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Cardiopulmonary response following administration of buprenorphine and butorphanol in cats anaesthetized with midazolam-ketamine-isoflurane

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Abstract
Clinical study was conducted to access the cardiovascular effect of buprenorphine and butorphanol in 18 female cats anaesthetized with midazolam-ketamine- isoflurane. The cats were divided in to three Groups. In Group I, anaesthesia was induced by midazolam (@0.3mg/kg) ketamine (11mg/kg) mixture. In Group II and Group III cats, butorphanol and buprenorphine were administered @ 0.4 mg/kg and 0.01 mg/kg, 15 minutes prior to induction as in Group I and maintained with isoflurane. Pulse rate, Respiration rate, saturation of peripheral oxygen (SPO_2), inspired fraction of oxygen (FiO_2), end tidal oxygen (ETO_2), inspired fraction of carbon dioxide ($ETCO_2$), end tidal carbon dioxide and electrocardiography were recorded. A significant ($p<0.05$) increase in pulse rate during 5, 10 and 30th min. after induction in group III was observed. Statistical comparison revealed no significant change in the FiO_2, ETO_2 and $ETCO_2$. No life threatening cardiovascular emergencies were noticed during the ECG study.

Keywords: Buprenorphine, butorphanol, cat, midazolam, ketamine, isoflurane

Introduction
Recognition of pain in cats is very difficult and little emphasis is given for pain management owing to the unique pharmacological peculiarity of drug metabolism in this species. Xylazine-ketamine combination has been traditionally used as the anaesthetic regimen for surgical interventions in cats. The prolonged sedation of one to two hours duration and significant depression of cardiovascular function in normal cats associated with the above combination is now considered as unwarranted. The postoperative analgesia provided by the xylazine – Ketamine is believed to be inadequate. Induction and recovery associated with newer midazolam-ketamine-isoflurane protocol in cats is predictably rapid and inclusion of an opioid analgesic in the above protocol is recommended to achieve balanced anaesthesia [5]. Opioid provide useful analgesia in cats without loss of proprioception or consciousness and are effective in the control and management of acute or postoperative visceral pain. Good cardiovascular stability and attenuation of stress response of anaesthesia and surgery are the major advantages provided by the opioid. This paper reports the effect of inclusion of opioid analgesics in the anaesthetic protocol of cats on cardiopulmonary function.

Materials and methods
The study was conducted eighteen apparently healthy queen cats subjected for ovariohysterectomy at Veterinary College and Research Institute, Namakkal. The selected eighteen queens were randomly divided into three groups viz; Group I, Group II and Group III comprising of six animals in each group. Ovariohysterectomy was performed in all the animals through ventral midline/right flank approach as per standard surgical procedure with the following anaesthetic protocol. In Group I, anaesthesia was induced by intramuscular administration of midazolam (@0.3mg/kg body weight) ketamine (11mg/kg body weight) mixture. In Group II and Group III cats, butorphanol and buprenorphine were administered intramuscularly @ 0.4 mg/kg and 0.01 mg/kg body weight respectively, 15 minutes prior to induction of anaesthesia as in Group I. Maintenance of anaesthesia was carried out with isoflurane. About 0.5ml of 1% lignocaine solution was sprayed in to the larynx to prevent the laryngospasm before oroendotracheal intubation. Pulse rate, Respiration rate, saturation of peripheral oxygen (SPO_2), inspired fraction of oxygen (FiO_2), end tidal oxygen (ETO_2),

in spired fraction of carbon dioxide ($ETCO_2$), end tidal carbon dioxide and electrocardiography were recorded at 5 min interval during maintenance of anaesthesia using Schiller Argus multi gas monitor.

The statistical analysis was performed by using paired-t-test amongst the same group. Inter-group comparisons were done using one way ANOVA [3].

Results and discussions

Pain management in cats has led to the investigation of the pharmacokinetics and efficacy of opioid analgesic drugs in this species. Each opioid varies with dose, route of administration and the method used to assess them. The mean (±S.E) pulse and respiratory rates recorded before induction, 5, 10, 15, 20, 25, 30 min. of isoflurane maintenance and after recovery in all the groups were presented in Table 1. Comparison of pulse rate between the group I, II, and III revealed a significant ($p<0.05$) increase during 5, 10 and 30th min. of anaesthesia after induction in group III cats. The insignificant change in the pulse rate at different stages of anaesthesia and after recovery could be attributed to the non-influence of the premedicants, induction agent and maintenance agent on the pulse rate and indicated that the anaesthetic protocol employed in the present study provided better cardiovascular stability. Increase in heart rate during surgery could be ascribed to the inadequate analgesia causing sympathetic stimulation [5].

