13.33^{a*}	53.25±8.160^{a*}	58.40±22.67^{a*}
4	43.05±6.080^{ab}	47.90±10.63^{b}	50.75±17.09^{a*}	58.90±6.980^{a*}
6	42.30±7.510^{b}	45.95±18.28^{b}	40.60±7.690^{b}	47.10±7.160^{b*}
8	37.20±14.52^{b}	45.00±23.83^{b}	41.00±6.630^{b}	45.00±19.65^{c}
24	38.60±13.97^{b}	44.60±15.73^{b}	37.90±5.000^{b}	45.70±4.190^{c}
48	39.35±8.560^{b}	47.50±6.870^{b}	41.35±10.77^{b}	45.60±5.160^{c}
72	39.45±5.700^{b}	50.25±11.71^{b}	40.55±6.840^{b}	43.95±12.33^{c}
96	38.70±3.950^{b}	44.60±15.67^{b}	38.80±5.030^{b}	45.80±3.250^{c}
120	41.90±7.800^{b}	46.90±6.900^{b}	41.30±11.03^{b}	41.60±3.120^{c}
144	39.55±10.84^{b}	50.40±11.99^{b}	40.65±6.660^{b}	44.90±6.450^{c}
168	39.80±3.250^{b}	50.70±11.60^{b}	40.50±6.480^{b}	41.55±10.84^{c}

Table 5: Mean WBC counts in different groups (mean±standard deviation) (10^3 mm^{-3}) (n = 6)

Time (h)	G1	G2	G3	G4
BO	11.85±3.09^{b}	9.95±0.90^{c}	9.15±2.00^{b}	8.60±2.05^{c}
AO	9.20±2.32^{b}	8.90±1.00^{c}	9.95±2.30^{b}	8.95±1.43^{c}
1	9.80±1.83^{b}	10.00±0.46^{c}	10.30±1.55^{b}	9.00±1.17^{c}
2	11.00±2.67^{b}	11.10±1.17^{c}	11.95±1.30^{b}	11.10±2.29^{b*}
4	11.60±2.83^{b}	12.70±1.55^{c}	14.20±3.45^{a*}	13.75±1.14^{a*}
6	14.20±3.70^{a*}	14.55±2.41^{a*}	14.20±2.06^{a*}	14.55±3.88^{a*}
8	14.10±4.27^{a*}	12.20±2.62^{c}	12.15±3.99^{a*}	12.20±6.28^{ab*}
24	12.15±1.44^{b}	12.80±2.15^{c}	11.45±3.65^{ab}	10.75±1.71^{b*}
48	12.90±5.19^{b}	10.60±0.75^{c}	11.85±3.64^{ab}	10.10±3.10^{bc}
72	12.35±4.23^{b}	10.30±1.10^{c}	10.60±2.43^{b}	10.05±2.43^{bc}
96	11.15±2.41^{b}	10.80±2.24^{c}	11.55±3.64^{ab}	9.85±1.80^{c}
120	10.75±0.59^{b}	10.75±0.73^{c}	10.95±1.82^{b}	9.55±1.25^{c}
144	9.95±1.98^{b}	10.40±1.10^{c}	9.90±2.27^{b}	9.45±1.76^{c}
168	10.55±1.80^{b}	9.30±0.82^{c}	9.55±3.64^{b}	7.95±1.98^{c}

$^{a-c}$The difference between mean values in a column with different superscripts is statistically significant ($p<0.05$). BO: Before the Operation; AO: After the Operation

postoperative hour in G1 and G2 while they continued until the 6th h in G3 and G4. No statistically significant differences were detected between the PO_2 values of the groups (Table 4). Statistically significant increases in WBC values were detected at the 6th and 8th postoperative hours in G1 and at the 6th h in G2 ($p<0.05$). Statistically significant increases were detected at the 4th, 6th and 8th h in G3 and at the 2nd, 4th, 6th, 8th and 24th h in G2 ($p<0.05$) (Table 5).

