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Tramadol and Butorphanol in post-surgical pain management in canine

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Abstract
The present study was undertaken to evaluate the analgesic efficacy of Butorphanol and Tramadol as post-surgical analgesics in eighteen ovariohysterectomy bitches, divided into three groups' containing 6 animals in each. Group A and Group B were administered with Butorphanol @ 0.35 mg/kg IM and Tramadol @ 1.5 mg/kg IM respectively as single dose immediately after completion of operation and the animals of Group C were kept as control without any post-operative analgesic in entire observation period. The physiological parameters and pain assessment test were taken pre and postoperatively at 0 min, 15 min, 30 min, 1 hr, 2 hrs, 4 hrs and 6 hrs. The physiological parameters *viz.* heart rate, pulse rate, respiration rate, rectal temperature and Oxygen saturation (SpO_2) showed significant ($p<0.01$) variation between the groups but these variations were noted within physiological reference range. The Mean Arterial Pressure (MAP) did not show any significant variation between the groups or between time intervals in all the groups. The pain assessment test done by using University of Melbourne Pain Scale (UMPS) showed significantly ($p<0.01$) increased score in the post-operative period in Group C compared to Groups A and B; while in Groups A and B the pain scores remains relatively static till 4 hours after a initial rise in post-operative periods. Comparison between Group A and Group B, the scores were increased significantly from 4 hrs till 6 hrs post operation in Group A.
Based on the present study, it was found that degree of analgesia was better with Butorphanol while duration of analgesia was longer with Tramadol. Both the synthetic opioids were found to be economic and effective in alleviation of post-operative pain in dogs.

Keywords: Tramadol, butorphanol, pain management, canine

Introduction
Pain is an unpleasant sensory and emotional experience most commonly associated with actual or potential tissue damage or described in terms of such damage (Hellyer *et. al.*, 2007) [4]. As the subjects have inadequate expression to its suffering, it is hard to assess the level of post-surgical pain in animal. Therefore it is an ethical responsibility of the veterinarian to ensure trouble-free recovery of the animal following any surgical trauma. The Centre of Veterinary Medicine of the US Food and Drug Administration considers Ovariohysterectomy to cause moderate pain, making it suitable for clinical studies of analgesia.
Butorphanol is a synthetic agonist-antagonist opioid and its metabolites are agonist at kappa-opioid receptors and mixed agonist-antagonists at mu-opioid receptors (Chaithanya *et al.*, 2014) [2]. Tramadol is a synthetic, centrally active opioid like analgesic having agonist activity at mu-opioid receptor, as well as re-uptake inhibition of the neurotransmitters serotonin and nor-epinephrine. These two drugs have been used to treat moderate to severe pain in humans as well as in animals. Keeping this in view, the present study was undertaken to evaluate performance of Tramadol and Butorphanol as post-operative pain reliever following elective ovariohysterectomy in bitch.

Material and Methods
The entire experiment as carried out as per the guidance of Institutional Animal Ethics Committee. The experiment was carried out on 18 numbers of clinically healthy mongrel bitches of 3-4 years age group and body weight ranging from 10-15 kgs presented for elective ovariohysterectomy. The selected animals were divided into 3 (three) groups consisting of 6 (six) animals in each group.

Animals of Group-A received Butorphanol @ 0.35 mg/kg body weight i/m immediately after surgery as single dose, Group-B received Tramadol @ 1.5 mg/kg body weight i/m immediately after surgery as single dose and Group-C was kept as control without any post-operative analgesic. The elective ovariohysterectomy was performed in all the animals through left flank approach under general anaesthesia by inducing with Propofol at 5 mg/kg IV and maintenance was done with Diazepam @ 1mg/kg and Ketamine @ 10 mg/kg BW till the end of surgical procedure. The post-operative care and medication were identical in each individual animal. Physiological parameters (heart rate, pulse rate, respiration rate, and rectal temperature) were recorded as per standard protocol. The mean arterial pressure was recorded with the help of Automatic Blood Pressure Monitor; while oxygen saturation was determined from the Pulse Oximeter with the help of a sensor clip placed on the tip of the ear and the values displayed in the monitor were expressed in percentage (%). The assessment of pain (University of Melbourne Pain Scale) was done as per the methods described by Firth and Haldane, 1999. The data were recorded at pre-operatively and 0 minute, 15 minutes, 30 minutes, 1 hour, 2 hours, 4 hours and 6 hours post-surgically. The results of various parameters at different time intervals were statistically analyzed as per the method described by Snedecor and Cochran (1994) [11].

