CLINICO-PHYSIOLOGICAL EFFECTS OF BUTORPHANOL-XYLAZINE/DEXMEDETOMIDINE-KETAMINE ANAESTHESIA IN DOGS UNDERGOING ORTHOPAEDIC SURGERY

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The study was conducted on 12 dogs in two groups undergoing orthopaedic surgery to assess the clinicophysiological effects of xylazine/dexmedetomidine along with buorphanol for ketamine anaesthesia. After 10 minutes, anaesthesia was induced with ketamine in both groups followed by maintenance with ketamine IV as and when needed. Adequate muscle relaxation, sedation and analgesia was recorded in both groups. A significant ($P<0.05$) reduction in induction dose of ketamine was recorded in group B. Heart rate values were significantly ($P<0.05$) values from 30 to 60 min interval in group A. Significant ($P<0.05$) reduction in values of respiration rate, rectal temperature and SpO_2 were observed in both groups. Xylazine/dexmedetomidine-butorphanol combination produced a comparable degree of clinico-physiological stability during ketamine anaesthesia in dogs undergoing orthopaedic surgery.
Keywords: Xylazine, Dexmedetomidine, Butorphanol, Ketamine, Orthopaedic Surgery.

An ideal anaesthetic produces sedation, amnesia, analgesia and muscle relaxation. Multimodal or balanced analgesia results from the administration of combinations of different analgesic drugs, acting at multiple or different sites that leads to an absence of pain by affecting different parts of the nociceptive pathway (Lamont, 2008). Alpha-2 agonists are the most commonly used sedatives in veterinary practice as they induce reliable and dose dependent sedation, analgesia and muscle relaxation that can be readily reversed by administration of selective antagonists (Lemke, 2004). In dogs and cats, xylazine has been used alone or in combination with opioids to provide sedation and analgesia for diagnostic and minor surgical procedures (Thurmon *et al*., 1996). Ketamine increases muscle tone and induces spontaneous movement and, occasionally, convulsions but these undesirable effects are avoided by using ketamine in conjunction with benzodiazepines or alpha-2 agonists (Sika, 2013; Sethi *et al*., 2017). The present study was undertaken to compare the clinico-physiological effects of ketamine anaesthesia in dogs undergoing orthopaedic surgery premedicated with butorphanol-xylazine/ dexmedetomidine combination.

Materials and Methods

A prospective blinded clinical anaesthetic study on 12 randomly chosen (irrespective of age, sex, breed and body weight) dogs with tibial fracture having normal hematological parameters subjected to tibial plating were subject of study. Animals were fasted for 12 hours and undergone clinical examination before start of procedure. Atropine sulphate was administered @ 0.04 mg/kg IM followed after 5 minutes with butorphanol @ 0.2mg/kg in both groups. Xylazine @ 0.5 mg/kg body weight IM was administered in group A while dexmedetomidine @ 10 µg/kg body weight IM was administered in group B in separate syringe along with butorphanol. After 10 minutes of premedication, anaesthesia was induced with ketamine administered IV in both groups. Maintenance of surgical anaesthesia was made by incremental doses of ketamine IV as and when needed during surgical procedure.

Weak time and down time were recorded as the time elapsed from the time of injection of drugs to the time of onset on

incoordination/ataxia or drowsiness, and till the animal attained sternal recumbency, respectively. Recovery time was recorded as time elapsed from completion of surgery till reappearance of pedal reflex. Sternal recumbency time and complete recovery time were recorded as the time elapsed after completion of surgical procedure until the animals attained sternal recumbency for recovery, and stood and walked unassisted, respectively.

Palpebral reflex as a measure of depth of sedation, jaw relaxation as a measure of muscle relaxation and pedal reflex as measure of analgesia were used to monitor the depth of anaesthesia at 0, 10, 15, 30, 45, 60, 75 and 90 min.

Jaw relaxation, palpebral reflex and pedal reflex were scored as; 0: Animal not allowing to open the jaw, intact and strong reflex (strong withdrawal), 1: Animal resists opening of jaws and closes quickly, intact but weak blink (slow response), intact but weak pedal reflex (animal responding slowly), 2: Less resistance to opening the jaws and closed slowly, very weak (very slow and occasional response), 3: No resistance and jaws remain open, abolished blink reflex and pedal reflex, respectively.