Postoperative pain is inevitable after operations. Many anaesthetic drugs do not have analgesic effects or the period of effectiveness is rather short. Therefore, a suitable selection of analgesic drugs for the postoperative period is highly important for animal welfare. Many metabolic alterations are known to occur as a result of pain. The most important changes are increasing levels of the stress hormones noradrenaline, adrenaline, cortisol and ACTH. Increasing levels of these hormones is the first defense mechanism of the body. Long-term and intensive release of these hormones delay the wound-healing period and cause certain undesired situations such as deterioration of the immune system

(Jezova *et al*., 1996; Lariviere and Melzack, 2000; Mastrocinque and Fantoni, 2003; Short, 1998). Many drugs and methods are currently used for the treatment of postoperative pain. The analgesic effects of NSAIDs are attributed to their cyclooxygenase inhibition. Cyclooxygenase enzymes have 2 isoforms: COX-1 and COX-2. COX-1 is responsible for many physiologic events including the regulation of renal blood flow and gastric mucus production. On the other hand, COX-2 is involved in the production of prostaglandins and prostanoids in damaged or inflamed tissues (Lafuente *et al*., 2005). Carprofen is an NSAID of the carbazole group and is a propionic acid derivative. It is especially effective in controlling the pain caused by degenerative joint disease and is also quite effective in eliminating postoperative soft tissue and orthopaedic pain (Nolan and Reid, 1993). The COX-2 selectivity of carprofen is higher than its COX-1 selectivity.

NSAIDs have significant side effects including gastrointestinal hemorrhage, prolonged bleeding times and kidney disorders. However, carprofen has fewer side effects on account of its COX-2 selectivity (Leece *et al*., 2005; Nolan and Reid, 1993). In fact, no clinical side effect was detected in the animals of the 2 groups given carprofen (G1 and G2) in the present study. Dopamine an amine neurotransmitter is present in free nerve endings. The formation of Dihydroxyphenyl Alanine (DOPA) is mediated by tyrosine hydroxylase and dopamine is subsequently formed by the decarboxylation of DOPA. Dopamine is then transformed into noradrenaline and dopamine β-hydroxylase (Goldstein, 2006). In the present study, increases of 11 and 11.9% were observed in G1 at the 4th and 6th postoperative hours, respectively while increases of 69.2 and 73.1% were observed in G3 at the 6th and 8th h, respectively (Table 1). The increase in the dopamine level was higher in the laparotomy group (G3) in which no analgesic was used. Increases of 55.9 and 49.7% were observed in G2 at the 1st and 2nd postoperative hours while increases of 34.5, 28.2 and 34.6% occurred in G4 at the 2nd, 4th and 6th h, respectively (Table 1). The dopamine level was found to be higher in the osteotomy group (G2) until the analgesic drug showed efficacy.

The dopamine level reached its preoperative level in a longer period of time in G4 in which no painkiller was used than in G2. The dopamine level was increased in G2 in which an analgesic was used until the drug showed efficacy. Considering the dopamine levels of all groups, the preoperative levels of animals in G1 and G2 were statistically significantly higher than those of animals in G3 and G4 ($p<0.05$). The same situation was observed at the 96th, 120th, 144th and 168th postoperative hours (Fig. 1). We concluded that this situation could be caused by individual differences between animals. ACTH is secreted by the frontal lobe of the hypophysis and increases cortisol release from the suprarenal glands (Bomholt *et al*., 2005; Nicholson *et al*., 1998). Lykkegaard *et al*. (2005) used a local anaesthetic around the laparotomy line in one group in the postoperative period and physiologic serum in another group and then examined the plasma ACTH levels. The ACTH levels started to increase at the 15th min in the group given physiologic serum and reached its maximum level at the 30th min in this group. It subsequently started to decrease at the 45th min. Statistically significant increases in the ACTH levels were detected between G1 and G2: 29.9 and 21.5% at the 1st h and 34.1 and 21.6% at the 2nd h, respectively ($p<0.05$). Statistically significant increases were detected in the ACTH levels of G3 at the 1st (27.5%), 2nd (36.3%), 4th (36.7%), 6th (42.8%) and 8th (41.5%) h ($p<0.05$).

ACTH levels returned to preoperative levels starting from the 24th h and no statistically significant difference was found compared with the post-operative period. Statistically significant increases in G4 were detected at the 1st (33.1%), 2nd (43.7%), 4th (31.7%), 6th (40.2%), 8th (43.4%) and 24th (11.8%) h ($p<0.05$) and the levels returned to the preoperative levels starting from the 48th h (Table 2). The ACTH level decreased at the 4th h in G1 and G2. The decrease in G3 occurred at the 24 and 48th h in G4 (Fig. 2). These decreases in the ACTH level are compatible with those in the literature (Lykkegaard *et al*., 2005; Prunier *et al*., 2005).

