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Clinical efficacy of multimodal analgesia for the management of visceral pain in canine abdominal surgery

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Abstract
The present study was undertaken to evaluate management of visceral pain on the basis of behavioural response using Carprofen and Tramadol following abdominal surgery pre and postoperatively in dogs. Twelve clinical cases of dogs presented with various abdominal surgery were divided into two groups. Group A animals received Carprofen @ 4 mg/kg b.wt s/c, 20 minutes before surgery, 6 hours after complete recovery and then repeated at every 24 hrs up to 3rd postoperative day. Group B animals received Tramadol @ 4 mg/kg b.wt. i/m., 20 minutes before surgery, 6 hours after complete recovery and then repeated at every 24 hrs up to 3rd postoperative day. Inj. Bupivacaine hydrochloride @ 1.0mg/kg b.wt. (0.5%) was infiltrated at laparotomy incision site for incisional block in each animal of both the groups. The behavioral responses were analyzed preoperatively, 30 minutes after recovery and at 24, 48 and 72 hours post-operatively. The pain assessment was made by multifactorial numerical rating scale (MNRS) system. Various behavioral parameters studied were posture, vocalization, appetite and thirst, response to palpation, facial expression and mental status. The mean score value of posture, vocalization and personality / attitude increased non-significantly at 30 minute after recovery and there after decreased significantly ($p<0.05$). Appetite / thirst, response to palpation and mental status varied non-significantly between and within the group at each time interval. A significance ($p<0.05$) variation was observed at 24 hour post-operative period in facial expression in both the groups. Mean total pain score decreased significantly ($p<0.05$) in group A and B after recovery till the end of observations. It was concluded that bupivacaine can be used as perioperative analgesic as incisional block and carprofen provides better analgesia as compared to tramadol in dogs for the management of visceral pain produced following major abdominal surgery.

Keywords: Bupivacaine, carprofen, incisional block, tramadol, visceral pain

Introduction
Multimodal or balanced anaesthesia is a technique that is suitable for both small and large animals experiencing pain that may be difficult to control with a single analgesic agent. By using drugs from more than one analgesic class, the chance of successfully preventing and treating pain can be increased (Hellyer, 1999) [9] and making the combination safe and more effective. In addition with multimodal analgesia, the painful impulse can be blocked at many points in the pain processing pathway, achieving a synergistic effect. It should be noted that the local anaesthetics block pain in all three pathways of nociception (Beckman, 2006) [1]. Visceral pain management is commonly achieved in dogs by administration of opioid drugs, non steroidal anti-inflammatory drugs and local anaesthetics. (Leece *et al.*, 2005) [11]. Use of local anaesthetics in combination with general anaesthesia can greatly reduce anaesthetic requirements and therefore anaesthetic risk (Zaki, 2013) [22]. The practice of drug administration prior to the induction of painful stimulus is more effective than giving the same drug after the stimulus is induced (Beckman, 2006) [1]. By alleviating the pain, autonomic endocrine responses associated with pain can be prevented resulting in decreased suffering, distress, delayed wound healing and post operative morbidity.
As evident, that animals are incapable of describing pain, the change in their behaviour and physiological parameters are helpful in determining the presence of pain (Bianchi *et al*., 1996, Firth and Haldane, 1999) [2, 6]. Various Opioids and NSAIDS have been used successfully either alone or in combination as an analgesic in invasive surgery. Earlier studies suggest that the drug administered before surgery is more effective from analgesia point of view as compared to drug administered in the post surgical phase (Grape and Tramer, 2007) [7].

Preoperative incisional /wound infiltration with bupivacaine is simple and effective technique to reduce post operative pain for longer duration of time (Sarvas *et al*., 2008) [16]. Tramadol being a racemic mixture of two enatiomers, of which the (+) enantiomer is a weak mu opioid agonist with analgesic potency about 1/10th that of morphine and inhibits serotonin neural reuptake whereas (-) enantiomer inhibits nor epinephrine neuronal reuptake (Sevcik *et al*., 1993) [17]. Carprofen provides analgesia by reducing prostaglandin synthesis in injured tissues by virtue of cyclooxygenase 2 inhibition. Effective analgesia is provided by inhibition of sodium channels, complete blocking of the generation and conduction of nerve impulses induced by local nerve block techniques. Bupivacaine hydrochloride is approximately four times as potent as lignocaine hydrochloride and most widely used in small animal practice. Bupivacaine has slower onset of action (~15 min) and provides prolonged period of analgesia as compared to lignocaine (Woodward, 2008). Considering the paucity of literature, involving the use of NSAID Carprofen (Cox-2) and Tramadol (centrally acting analgesic) for preemptive analgesia along with incisional block with bupivacaine (long acting local anaesthetic), the present study was planned to assess the visceral pain by studying various behavior parameters in dogs undergoing abdominal surgery.