Heart rate (HR-beats/min) was monitored with non-invasive blood pressure monitor from ulnar artery and respiratory rate (RR- breaths/min) was measured by counting the excursion of thoracoabdomen at 0, 10, 15, 30, 45, 60, 75 and 90 min intervals. Rectal temperature (RT) was recorded with the help of a digital thermometer. Oxygen saturation of hemoglobin (SpO_2) was measured with pulse oxymeter applied over tip of tongue.

Analysis of variance (ANOVA) and Duncan's multiple range tests (DMRT) were used to compare the means at different intervals among different groups. Paired "t" test was used to compare the mean values at different levels with their respective base value in each group. For non-parametric observations Kruskal-Wallis one-way test was used to compare the mean between the groups at corresponding intervals. Statistical significance was assessed at $P<0.05$.

Results and Discussion

A non-significantly ($P>0.05$) lower weak time (4.92±0.44 v/s 3.47±0.32 min) and down time (6.64±0.38 v/s 4.56±0.27 min) was recorded in the animals of group B which could be due to lipophilic property of dexmedetomidine leading to rapid onset of action as also reported earlier by Sika (2013). Concurrent administration of dexmedetomidine along with butorphanol leading to reduced weak time interval has also been earlier documented in dogs (Rafee *et al*., 2015). A non-significantly ($P>0.05$) increased recovery time (16.18±1.38 v/s 19.46±1.89 min), sternal recumbency time (22.67±1.56 v/s 27.72±2.83 min) and standing time (33.12±1.25 v/s 36.63±2.56 min) were observed in animals of group B in comparison to group A which could be attributed to synergistic action of dexmedetomidine and butorphanol leading to enhanced effects of ketamine.

Less resistance to opening jaws was observed in animals of group B at 15 minute interval. However, resistance to opening jaws was observed in animals of both groups at most of time intervals from 10 to 60 min in followed by no jaw relaxation at 75 and 90 min (Table- 1). Mild jaw relaxation as indicated by resistance to opening the mouth from 10 min onwards could be due to muscle poor relaxant effect of alpha- 2 agonists palpebral reflex recorded mild response from 10 min till 45 min interval followed by moderate response at 75 and 90 min interval in animals of both groups. Very weak pedal reflex was recorded in animals of group A at 15 min while pedal reflex was completely abolished from 15 min onwards till 60 min interval in animals of group B. Thereafter, pedal reflex was moderate at 75 min followed by strong withdrawal of limb at 90 min interval in animals of both groups. Complete abolishment of pedal reflex after administration of ketamine might be due to

excellent analgesic property of ketamine and addition of alpha-2 agonist along with butorphanol produced analgesia of longer duration.

A significantly (P<0.05) lower induction dose of ketamine was recorded in animals of group B as compared to group A (8.34±0.42 and 6.29±0.39 mg/kg). Synergestic interaction between dexmedetomidine and butorphanol could have led to reduction in induction dose of ketamine in our study. Maintenance dose values of ketamine did not differ significantly (P>0.05) between groups (2.39±0.26 and 2.94±0.37 mg/kg) in our study. Heart rate increased non-significantly (P>0.05) after premedication at 10 min in animals of both groups (Table-2). Thereafter, HR improved from 15 min onwards and remained significantly (P<0.05) higher than baseline values in animals of group A from 30 to 60 min interval. However, in animals of group B, the values of HR were non-significantly (P>0.05) higher than baseline values from 15 min onwards till completion of observation period. Comparison between groups revealed no significant (p>0.05) difference in HR at different time intervals. The increase in HR during initial phase of experiment even after the administration of alpha-2 agonists with opioids might be attributed to the effect of atropine .

Respiratory rate values recorded a significant (P<0.05) decrease in both groups as compared to the baseline values at most of time intervals during the observation period. Comparison between groups revealed no significant (p>0.05) differences in RR at any time interval. Secondary CNS depression as well as direct depression of respiratory centre produced by alpha- 2 agonists might have caused respiratory depression in our study Administration of alpha-2 agonists along with butorphanol prior to ketamine anaesthesia leading to decrease in RR has also been reported earlier in dogs (Rafee *et al*., 2016; Singh *et al*., 2019).

The values of rectal temperature decreased significantly (p<0.05) below the baseline in both groups till 45 min interval followed by non-significantly (p>0.05) decreased RT till the end of observation period. Decreased skeletal muscle tone, reduction in metabolic rate, depression of thermoregulatory center and peripheral vasodilation could be probable causation factor for decreased RT values which has also been reported by Virtanen (1989). The values of SpO_2 revealed a highly significant (P<0.01) decrease at most time intervals in both groups which might be due to certain degree of respiratory depression in both groups. Comparison between groups revealed that SpO_2 value in animals of group A were significantly (P<0.05) lower at 75 min interval.Decreased $Sp0_2$ values during initial phase of observation period could be due to vasoconstriction produced by alpha-2 agonists. Decreased SpO_2 values following administration of butorphanol along with alpha-2 agonists and ketamine anaesthesia in dogs which has also been reported (Muir *et al*., 1999).