The decreases in blood PCO_2 levels of all groups at the 1st and 2nd postoperative hours were attributed to the increased respiration. The decreasing PCO_2 levels in G2 and G3 lasted until the 4th h while they continued in G4 until the 6th h (Table 3). This situation could be caused by increased respiration due to pain. Blood PO_2 increased in all groups at the initial hours. Significant increases were detected at the 1st h in G1 at the 1st and 2nd h in G2 at the 1st, 2nd and 4th h in G3 and at the 1st, 2nd, 4th and 6th h in G4 ($p<0.05$) (Table 4). These changes took place in parallel with those of the blood PCO_2 level. An increase was observed in the PCO_2 level based on the increased respiration.

Statistically significant increases were detected in WBC numbers at the 6 and 8th h in G1 at the 6th h in G2 at the 4th, 6th and 8th h in G3 and at the 2nd, 4th, 6th, 8th and 24th h in G4 compared with the initial values ($p<0.05$) (Table 5). Organisms release leukocytes in storage organs as a defense mechanism that depends on the cortisol secreted under stress. No statistically significant differences in blood gases or blood counts were detected between the groups. However, statistically significant differences in PCO_2, PO_2 and WBC values were found in

inter-group comparisons. This situation may have been caused by the good health of dogs included in the study. Blood gas and blood count results may not have had much effect on postoperative pain however, they supported the ACTH and dopamine results.

CONCLUSION

In this study, significant increases were detected in ACTH and dopamine levels in the present study. Values returned to normal within a shorter period of time in the group subjected to hard tissue operation (osteotomy) than in the groups subjected to soft tissue operation (laparotomy) and in which painkillers were not used. These findings may indicate better effectiveness of carprofen in soft tissue operations. Hard tissue operations were determined to involve more pain and cause more metabolic alterations in the body compared with soft tissue operations. However, the application time of the painkiller used in the study was highly important.

Based on the results obtained in the present study, procurement of effective postoperative analgesia was found quite necessary after both hard and soft tissue operations. It is evident that effective analgesia should be immediately implemented in the interest of animal welfare and to ensure rapid return to normal physiologic functions.

ACKNOWLEDGEMENTS

This study was summarised from a PhD thesis and supported by SUBAPK (The Coordination of Scientific Research Projects, University of Selcuk, Project No. 2003/302).

REFERENCES

Bomholt, S.F., J.D. Mikkelsen and G. Blackburn-Munro, 2005. Normal hypothalamo-pituitary-adrenal axis function in a rat model of peripheral neuropathic pain. Brain Res., 1044: 216-226.

Dahl, J.B. and H. Kehlet, 1991. Non-steroidal anti-ýnflammatory drugs: Rationale for use in severe postoperative pain. Br. J. Anaesthesia, 66: 703-712.

Deneuche, A.J., C. Dufayet, L. G oby, P. Fayolle and C. Desbois, 2004. Analgesic comparison of meloxicam or ketoprofen for orthopedic surgery in dogs. Vet. Surg., 33: 650-660.

Dzikiti, T.B., K.E. Joubert, L.J. Venter and L.N. Dzikiti, 2006. Comparison of morphine and carprofen administered alone or in combination for analgesia in dogs undergoing ovariohysterectomy. J. S. Afr. Vet. Assoc., 77: 120-126.

Fox, S.M. and S.A. Johnston, 1997. Use of carprofen for the treatment of pain and inflammation in dogs. J. Am. Vet. Med. Assoc., 210: 1493-1498.

Goldstein, D.S., 2006. L-Dihydroxyphenylserine (L-DOPS): A norepinephrine prodrug. Cardiovasc. Drug Rev., 24: 189-203.

Grisneaux, E., J. Dupuis, P. Pibarot, N.H. Bonneau, B. Charette and D. Blais, 2003. Effects of postoperative administration of ketoprofen or carprofen on short- and long-term results of femoral head and neck excision in dogs. J. Am. Vet. Med. Assoc., 223: 1006-1012.