Materials and Methods

The study was conducted on 12 clinical cases of dogs irrespective of breed and sex that were presented and operated for abdominal surgery. The dogs were randomly divided into two groups. In group A, Inj. Carprofen was administered @ 4 mg/kg b.wt. S/C 20 minutes before surgery, and then repeated with the same dose rate at 6 hrs after complete recovery and then at 24, 48 and 72 hours postoperatively. In group B, Inj. Tramadol was administered @ 4 mg/kg b.wt.I/M 20 minutes before surgery, and then repeated with the same dose rate at 6hrs after complete recovery and then at 24,48 and 72 hours postoperatively. Inj. Bupivacaine @ 1.0 mg/kg b.wt (5%) was infilterated at the site of incision as incisional block in all the animals of Group A and Group B. The animals of both the groups were operated by using Inj. Atropine sulphate @ 0.04 mg/kg b.wt. I/M, Inj. Xylazine hydrochloride @ 1 mg/kg b.wt. and Inj Ketamine @5mg/Kg b.wt. intramuscularly. Major abdominal surgery were performed in animal of both the groups in similar ratio of clinical cases viz., Cystotomy, Gastrotomy, Ovariohysterectomy and Caesarean section. Pain assessments were conducted using a multifactorial numerical rating scale (MNRS) (Table 1). Postoperative assessments were done at the owner's premises and Department of Veterinary Surgery and Radiology. Various behavioural parameters related to visceral pain like posture, vocalization, appetite and thirst, response to palpation, facial expression and mental status were observed/recorded preoperatively (0 min), 30 mts after recovery and at 24, 48 and 72 hour postoperatively. The data obtained during the study was analyzed using “Kruskal wallis non-parametric test” for knowing any difference existing among the groups.

Table 1: Multifactorial Numerical Rating Scale (NRS)

Behavioural parameters	Scale	Observation
A) Posture	0	Sitting or standing head up
	1	Lateral recumbancy
	1	Standing head down
	2	Restless
	3	Tucked up appearance
B) Vocalization	0	No Vocalization
	1	Vocalization when forced to move
	2	Vocalization when touched
	2	Intermittent
	3	Continuous
C) Appetite and thirst	0	Taking food and water
	1	Taking liquid only
	2	Not taking anything
D) Personality/Attitude	0	At rest
	1	Quiet and docile animal may become aggressive
	2	Licking /Biting/Scratching the painful area
	3	Self mutilation
E) Response to palpation	0	No change
	1	Guards/reacts when touched
	2	Reacts before touched
	3	Severe response
F) Facial expression	0	Active
	1	Dull eyes
	2	Staring in space
	2	Appears sleepy
	3	Photophobic appearance
G) Mental status	0	Submissive
	1	Overfriendly
	2	Wary
	3	Aggressive

Result and Discussion

Successful management of pain in animals must begin with an accurate assessment of the degree of pain. Accurate measurement of intensity of pain shown by animal is nearly impossible. In veterinary patients, behaviour observation, through an imprecise method to assess discomfort, remains the cornerstone in evaluating the effectiveness of treatment (Johnston, 2000) [10]. Therefore, various scales were developed such as simple descriptive scale, numerical rating scale and visual analogue scale. MNRS is the most suitable of the three scales for assessing pain in dogs (Robertson, 2003 and Paul-Murphy *et al.*, 2004) [3, 14]. It provides a suitable compromise between over interpretation and difficulty in use that can be a feature of VAS and lack of sensitivity that has been seen with the use of SOS (Downie *et al.*, 1978) [5]. In multifactorial NRS pain associated behaviours are assigned scores which are summed up to create a total pain score of the patient. To add, in contrast to MNRS, different behaviours can be assigned the same value or weight (Pascoe and Dyson, 1993; Conzemius *et al.*, 1997; Firth and Haldane, 1999) [13, 3, 6]. In the present study, the modified NRS scale i.e. Multifactorial numerical rating scale was used for calculation of mean total pain score (MTPS).

1: Posture

Table 2: Showing mean score values of posture in dog (Mean ± S.E.)

