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Evaluation of Propofol Anaesthesia inMedetomidine-Pentazocine and Midazolam-Pentazocine Premedicated Buffalo Calves

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ABSTRACT

Twelve buffalo calves of either sex presented to the college clinic with various surgical conditions were utilized to study the effect of continuous intravenous infusion of propofol after premedication with medetomidine – pentazocine and midazolam – pentazocine. The animals were divided into two groups of six animals each. Group I animals were premedicated with Medetomidine @ 2.5 µg/kg b.wt. – pentazocine @ 0.5 mg/kg b.wt IV and Group II animals received midazolam @ 0.25 mg/kg b.wt. – pentazocine @ 0.5 mg/kg b.wt. IV.. Propofol was given @ 4 mg/kg b.wt. IV after premedication and maintained by continuous intravenous infusion of propofol @ 0.4 mg/kg b.wt. in 5 % dextrose normal saline in both groups. Induction quality was excellent, smooth and attained sternal recumbency rapidly without struggling in both groups. Anaesthetic character, Physiological & haematobiochemical parameters were studied at 0, 5,10,15,30 and 60 minutes following anaesthetic injections. No significant changes were recorded in both the groups. ECG studies did not reveal any abnormalities except slight variations in the amplitude of P wave, T wave and QRS complex in both groups. The study suggests that medetomidine – pentazocine premedication with continuous intravenous infusion of propofol provided better surgical anaesthesia and was compatable and safe in buffalo calves.

Keywords: Buffalo calves, ECG, haematobiochemical, physiological, Propofol,

In bovines, general anaesthesia is challenging because of various complications like excessive salivation, regurgitation, tympany and cardiopulmonary depression. To minimize the undesirable effects, the search for new drug combinations with appropriate pharmacokinetic and pharmacodynamic profiles for use in bovines is ongoing. Propofol is a short acting intravenous anaesthetic agent with reduced post anaesthetic complications, because of its rapid metabolism. Medetomidine is a new alpha 2-agonist which is about 30 to 40 times as potent as xylazine. It produces immediate and reliable degree of sedation, muscle relaxation and analgesia. Midazolam is a sedative with early induction, short duration of action, rapid elimination and total body clearance time. Pentazocine is an agonist-antagonist opioid to treat moderate to moderately severe pain. However, no reports are available on combination of medetomidine, midazolam, pentazocine with propofol as total intravenous anaesthesia in buffaloes. The present paper reports the evaluation of propofol anaesthesia in medetomidine – pentazocine and midazolam – pentazocine premedicated buffalo calves.

MATERIALS AND METHODS

Twelve buffalo calves of either sex aged between 6 – 8 months presented to the College clinic with various surgical problems like umbilical hernia (n = 4), urolithiasis (n = 4) and fractures (n = 4) were selected and used for present study. The animals were fasted for 48 hrs and water was withheld for 24 hrs prior to start of the experiment. Group I animals were premedicated with Medetomidine @ 2.5 µg/kg b.wt. – pentazocine @ 0.5 mg/kg b.wt IV

and Group II animals received midazolam @ 0.25 mg/kg b.wt. – pentazocine @ 0.5 mg/kg b.wt. IV.. In both the "groups", anaesthesia was induced by Propofol given @ 4 mg/kg b.wt. IV and maintained by continuous intravenous infusion of propofol @ 0.4 mg/kg/min in 5 % dextrose normal saline. The character of anaesthesia during induction, surgical plane of anaesthesia and recovery was assessed. Physiological parameters like temperature, heart rate and respiratory rate & haematobiochemical parameters such as haemoglobin, packed cell volume, erythrocyte sedimentation rate, alanine aminotransferase (ALT), aspertate aminotransferase (AST), and alkaline phosphatise (ALP) were recorded before and at 5,10,15,30 and 60 minutes after propofol administration. Subcutaneous needle electrodes were placed at the posterior border of the scapula and at the 5th costochondral junction (base apex lead) for recording of ECG at 1mv and 25 mm/sec paper speed (Mark's micro RcP_2) at 0 ,5 ,10 ,15 ,30 and 60 minutes after intravenous propofol infusion. The base line data for arterial O_2 saturation were obtained by applying sensor of a pulse oximeter (Datex Ohmeda 3800 Pulse oximeter) to the tip of ear before and at 5,10,15,30, and 60 minutes after administration of propofol.