The findings of our study revealed that premedication with butorphanol along with xylazine/dexmedetomidine produced comparable degree of clinicophysiological and hemodynamic effects during ketamine anaesthesia in dogs undergoing orthopaedic surgery and may be recommended for balanced anaesthesia in clinical practice.

Table-1: MEAN ±S.E. VALUES OF JAW RELAXATION, PALPEBRAL REFLEX AND PEDAL REFLEX AT DIFFERENT TIME INTERVALS IN DIFFERENT GROUPS

Parameter	Group	Time intervals (min)							
		0	10	15	30	45	60	75	90
Jaw	A	0.00± 0.00	1.33± 0.23	1.50± 0.34	1.67± 0.21	1.50± 0.22	1.00± 0.26	0.67± 0.26	0.53± 0.14

relaxation	B	0.00± 0.00	1.87± 0.26	2.00± 0.16	1.93± 0.40	1.64± 0.28	1.45± 0.19	0.83± 0.21	0.64± 0.15
Palpebral reflex	A	0.00± 0.00	1.35± 0.23	1.63± 0.17	1.54± 0.25	1.37± 0.22	1.21± 0.14	0.64± 0.29	0.37± 0.18
	B	0.00± 0.00	1.69± 0.11	1.86± 0.21	1.71± 0.24	1.55± 0.32	1.34± 0.28	0.83± 0.32	0.50± 0.22
Pedal reflex	A	0.00± 0.00	2.00± 0.23	2.81± 0.32	3.00± 0.00	3.00± 0.00	2.82± 0.26	1.00± 0.45	0.50± 0.22
	B	0.00± 0.00	2.69± 0.31	3.00± 0.00	3.00± 0.00	3.00± 0.00	3.00± 0.00	1.17± 0.34	0.57± 0.26

Table-2: MEAN ±S.E. VALUES OF HEART RATE (BEATS/MIN), RESPIRATORY RATE (BREATHS/MIN), RECTAL TEMPERATURE (^{0}C) AND OXYGEN SATURATION (SP0_2%) AT DIFFERENT TIME INTERVALS IN DIFFERENT GROUPS

Parameter	Group	Time intervals (min)							
		0	**10**	**15**	**30**	**45**	**60**	**75**	**90**
Heart rate	A	114.57 ± 4.23	118.32 ± 5.24	121.71 ± 4.21	132.34± 4.87**	137.73± 4.01**	129.38± 4.24**	126.24 ± 3.67	122.34 ± 5.24
	B	119.24 ± 5.27	121.73 ± 5.75	114.35 ± 4.23	125.72± 4.54	130.26± 4.21	122.43± 3.87	121.38 ± 4.08	124.71 ± 3.84
Resp. rate	A	32.13± 3.89	26.38± 3.18**	23.84± 3.54**	22.28± 2.76**	21.76± 3.72**	23.94± 3.41*	25.04± 4.45*	29.87± 4.78
	B	29.87± 3.47	24.07± 3.16**	24.67± 2.28*	21.54± 2.47**	21.14± 1.54*	20.46± 2.12*	21.13± 3.40	26.38± 3.69
Rectal temp.	A	37.92± 0.43	37.14± 0.34**	36.97± 0.46**	36.89± 0.52**	36.63± 0.31*	36.42± 0.41*	37.62± 0.36	37.27± 0.32
	B	37.82± 0.56	37.55± 0.46	37.22± 0.33*	36.67± 0.48*	36.28± 0.34*	36.67± 0.52*	37.96± 0.42*	37.04± 0.24
SpO_2	A	89.65± 1.48	83.78± 2.39**	82.96± 2.04**	82.12± 1.73**	80.84± 1.69**	82.32± 1.42*	79.82± 3.24*^{a}	84.47± 0.85
	B	90.29± 1.78	82.07± 2.24**	80.96± 2.62**	79.23± 2.49**	77.02± 2.33**	81.13± 2.85**	86.27± 1.89*^{b}	82.24± 2.86**

*Significantly different from base value (P<0.05)
**Significantly different from base value (P<0.01)
Values with different superscripts differ significantly (P<0.05)

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