There was no significant change in the respiratory rate at different stages of anaesthesia between the groups. The significant decrease in respiratory rate at minutes of anaesthesia in group II animal could be attributed to the depressant effect of buprenorphine on the respiratory system. Butorphanol was reported to have respiratory depression ceiling effect and this could explain the significant decrease in cats administered with buprenorphine compared to butorphanol administered cats [6].

The mean (±S.E) saturation of peripheral oxygen (SpO_2), inspired fraction of oxygen (FiO_2), end-tidal oxygen (ETO_2), inspired fraction of carbon dioxide ($FiCO_2$) and end-tidal carbon dioxide ($ETCO_2$) recorded in per cent at 5 min. interval during maintenance of anaesthesia and were presented in Table 2. There was no significant change in the SpO_2 during maintenance phase of anaesthesia between the groups. The saturation of peripheral oxygen was maintained above 95 per cent at different time intervals of maintenance of anaesthesia and could be attributed to the administration of 100 per cent oxygen as carrier gas. The resulting increase in the partial pressure of oxygen at alveoli could maintain saturation of peripheral oxygen above 95 per cent [4, 5]. In all the cats, saturation of peripheral oxygen level was maintained above 95 per cent. Statistical comparison revealed no significant change in the FiO_2, ETO_2 and $ETCO_2$ at different time interval of isoflurane maintenance within the group and between the groups. The FiO_2 in the present study was maintained above 70 per cent in all the cats and indicated that the FGF employed was sufficient [2]. The FGF of 1 litre per minute employed in the study was sufficient to maintain high FiO2 and SpO2. The difference between the inspired and end-tidal oxygen ranged between 4 to 7 per cent in all the animals during maintenance of anaesthesia. Comparison of inspired and end-tidal oxygen revealed a normal uptake of oxygen during anaesthesia to meet metabolic oxygen demand. The normal uptake of oxygen maintained oxygenation and prevented development hypoxemia [6].

The $FiCO_2$ throughout the study period in all the groups had not exceeded one per cent. The $FiCO_2$ was less than one per cent during maintenance of anaesthesia and this could be attributed to the sufficient FGF employed to prevent rebreathing of exhaled air from the Bain¨s circuit [6]. The $ETCO_2$ in the present study was within the physiological limits and this could be attributed to the maintenance of adequate ventilation in all the anaesthetized cats. No life threatening cardiovascular emergencies were noticed in any of the cats during the ECG study. This indicates that, the selected anaesthetic protocol provided good cardiovascular stability [1].

Table 1: Mean (±S.E) Pulse rate and Respiratory rate per min. during different stages of anaesthesia

Parameter	Group	Before Induction	During maintenance (min.)						After Recovery
			5	10	15	20	25	30	
Pulse Rate (beats per min.)	I	$101.00^{a} \pm 19.91$	$87.50^{a} \pm 22.98$	$105.33^{ab} \pm 23.42$	$117.00^{a} \pm 21.05$	$121.50^{a} \pm 20.63$	$113.67^{a} \pm 20.88$	$107.56^{a} \pm 21.88$	$118.83^{a} \pm 12.27$
	II	$119.00^{a} \pm 18.21$	$124.50^{ab} \pm 19.38$	$121.17^{a} \pm 20.29$	$123.83^{a} \pm 19.96$	$136.67^{a} \pm 19.99$	$153.00^{a} \pm 22.19$	$142.17^{ab} \pm 18.82$	$121.16^{a} \pm 17.30$
	III	$133.66^{a} \pm 14.08$	$144.33^{b} \pm 17.56$	$142.00^{b} \pm 18.82$	$145.00^{a} \pm 17.89$	$155.17^{a} \pm 11.29$	$159.17^{a} \pm 13.60$	$159.00^{b} \pm 13.79$	$133.50^{a} \pm 14.62$
Respiratory Rate (breaths per min.)	I	$14.50^{a} \pm 3.06$	$18.17^{b} \pm 5.50$	$19.17^{b} \pm 4.25$	$20.67^{b} \pm 5.27$	$15.17^{b} \pm 4.03$	$18.33^{b} \pm 5.05$	$20.33^{b} \pm 5.21$	$15.67^{a} \pm 5.27$
	II	$15.66^{a} \pm 1.83$	$11.67^{a} \pm 2.27$	$15.17^{ab} \pm 2.67$	$11.00^{a} \pm 2.03$	$11.07^{a} \pm 1.75$	$10.67^{a} \pm 1.48$	$9.17^{ab} \pm 1.01$	$12.17^{a} \pm 2.25$
	III	$16.33^{a} \pm 2.33$	$16.67^{ab} \pm 2.20$	$14.67^{a} \pm 2.15$	$16.33^{ab} \pm 2.52$	$14.50^{a} \pm 2.14$	$17.50^{a} \pm 3.28$	$16.67^{a} \pm 2.69$	$16.50^{a} \pm 3.28$