Horstman, C.L., M.G. Conzeminus, R. Evans and W.J. Gordon, 2004. Assessing the efficacy of perioperative oral carprofen after cranial cruciate surgery using noninvasive, objective pressure platform gait analysis. Vet. Surg., 33: 286-292.

Jezova, D., E. Jurankova, A. Mosnarova, M. Kriska and I. Skultetyova, 1996. Neuroendocrine response during stress with relation to gender differences. Acta Neurobiol., 56: 779-785.

Johnson, C.B., P.M. Taylor, S.S. Young and J.C. Brearley, 1993. Postoperative analgesia using Phenylbutazone, Flunixin or Carprofen in horses. Vet. Rec., 133: 336-338.

Lafuente, M.P., J. Franch, I. Durall, M.C. Diaz-Bertrana and R.M. Marquez, 2005. Comparison between meloxicam and transdermally administered fentanyl for treatment of postoperative pain in dogs undergoing osteotomy of the tibia and fibula and placement of a uniplanar external distraction device. J. Am. Vet. Med. Assoc., 227: 1768-1774.

Laredo, F.G., E. Belda, J. Murciano, M. Escobar, A. Navarro, K.J. Robinson and R.S. Jones, 2004. Comparison of the analgesic effects of meloxicam and carprofen administered preoperatively to dogs undergoing orthopaedic surgery. Vet. Rec., 155: 667-671.

Lariviere, W.R. and R. Melzack, 2000. The role of corticotropin-releasing factor in pain and analgesia. Pain, 84: 1-12.

Lascelles, B.D., S.J. Butterworth and A.E. Waterman, 1994. Postoperative analgesic and sedative effects of carprofen and pethidine in dogs. Vet. Rec., 134: 187-191.

Leece, E.A., J.C. Brearley and E.F. Harding, 2005. Comparison of carprofen and meloxicam for 72 hours following ovariohysterectomy in dogs. Vet. Anaesthesia Analgesia, 32: 184-192.

Lobetti, R.G. and K.E. Joubert, 2000. Effect of administration of nonsteroidal anti-inflammatory drugs before surgery on renal function in clinically normal dogs. Am. J. Vet. Res., 61: 1501-1507.

Lykkegaard, K., B. Lauritzen, L. Tessem, P. Weikop and O. Svendsen, 2005. Local anaesthetics attenuates spinal nociception and HPA-axis activation during experimental laparotomy in pigs. Res. Vet. Sci., 79: 245-251.

Martin, T.J., N.L. Buechler and J.C. Eisenach, 2006. Intrathecal administration of a cylcooxygenase-1, but not a cyclooxygenase-2 inhibitor, reverses the effects of laparotomy on exploratory activity in rats. Anesthesia Analgesia, 103: 690-695.

Mastrocinque, S. and D.T. Fantoni, 2003. A comparison of preoperative tramadol and morphine for the control of early postoperative pain in canine ovariohysterectomy. Vet. Anaesthesia Analgesia, 30: 220-228.

Nicholson, G., J.M. Burrin and G.M. Hall, 1998. Perioperative steroid supplementation. Anaesthesia, 53: 1091-1104.

Nolan, A. and J. Reid, 1993. Comparasion of the postoperative analgesic and sedative effects of Carprofen and Papaveretum in the dog. Vet. Rec., 133: 240-242.

Prunier, A., A.M. Mounier and M. Hay, 2005. Effects of castration, tooth resection, or tail docking on plasma metabolites and stres hormones in young pigs. J. Anim. Sci., 83: 216-222.

Schecter, W.P., F.S. Bongard, B.J. Gainor, D.L. Weltz and J.K. Horn, 2002. Pain control of outpatient surgery. J. Am. Coll. Surg., 195: 95-104.

Short, C.E., 1998. Fundamentals of pain perception in animals. Appl. Anim. Behav. Sci., 59: 125-133.

Slingsby, L.S., P.J. Murison, L. Goossens, M. Engelen and A.E. Waterman-Pearson, 2006. A comparison between pre-operative carprofen and a long-acting sufentanil formulation for analgesia after ovariohysterectomy in dogs. Vet. Anaesthesia Analgesia, 33: 313-327.

Zhu, X., D. Conklin and J.C. Eisenach, 2003. Cyclooxygenase-1 in the spinal cord plays an important role in postoperative pain. Pain, 104: 15-23.