RESULTS AND DISCUSSION

The mean values of propofol induction time were 21 ± 0.516 (seconds) and 22 ± 0.408 (seconds) in group I and group II respectively. Induction quality was excellent, smooth and attained recumbency rapidly without struggling in all animals in both groups.

The mean preanaesthetic rectal temperature (RT) values in group I and group II were 99.28°F ± 0.14 and 100.45°F ± 0.32 respectively (Table 1). There was a non-significant decrease in temperature in both groups till the entire period of observation. The variation in the temperature between the groups was significant ($P \leq 0.05$). Decrease in RT was recorded in both groups during post anaesthetic period i.e. after premedication and induction of anaesthesia. Medetomidine, midazolam and propofol were known to cause a decrease in RT by depression of thermoregulatory center, reduced BMR and muscle activity, depression of peripheral circulation and vasodilatation Weaver and Raptopoulos, 1990; Surbhi *et al.,* 2010). Reduced BMR and muscle activity on one hand and depression of thermoregulation on the other might have resulted in hypothermia in this study. Similar findings were reported after medetomidine administration in buffalo calves (Singh *et al.,* 2003; Singh *et al.,* 2010) and dogs (Surbhi *et al.,* 2010). Medetomidine induced CNS depression along with depressed hypothalamic noradrenergic μ_2 receptors might have led to hypothermia in group I animals as reported by Singh *et al.,* (2010).

The mean preanaesthetic respiratory rate (RR) values in group I and group II were 10.16 ± 0.30 and 10.50 ± 0.22 per minute respectively (Table 1). A significant decrease in RR was observed in both groups following permedication and induction of anaesthesia. In the present study, respiratory depression was a consistent finding in both groups, which persisted upto 30 min interval. Respiratory depression associated with alpha 2 adrenergic agonists might be secondary to the CNS depression produced by alpha 2 adrenoceptor stimulation or due to direct depression of the respiratory centers by preanaesthetics. These findings were in accordance with the earlier studies in which a greater respiratory depression was observed when alpha 2 agonists were used in combination with opioids in dogs (Singh *et al.,* 2010). Propofol caused a further decrease in mean RR by depressing central inspiratory drive and the ventilatory response to arterial CO_2 tension. In the present study, transient apnoea was observed immediately after propofol induction in both groups (Muir and Gadawski, 1998;Murison, 2001). Bufalari *et al.,* (1998) also opined that respiratory depression might cause transient apnoea. A similar decrease in RR was reported following medetomidine premedication in buffaloes (Singh *et al.,* 2003; Malik *et al.,* 2011b). This is in contrary with the findings of Vijay *et al.* (2010) who reported increase in RR after midazolam administration in buffalo calves. Propofol caused a further decrease in mean RR in both groups, plausibly by depressing central inspiratory drive and ventilator response to arterial CO_2 response (Khattri *et al.,* 2013). Similar findings were reported with propofol as a single agent or in combination with other anaesthetic drugs in various species, midazolam and propofol in dogs (Kushwaha *et al.,* 2012; Singh *et al*., 2012b), zolazepam and propofol in dogs (Cullen and Reynoldson,1997). Whereas, Kumar *et al.,* (2011) noticed increase in RR after propofol administration in buffalo calves.

The mean pre anaesthetic heart rate (HR) values were 54.00 ± 4.58 and 50.66 ± 1.72 per minute in group I and group II respectively (Table 1). A non-significant decrease