Result and Discussion

The mean values of the heart rate, pulse rate, respiration rate and rectal temperature have been depicted in Table-1. In all the Groups the heart rate was decreased significantly immediately after operation; however in Group C animals showed increasing trend after surgery, might be due to acute pain, anxiety and fear. The heart rates showed a mild decreasing trend in Group A and B, but within physiological range throughout the examination period. The results were in accordance with the findings of Mich and Hellyer (2008) [6] and Phillip *et al*. (1991) [9]. There was significant (p<0.01) decrease of pulse rate in all the groups immediately after surgery which might be due to the action of anaesthetics during operation. Similar findings were also recorded by Laiju *et al.* (2011) [5] in ovariohysterectomized bitches. The respiration rate (breaths/min) was reduced significantly (p<0.01) in all the groups, which might be due to the anaesthetic effect. However the animals of Group C showed increased significantly at 2 hours compare to treated groups. The findings were in accordance with the experiment of Tantry *et al.* (2010) [12] in goat and Parker (2004) [8] in human following butorphanol and tramadol administration respectively. A significant decrease of rectal temperature was recorded in all the groups immediately after surgery, followed by increasing trend towards the base values; however quick return was recorded in Group C. This might be due to acute pain in Groups C animals. Similar findings were recorded by Mich and Hellyer (2008) [6].

The mean values of the mean arterial pressure (mmHg), oxygen saturation (%) and University of Melbourne Pain Scale (UMPS) have been depicted in Table-2. In all the groups, the Mean Arterial Pressure (mmHg) was recorded non-significant (p<0.05) variation in entire observation period. The findings were in accordance with experiment of Rauser *et al*. (2008) [10] in pigs following administration Butorphanol and Natalini *et al*. (2007) [7] in dog after premedication with Tramadol in dog. The Oxygen saturation (%) was found significantly (p< 0.01) decreased significantly immediately after surgery; however these were within the normal reference range. The values gradually returned to normal by the end of the observation in all the groups. Similar findings were also recorded by Rauser *et al.* (2008) [10]. The values of University of Melbourne Pain Scale (UMPS) increased significantly (p<0.01) from the pre-operative values in all the groups immediately after operation. The pain score in group C was recorded sharp rise to '10' at 1 hour while in group A and group B rise of pain score significantly less till the end of observation. The findings were in accordance with observations of Almeida *et al.* (2009) [1] in dog. Between the treated groups the pain score was recorded significantly less in Group A and B after 2 hours. From the observations in the present study indicated that the degree of analgesia was recorded better with butorphanol while duration of analgesia is longer with tramadol in dog.

Table 1: Effects of various treatment on heart rate (beats/min), pulse rate (beats/min), respiration rate (breaths/min) and temperature (^{0}f) at different time intervals

Parameter	Groups	Time Interval							
		Pre-operative	Post-operative						
			0 min	15 min	30 min	1 hr	2hrs	4hrs	6hrs
Heart Rate (Beat/Min)	A	94.33 ± 2.16^{a}	88.50 ± 1.52^{b}	86.50 ± 1.06^{bc}	84.67 ± 1.17^{cd}	82.00 ± 0.52^{de}	80.33 ± 0.42^{e}	85.00 ± 0.34^{e}	86.33 ± 0.65^{bc}
	B	92.50 ± 2.00^{a}	87.50 ± 1.41^{b}	87.83 ± 1.19^{b}	84.33 ± 1.20^{c}	84.17 ± 1.09^{c}	84.50 ± 1.08^{c}	85.33 ± 1.06^{e}	85.83 ± 0.79^{e}
	C	91.00 ± 1.32^{a}	86.83 ± 1.09^{b}	89.83 ± 0.83^{c}	90.83 ± 0.60^{ac}	91.50 ± 0.52^{a}	92.17 ± 1.05^{a}	95.83 ± 0.48^{d}	96.00 ± 0.21^{d}
Pulse Rate (Beat/Min)	A	91.17 ± 1.40^{a}	85.83 ± 0.95^{b}	84.17 ± 0.98^{bc}	83.00 ± 0.93^{cd}	81.83 ± 0.60^{cd}	81.17 ± 0.70^{d}	81.33 ± 0.49^{d}	81.50 ± 0.34^{d}
	B	90.17 ± 0.60^{a}	85.50 ± 0.67^{bcd}	84.50 ± 1.43^{bc}	84.00 ± 0.58^{b}	86.17 ± 0.31^{cd}	87.17 ± 0.31^{de}	87.33 ± 0.33^{de}	88.33 ± 0.49^{ae}
	C	91.00 ± 1.15^{a}	85.00 ± 1.02^{b}	84.00 ± 0.68^{b}	84.67 ± 0.67^{b}	88.17 ± 0.79^{c}	90.00 ± 0.52^{ac}	90.50 ± 0.43^{a}	91.50 ± 0.43^{a}
Respiration Rate (Rate/Minute)	A	32.00 ± 1.34^{a}	20.00 ± 0.86^{b}	21.50 ± 1.15^{b}	24.17 ± 0.70^{c}	25.67 ± 0.49^{cd}	25.83 ± 0.31^{cd}	26.17 ± 0.79^{cd}	27.50 ± 0.43^{d}
	B	31.33 ± 0.67^{a}	21.83 ± 1.35^{b}	24.67 ± 1.09^{c}	25.00 ± 0.26^{c}	25.67 ± 0.49^{bc}	25.17 ± 0.83^{c}	25.50 ± 0.67^{c}	28.50 ± 0.50^{d}
	C	32.67 ± 0.88^{a}	21.33 ± 0.33^{b}	25.33 ± 0.42^{c}	30.17 ± 0.65^{d}	31.67 ± 0.80^{ad}	34.83 ± 1.19^{ae}	37.00 ± 1.29^{ef}	38.00 ± 1.44^{f}
Rectal Temperature (°F)	A	102.07 ± 0.10^{a}	99.75 ± 0.27^{b}	99.70 ± 0.33^{b}	99.90 ± 0.25^{b}	99.85 ± 0.24^{b}	100.10 ± 0.21^{b}	100.40 ± 0.20^{bc}	100.83 ± 0.16^{c}
	B	101.98 ± 0.13^{a}	99.88 ± 0.54^{b}	99.78 ± 0.54^{b}	99.55 ± 0.52^{b}	99.48 ± 0.40^{b}	99.53 ± 0.32^{b}	99.87 ± 0.30^{b}	100.13 ± 0.30^{b}
	C	101.97 ± 0.11^{a}	99.83 ± 0.13^{b}	99.87 ± 0.10^{b}	99.95 ± 0.08^{b}	100.30 ± 0.12^{c}	101.20 ± 0.18^{d}	101.65 ± 0.09^{a}	101.75 ± 0.09^{a}