Group	Time interval after recovery				
	0 min.	30 min.	24 hrs	48 hrs	72 hrs
A	1.33^{ab}±0.49	1.48^{a}±0.21	0.83^{b}±1.16	0.67^{b}±0.21	0.33^{b}±0.20
B	1.33^{ab}±0.95	1.50^{a}±0.22	1.00^{b}±1.26	0.50^{b}±0.22	0.31^{b}±0.21

In the present study, the mean score value of posture behaviour increased non-significantly (p>0.05) at 30 minute after recovery within both the groups and then varied significantly (p<0.05) at 24 and 48 hr time interval in each group (Table 2). However, the low pain score deviations like lateral recumbency and standing head down were noticed at 72 hours in post-operative period in few animals of both the groups but postural abnormalities like tucked up appearance and restlessness were noticed in one and two animals of group A and group B respectively. There was non-significant (p>0.05) difference between the groups at each time interval. Low hung head, recumbency and tensing of abdominal and back muscles resulting in tucked up appearance which are indicative of pain in dogs as reported by Spinelli and Markowitz (1987) [19]; Watson *et al.* (1996) [20] and Robertson (2003) [15].

2: Vocalization

Table 3: Showing mean score values of vocalization in dog (Mean ± S.E.)

Group	Time interval after recovery				
	0 min.	30 min.	24 hrs	48 hrs	72 hrs
A	1.00^{ab}±0.36	1.50^{a}±0.22	1.67^{a}±0.31	0.33^{c}±0.21	0.17^{c}±0.17
B	1.50^{ab}±0.50	1.67^{a}±0.21	1.50^{b}±0.26	0.30^{c}±0.22	0.33^{c}±0.21

The mean score value of vocalization behaviour increased significantly (p<0.05) upto 24 hr after recovery in Group A whereas in group B, vocalization increased significantly at 30 min. after recovery and then varied significantly (p<0.05) at various time interval of the study period (Table 3). There was non-significant difference between the groups at each time interval. Intermittent vocalization before or only after touching the animal was detected in many animals of both the groups during the preoperative and postoperative periods also. Vocalization was the most frequently nominated indicator of pain in dogs and cats as surveyed by 5054 Australian Veterinarians (Watson *et al.*, 1996) [20].

3: Appetite and Thirst

Table 4: Showing mean score values of appetite and thirst in dog (Mean ± S.E.)

Group	Time interval after recovery				
	0 min.	30 min.	24 hrs	48 hrs	72 hrs
A	1.00^{b}±0.36	1.80^{a}±0.22	0.83^{b}±0.41	0.50^{b}±0.34	0.17^{b}±0.17
B	1.17^{b}±0.40	1.83^{a}±0.21	1.00^{b}±0.36	0.33^{b}±0.33	0.19^{b}±0.21

The mean score value of appetite and thirst behaviour significantly (p<0.05) increased at 30 minute after recovery in animals of both the groups and then decreased significantly (p<0.05) at 24, 48 and 72 hr time interval (Table 4). However, non-significant difference was observed between the groups at various time interval. In the present study, the appetite and thirst significantly increased at 30 min. after complete recovery in both the groups.

4: Personality and Attitude

Table 5: Showing mean score values of personality and attitude in dog (Mean ± S.E.)

Group	Time interval after recovery				
	0 min.	30 min.	24 hrs	48 hrs	72 hrs
A	1.17^{a}±0.40	1.33^{a}±0.22	0.43^{b}±0.21	0.33^{b}±0.21	0.17^{b}±0.17
B	1.10^{a}±0.36	1.17^{a}±0.17	0.67^{b}±0.74	0.50^{b}±0.34	0.19^{b}±0.21

The mean score value of personality and attitude behaviour increased non-significantly at 30 minute after recovery within both the groups and then decreased significantly (p<0.05) at 24, 48 and 72 hr time interval in group A and B (Table 5). There was non-significant difference between the groups at each time interval. Two animals of group A and four animals of group B were found licking the painful area during postoperative periods. In the present study, all the animals prior to surgery were quite and docile but during postoperative period same animals became aggressive which might be due to pain. Excessive licking, biting, scratching or shaking of a painful area can lead to self mutilation as reported by Haskins (1987) [8] and Moberg (1987) [12].

5: Response to palpation

Table 6: Showing mean score values of response to palpation in dog (Mean ± S.E.)

Group	Time interval after recovery				
	0 min.	30 min.	24 hrs	48 hrs	72 hrs
A	0.93^{a}±0.30	1.10^{a}±0.25	0.83^{a}±0.17	0.43^{a}±0.21	0.17^{a}±0.17
B	1.00^{a}±0.36	1.17^{a}±0.40	0.86^{a}±0.30	0.67^{a}±0.22	0.18^{a}±0.10

In the present study, mean score values for response against palpation showed non-significant variation within and between the group A and B at different time intervals (Table 6). Wound palpation is an important component of pain assessment in all species of animal (Watson *et al.*, 1996 and Robertson, 2003a) [20, 15]. In the present study, all the animals prior to surgery were quite and docile but during wound palpation postoperatively some animals became aggressive, which might be due to pain.