in HR was recorded after administration of medetomidine and pentazocine in group I animals. This was due to central sedative, autonomic and peripheral vascular effects of medetomidine. Inhibition of sympathetic tone due to reduction in norepinephrine release from the CNS, vagal activity in response to alpha 2 agonists induced vasoconstriction and direct increase in the release of acetylcholine from parasympathetic nerves in the heart have been reported as the possible mechanisms by which alpha 2 agonists induced bradycardia (Surbhi *et al.,* 2010;Singh *et al.,* 2012a). It has also been reported that pentazocine facilitates the increase in the parasympathetic tone and there by contributes to bradycardia (Khattri *et al.,* 2013). Similar findings were observed in goats (Amarpal *et al.,* 1998), buffalo calves (Singh *et al.,* 2003) and dogs (Surbhi *et al.,* 2010). A non-significant tachycardia was observed in animals premedicated with midazolam and induced with propofol. The increase in HR was recorded throughout the period of observation. This correlates with the findings of Komar *et al.,* (1992) who observed tachycardia without any change in cardiac output in dogs with propofol anaesthesia. Midazolam has been reported to cause transient hypotension in humans and, as the baro reflex is preserved, the increase in HR might be a reflex response to decreased blood pressure in humans. A similar finding was recorded in the present study, where midazolam caused tachycardia. This is in agreement with findings of Lin *et al.,* (1997) in sheep, Cullen and Reynoldson (1997), Muir and Gadawski (1998) and Kushwaha *et al.* (2012) in dogs. This contradicts with the findings of Jangra *et al.* (2008) who observed decrease in HR after midazolam administration in goats.

Means bearing different superscripts within a row (a, b...) vary significantly ($P \leq 0.05$)

Group I animals showed a significant ($P \leq 0.05$) decrease in haemoglobin & PCV during the period of observation. In group II also , haemoglobin & PCV values showed a significant ($P \leq 0.05$) decrease during entire period of observation. But these fluctuations were non significant between the groups. Pooling of circulatory blood cells in the spleen or other reservoirs secondary to decreased sympathetic activity explained the decrease in Hb and PCV. Further this decrease in Hb and PCV might be due to shifting of fluid from extravascular compartment to intravascular compartment in order to maintain normal cardiac output in animals (Khattri *et al.,* 2013).

In group I, a significant ($P \leq 0.05$) increase in ESR was recorded in the entire period of observation with a maximum of 8.00 ± 0.00 at 60 minutes. Group II animals showed a significant ($P \leq 0.05$) increase in ESR with a maximum of 7.66 ± 0.21 at 60 minutes. The changes in ESR values differed significantly ($P \leq 0.05$) within the group but no significant difference was seen between the groups. In the present study, ESR values were found to be increased significantly from the base line value throughout the period of observation in both groups. This is in contrary to the findings of Kumar *et al.* (2011) who reported no significant change in ESR after administration of propofol in buffalo calves.

In group I animals, AST values increased significantly ($P \leq 0.05$) throughout the period of study reaching a maximum of 164.33 ± 1.47 at 60 minutes. In group II,

Table 1. Variations in mean values (± SE) of different physiological parameters before, during and after anaesthesia in buffalo calves

Parameters	Groups	Minutes					
		0	5	10	15	30	60
Temperature (°F)	Group I	99.28 ± 0.14	99.25 ± 0.07	98.80 ± 0.03	98.63 ± 0.03	98.46 ± 0.02	98.25 ± 0.04
	Group II	100.45 ± 0.32	99.80 ± 0.28	99.23 ± 0.39	98.51 ± 0.23	98.13 ± 0.18	97.96 ± 0.11
Respiratory rate (breaths/ minute)	Group I	10.16 ± 0.30^{a}	10.83 ± 0.30^{ab}	8.83 ± 0.30^{abc}	8.33 ± 0.21^{abc}	11.83 ± 0.30^{abc}	13.8 ± 0.30^{ab}
	Group II	10.50 ± 0.22^{a}	8.83 ± 0.30^{ab}	10.50 ± 0.34^{ab}	9.83 ± 0.30^{abc}	8.83 ± 0.37^{abc}	12.66 ± 0.49^{ab}
Heart rate (beats/ minute)	Group I	54.00 ± 4.58^{a}	45.66 ± 4.41^{a}	40.50 ± 3.83^{a}	42.16 ± 5.97^{a}	47.00 ± 5.39^{a}	47.83 ± 4.06^{a}
	Group II	50.66 ± 1.72^{a}	57.00 ± 2.35^{a}	64.33 ± 2.30^{a}	72.33 ± 2.04^{a}	63.50 ± 2.06^{a}	58.50 ± 2.06^{a}