Means superscripts with different letter differ significantly.

Table 2: Effects of various treatment on mean arterial pressure (MMHG), oxygen saturation (%) and university of melbourne pain scale (score) at different time intervals

Parameter	Groups	Time Interval							
		Pre-operative	Post-operative						
			0 min	15 min	30 min	1 hr	2hrs	4hrs	6hrs
Mean Arterial Pressure (mmHg)	A	102.42± 4.35^{a}	101.92± 4.10^{a}	100.83± 3.78^{a}	100.17± 3.40^{a}	99.00± 3.13^{a}	98.33± 2.49^{a}	98.67± 2.02^{a}	100.25± 2.06^{a}
	B	101.67± 1.67^{a}	101.42 ±1.45^{a}	101.75 ± 1.31^{a}	101.42± 1.10^{a}	101.42± 0.92^{a}	101.84 ± 0.76^{a}	101.00 ± 0.68^{a}	101.33 ± o.76^{a}
	C	101.25± 2.74^{a}	100.92± 2.72^{a}	101.09± 2.61^{a}	100.92± 2.29^{a}	101.59± 2.56^{a}	101.58± 2.67^{a}	100.92 ±2.43^{a}	101.00± 2.16^{a}
Oxyhaemoglobin Saturation (%)	A	100 ± 0.00^{a}	98.67 ± 0.42^{b}	98.83 ± 0.17^{b}	99.00 ± 0.26^{b}	99.67 ± 0.21^{a}	99.83 ± 0.17^{a}	99.83 ± 0.17^{a}	100 ± 0.00^{a}
	B	100 ± 0.00^{a}	98.50 ± 0.56^{b}	99.50 ± 0.34^{a}	99.33 ± 0.21^{ab}	99.67 ± 0.33^{a}	99.67 ± 0.33^{a}	99.83 ± 0.17^{a}	100 ± 0.00^{a}
	C	100 ± 0.00^{a}	98.67 ± 0.42^{b}	98.50 ± 0.43^{b}	98.83 ± 0.40^{b}	99.83 ± 0.17^{a}	99.83 ± 0.17^{a}	100 ± 0.00^{a}	100 ± 0.00^{a}
University of Belbourne Pain Scale (Score)	A	0.00^{a}	1.83 ± 0.17^{b}	4.67 ± 0.33^{c}	5.33 ± 0.21^{d}	5.50 ± 0.22^{d}	6.33 ± 0.21^{e}	9.50 ± 0.22^{f}	10.50 ± 0.22^{g}
	B	0.00^{a}	1.67 ± 0.33^{b}	4.83 ± 0.17^{c}	5.83 ± 0.31^{d}	6.17 ± 0.31^{de}	6.83 ± 0.31^{e}	8.17 ± 0.31^{f}	8.50 ± 0.22^{f}
	C	0.00^{a}	1.83 ± 0.31^{b}	5.50 ± 0.22^{c}	9.67 ± 0.21^{d}	10.00 ± 0.37^{de}	10.17 ± 0.31^{de}	10.50 ± 0.22^{e}	10.67 ± 0.21^{e}

Means superscripts with different letter differ significantly.

Conclusion: In conclusion, the use of butorphanol and tremadol immediately after major abdominal surgery found successful in alleviate post-surgical pain in animal; however butorphanol was found more effective pain reliever for short duration compare to long term effect of tramadol.

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