Statistical analysis for row-wise group were performed by the comparison of baseline value with the data obtained from each time intervals.
Row-wise group mean (± SE) with different superscript (ab) differ significantly ($p<0.05$)

Table 2: Mean (±S.E) saturation of peripheral oxygen (%), inspired fraction of oxygen (%), end-tidal oxygen (%), inspired fraction of carbon dioxide (%) and end- tidal carbon dioxide (%) during maintenance stages of anaesthesia

Parameter	Group	During maintenance (min.)					
		5	10	15	20	25	30
SpO2 (%)	I	96.66 ± 1.40	97.10 ± 1.63	95.00 ± 3.41	97.60 ± 1.16	97.83 ± 1.19	95.33 ± 3.67
	II	98.22 ± 0.26	95.20 ± 3.04	95.06 ± 3.02	96.23 ± 1.86	97.66 ± 0.42	96.16 ± 2.03
	III	97.00 ± 0.93	97.66 ± 0.76	98.16 ± 0.87	98.83 ± 0.16	98.16 ± 0.87	98.00 ± 0.81
FiO2 (%)	I	73.08 ± 8.13	84.13 ± 1.40	87.40 ± 2.37	87.70 ± 0.95	86.63 ± 1.66	86.44 ± 2.86
	II	89.46 ± 6.02	92.30 ± 3.08	93.70 ± 2.73	93.23 ± 2.62	93.93 ± 2.33	91.03 ± 4.24
	III	75.90 ± 4.72	80.40 ± 4.01	82.16 ± 3.50	82.43 ± 3.01	84.20 ± 2.71	82.36 ± 2.97
ETO2 (%)	I	66.41 ± 7.49	74.63 ± 2.62	79.63 ± 3.63	79.86 ± 3.26	78.30 ± 2.67	81.00 ± 4.47
	II	85.88 ± 5.93	88.73 ± 2.75	89.50 ± 2.74	89.06 ± 2.70	89.10 ± 2.59	86.48 ± 3.78
	III	68.38 ± 5.05	74.50 ± 3.96	77.43 ± 2.84	76.23 ± 2.87	79.06 ± 2.03	78.00 ± 2.49
FiCO2 (%)	I	0	0.50 ± 0.22	0	0.33 ± 0.21	0	0
	II	0	0	0.50 ± 0.22	0	0	0.33 ± 0.21
	III	0.33 ± 0.21	0	0	0.50 ± 0.22	0	0
ETCO2 (%)	I	4.97 ± 0.37	4.91 ± 0.46	4.93 ± 0.46	4.73 ± 0.65	4.64 ± 0.57	4.38 ± 0.68
	II	4.58 ± 0.62	4.56 ± 0.49	4.56 ± 0.46	5.19 ± 0.53	5.08 ± 0.52	4.62 ± 0.48
	III	4.89 ± 0.36	5.61 ± 0.38	5.32 ± 0.35	5.81 ± 0.39	5.98 ± 0.43	5.00 ± 0.63

Conclusion

To conclude, the inclusion of buprenorphine and butorphanol in the anaesthetic protocol provided better cardiopulmonary function during maintenance phase. Butorphanol produced effective analgesia and possess respiratory depression ceiling effect. The duration of analgesia provided by the buprenorphine is comparatively longer and avoids repetitive administration.

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Conflict of interest

Authors declare that there is no conflict of interests regarding the publication of this article.

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