AST values increased significantly (P≤0.05) throughout the period of observation reaching a maximum of 165.33 ± 1.81. The changes in AST values were significant (P≤0.05) within the group and no significant (P≤0.05) difference was observed between the groups. In group I, there was significant (P≤0.05) increase in ALP values reaching a maximum of 345.82 ± 7.73 at 30 minutes. In group II, there was a significant (P≤0.05) increase in ALP values reaching a maximum of 305.77 ± 4.46 at 30 minutes. The changes in ALP differed significantly (P≤0.05) among the animals in the group and between the groups. A significant increase in AST and ALP was noticed in both the groups throughout the period of observation but this increase was within the physiological limit which indicated the possibility of pathological changes in the liver could therefore, be ruled out. It corroborates with the findings of many workers, following administration of medetomidine – butorphanol in buffaloes (Malik *et al.,* 2011a) and propofol in dogs (Bayan *et al.,* 2002).

In group I, there was significant (P≤0.05) decrease in ALT values upto 15 minutes, with a significant (P≤0.05) increase at 30 minutes and a sudden fall at 60 minutes reaching a minimum of 70.55 ± 1.23. In group II, ALT values decreased significantly (P≤0.05) upto 10 minutes with a gradual increase upto 30 minutes. These fluctuations in ALT values differ significantly (P≤0.05) within the group and between the groups. In our study, a significant decrease in ALT was observed in both the groups during entire period of observation as reported by Kwon – Youngsam *et al.,* (1999) during propofol anaesthesia in dogs (Malik *et al.,* 2011a) following midazolam – butorphanol premedication in buffaloes.

SPO_2 decreased significantly ($P \leq 0.05$) during the entire period of observation in both groups, with a significant difference (P≤0.05) between the groups and within the groups (Table 2). This decrease was significant after 10 minutes of drug administration in both groups, which might be due to a certain degree of respiratory depression by the anaesthetics as mentioned by Khattri *et al.,* (2013). Similar findings were reported following administration of midazolam in goats (Jangra *et al.,* 2008), medetomidine and butorphanol in dogs (Surbhi *et al.,* 2010), midazolam and propofol in dogs (Kushwaha *et al.,* 2012), xylazine – midazolam with propofol in dogs (Singh *et al.,* 2012b) and medetomidine – butorphanol and midazolam – butorphanol in buffaloes (Malik *et al.,* 2011a) and medetomidine – fentanyl in water buffaloes (Singh *et al.,* 2012a). On the contrary, Redondo *et al.,* (2000) and Surbhi *et al.,* (2010) observed no significant difference in SpO_2 after propofol anaesthesia and medetomidine and butorphanol premedication in dogs respectively.

ECG studies add additional information related to the changes in heart rate, rhythm, presence of conduction defects and arrhythmic changes during anaesthesia and surgery. It is a reliable source to evaluate patient oxygenation capacity by observing T wave and ST segment.

ECG findings of medetomidine – pentazocine premedicated buffalo calves showed a marked reduction in the heart rate (bradycardia). There was a decrease in the amplitude of P wave after 5 min of premedication and remain decreased until the end. This is in concurrent with the findings of Malik *et al.,* (2011b) who observed a decrease in amplitude of P wave in medetomidine – butorphanol premedicated buffaloes. The myocardial contraction increased markedly as denoted by the increase in the amplitude of QRS complex starting at 5 min post injection. Similar findings were reported by Shekidef *et al.,* (2007) and Malik *et al.,* (2011b) after premedication with medetomidine in buffalo calves. There was insignificant decrease in PR interval from 15 min to 60 min in 3 animals. Animals of this group showed increase in QT interval (Figure 1) after 15 min of

Table 2. Variations in mean values (± SE) of per cent SPO_2 before, during and after propofol anaesthesia in premedicated buffalo calves

Parameters	Groups	Minutes					
		0	5	10	15	30	60
SPO_2 (Percentage)	I	95.33 ± 0.33 [a]	94.16 ± 0.40 [b]	91.16 ± 0.60 [c]	89.50 ± 0.56 [d]	85.83 ± 0.83 [e]	89.50 ± 0.99 [f]
	II	97.00 ± 0.36 [a]	95.83 ± 0.47 [b]	94.16 ± 0.30 [c]	91.00 ± 0.51 [d]	86.50 ± 0.42 [e]	88.66 ± 0.61 [f]