6: Facial expression

Table 7: Showing mean score values of facial expression in dog (Mean ± S.E.)

Group	Time interval after recovery				
	0 min.	30 min.	24 hrs	48 hrs	72 hrs
A	1.17^{ab}±0.40	1.95^{a}±0.30	0.83^{b}±0.40	0.50^{b}±0.22	0.17^{b}±0.17
B	1.33^{ab}±0.33	2.00^{a}±0.17	0.89^{b}±0.17	0.33^{b}±0.21	0.19^{b}±0.21

The mean score value of facial expression behavior increased significantly (p<0.05) at 30 minute after recovery within both the groups and then decreased non-significantly at 24hr, 48 hr and 72 hr time interval in group A and B (Table 7). However, there was a non-significant difference between the groups at each time interval. None in the group had photophobic appearance post operatively. In both the groups, most of the animals were found staring in space during the preoperative period. However, during the various postoperative assessment period most animals of group A were active but some of group B had dull eyes. Dull eyes, dilated pupils, sleepy or photophobic appearance have been reported to be signs of pain by Robertson (2003) [15].

7: Mental status

Table 8: Showing mean score values of mental status in dog (mean ±SE)

Group	Time interval after recovery				
	0 min.	30 min.	24 hrs	48 hrs	72 hrs
A	1.27^{ab}±0.40	1.83^{a}±0.22	0.83^{b}±0.40	0.50^{b}±0.22	0.18^{b}±0.35
B	1.35^{ab}±0.36	2.00^{a}±0.17	0.87^{b}±0.17	0.33^{b}±0.21	0.19^{b}±0.21

The mean score value of mental status behaviour increased significantly (p<0.05) at 30 minute after recovery within both the groups and then decreased non significantly at 24, 48 and 72 hr time interval in group A and B respectively (Table 8). One animal of group A was aggressive and most of them in both the groups were wary during the preoperative period. During the early postoperative period, few dogs appeared over friendly but majority were submissive in both the groups. The importance of an aggressive change in behaviour should be evaluated in light of the fact that dogs and cats develop an intensive care psychosis of sorts, a syndrome that has been described in critically ill human patients (Haskins, 1987) [8].

(B) Mean Total Pain Score (MTPS)

Table 9: Showing mean score values of Mean Total Pain Score (MTPS) in dog (mean±SE)

Group	Time interval after recovery				
	0 min.	30 min.	24 hrs	48 hrs	72 hrs
A	7.87^{b}±0.06	10.99^{a}±0.16	6.25^{c}±0.16	3.26^{d}±0.04	1.36^{e}±0.02
B	8.78^{b}±0.07	11.34^{a}±0.11	6.79^{c}±0.18	2.96^{d}±0.47	1.58^{e}±0.29

The highest MTPS was obtained at 30 minute after surgery (10.99 ±0.16 and 11.34 ±0.11) in group A and group B respectively and thereafter, decreased significantly (p<0.05) within both the groups. At 24 and 48 hour interval decreasing trend was observed in MTPS in both the groups. At the end of the study, the lowest MTPS recorded was 1.36±0.02 and 1.58 ±0.29 in group A and B respectively. Between the groups, the MTPS values did not differ significantly at any stage of observation period. But MTPS values were lower in case of group A as compared to animals of group B. Carprofen

provided superior analgesia up to about 18 hours post-surgery in dogs under gone ovariohysterectomy (Shih *et al*., 2008) [18]. Similar findings were also reported by Delgado *et al*. (2014) [4] in post-operative analgesia using carprofen and tramadol after enucleation in dogs. In our study, similar pattern was observed where both groups exhibited gradual reduction in pain score during postoperative period without significant difference between the groups.

In the present study, the mean score value of posture, vocalization and personality / attitude increased non-significantly at 30 minute after recovery and there after decreased significantly (p<0.05). Appetite / thirst, response to palpation and mental status varied non-significantly between and within the group at each time interval. A significant (p<0.05) variation was observed at 24 hour post-operative period in facial expression in both the groups. All the behavior parameters suggest that the analgesic effect with combination of carprofen and bupivacaine was better as compared to tramadol when combined with bupivacaine. It confirms the multimodal analgesic theory (Beckman, 2006) [1] as the local anaesthetic bupivacaine works on a different mechanism than the NSAID carprofen and opioid tramadol. Mean total pain score decreased significantly (p<0.05) in group A and B after recovery till the end of observation period. There was non-significant difference in between the groups but the MTPS was comparatively lower in animals of group A than group B.