Means bearing different superscripts within a row (a, b...) vary significantly ($P \leq 0.05$)

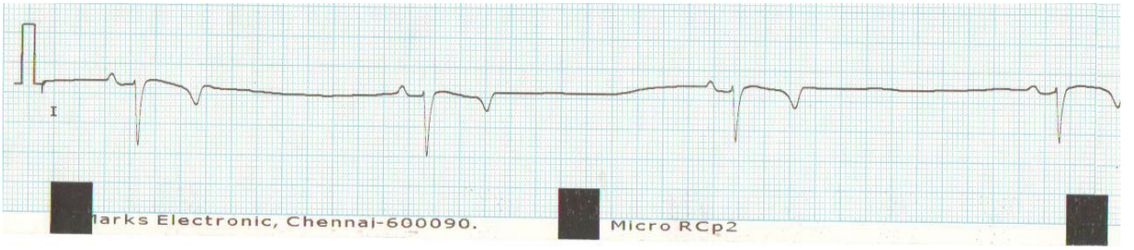

Figure 1: Photograph showing increased 'QT' interval on electrocardiograph during propofol anaesthesia in a buffalo calf after medetomidine – pentazocine premedication

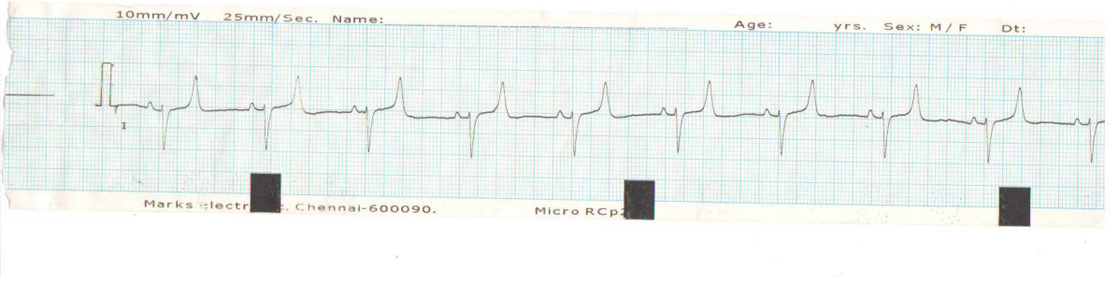

Figure 2: Photograph showing increased 'T' wave amplitude on electrocardiograph during propofol anaesthesia in a buffalo calf after midazolam – pentazocine premedication

anaesthesia. This finding was consistent with Malik *et al.,* (2011b) which might be due to decreased heart rate and a corresponding increase in the O_2 requirement of the heart after medetomidine – pentazocine administration. Elevated ST segment was observed from 15 min to 30 min in one animal in this group, which is in agreement with the findings of Sharma *et al.,* (2008) who administered medetomidine – ketamine in neonatal calves.

Sinus tachycardia was observed in animals premedicated with midazolam and pentazocine. A non significant increase in the amplitude of P wave was noticed from 15 min up to 60 min in two animals of this group. Amplitude of QRS complex was increased after 5 min of premedication in this group which indicates increase in myocardial contraction. PR interval increased non significantly throughout the period of observation. QT interval in this group recorded a decreasing trend towards the end of anaesthesia. Increase in amplitude of T wave (Figure 2) was observed in two animals of this group up to 5 min after the drug administration. This was in agreement with the findings of Malik *et al.,* (2011b) who evaluated midazolam – butorphanol premedication with propofol infusion in buffaloes. These changes indicated decrease in myocardial oxygenation as reported by Jangra *et al.,* (2008) in goats. None of the animals showed arrhythmias and conduction abnormalities.

CONCLUSION

It can be concluded from present study that both anaesthetic drug combinations were safe in buffalo calves for major surgical procedures. However, medetomidine provides better sedation, analgesia and muscle relaxation than midazolam. Addition of pentazocine can augment sedation and analgesia produced by medetomidine. Hence, medetomidine – pentazocine premedication with continuous intravenous infusion of propofol provides better surgical anaesthesia and therefore, may be recommended for anaesthesia in buffalo calves.

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