Conclusion

Carprofen along with incisional administration of bupivacaine provided better analgesia than tramadol along with incisional administration of bupivacaine for the management of visceral pain produced following major abdominal surgery in canines.

Reference

1. Beckman BW. Pathophysiology and management of surgical and chronic oral pain in dogs and cats. Journal of Veterinary Dentistry, 2006;23(1):50-60.
2. Bianchi P, Ardizzone S, Petrillo M, Caruso I, Montrone F. Endoscopic assessment of the effects of dipyrone (metamizole) in comparison to paracetamol and placebo on the gastric and duodenal mucosa of healthy adult volunteers. Digestion. 1996;57(3):186-190.
3. Conzemius MG, Hill CM, Sammarco JL, Perkowski SZ. Correlation between subjective and objective measures used to determine severity of postoperative pain in dogs. J Am. Vet. Med. Assoc. 1997;210(11):1619-1622.
4. Delgado C, Bentley E, Hetzel S, Smith LJ. Carprofen provides better post-operative analgesia than tramadol in dogs after enucleation: A randomized, masked clinical trial. J Am. Vet. Med. Assoc. 2014;245(12):1375.
5. Downie WW, Leatham PA, Rhind VM, Wright V, Branco JA, Anderson JA. Studies with pain rating scales. Annals of the Rheumatic Diseases. 1978;37(4):378.
6. Firth AM, Haldane SL. Development of a scale to evaluate postoperative pain in dogs. J Am. Vet. Med. Assoc. 1999;214(5):651-659.
7. Grape S, Tramèr MR. Do we need preemptive analgesia for the treatment of postoperative pain? Best Practice & Research Clinical Anaesthesiology. 2007;21(1):51-63.
8. Haskins SC. Use of analgesics postoperatively and in a small animal intensive care setting. J Am. Vet. Med. Assoc. 1987;191(10):1266-1268.
9. Hellyer PW. Minimizing postoperative discomfort in dogs and cats. Vet. Med. 1999;94(3):259-265.
10. Johnston SA. Pain: Identification. *In:* Text book of Veterinary Internal Medicine. Etinger, S.J. and Feldman, E.C. (Eds.) 5th Edn. W.B. Saunders Co., Tokyo. 2000;I:20-22.
11. Leece EA, Brearley JC, Harding EF. Comparison of carprofen and meloxicam for 72 hours following ovariohysterectomy in dogs. Veterinary Anaesthesia and Analgesia. 2005;32(4):184-192.
12. Moberg GP. Problems in defining stress and distress in animals. J Am. Vet. Med. Assoc. 1987;191(10):1207.
13. Pascoe PJ, Dyson DH. Analgesia after lateral thoracotomy in dogs epidural morphine vs. intercostal bupivacaine. Veterinary Surgery. 1993;22(2):141-147.
14. Paul-Murphy J, Ludders JW, Robertson SA, Gaynor JS, Hellyer PW, Wong PL. The need for a cross-species approach to the study of pain in animals. J Am. Vet. Med. Assoc. 2004;224(5):692-697.
15. Robertson SA. How do we know if they hurt? Pain assessment in small animals. Vet. Med. 2003;98(8):700-709.
16. Sarvas I, Papazoglou LG, Kazakos G, Anagnostou T, Tsioli V, Raptopoulos D. Incisional block with bupivacaine for analgesia after celiotomy in dogs. J. Am. Ani. Hosp. Assoc. 2008;44(2): 60-66.
17. Sevik J, Nieber K, Driessen B, Illes P. Effects of the central analgesic tramadol and its main metabolite O-desmethyltramadol on rat locus coeruleus neurons. Br. J. Pharmacol. 1993;110:169-176.
18. Shih AC, Robertson S, Isaza N, Pablo L, Davies W. Comparison between analgesic effects of buprenorphine, carprofen, and buprenorphine with carprofen for canine ovariohysterectomy. Vet Anaesth Analg. 2008;35(1):69-79.
19. Spinelli JS, Markowitz H. Clinical recognition and anticipation of situations likely to induce suffering in animals. J Am. Vet. Med. Assoc., 1987;191:1216-1218.
20. Watson ADJ, Nicholson A, Church DB, Pearson MRB. Use of anti-inflammatory and analgesic drugs in dogs and cats. Australian veterinary journal. 1996;74(3):203-210.
21. Woodward TM. Pain management and regional anesthesia for the dental patient. Top Companion Anim Med. 2008;23:106-114
22. Zaki S. Pain Assessment and Management in Companion Animals Veterinary Update. Boardtalk Insert. 2013;1:1-8.