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Chamanvali B
M.Sc. Scholar, Department of Veterinary Surgery and Radiology, Veterinary College, Bidar, Karnataka, India

Dilipkumar D
Dean, Veterinary College, Bidar, Karnataka, India

Vijay Kumar
Ph.D. Scholar, Department of Veterinary Surgery and Radiology, Veterinary College, Bidar, Karnataka, India

Bhagavantappa B
Associate Professor and Head, Department of Veterinary Surgery and Radiology, Veterinary College, Bidar, Karnataka, India

Shivaprakash BV
Director of Research, KVAFSU, Bidar, Karnataka, India

Shrikant Kulkarni
Professor and Head, Department of Veterinary Surgery and Radiology, Veterinary College, Bidar, Karnataka, India

Vinay P Tikare
Assistant Professor, Department of Veterinary Pharmacology and Toxicology, Veterinary College, Gadag, Karnataka, India

Usturge SM
RETD, DIPGs, KVAFSU, Bidar, Karnataka, India

Venkatgiri
Assistant Professor (OPG), Department of Veterinary Surgery and Radiology, Veterinary College, Bidar, Karnataka, India

Corresponding Author:
Chamanvali B
M.Sc. Scholar, Department of Veterinary Surgery and Radiology, Veterinary College, Bidar, Karnataka, India

Comparative evaluation of anaesthetic combination of romifidine-ketamine-isoflurane and romifidine-propofol-isoflurane on physiological parameters due to surgeries in goats

Chamanvali B, Dilipkumar D, Vijay Kumar, Bhagavantappa B, Shivaprakash BV, Shrikant Kulkarni, Vinay P Tikare, Usturge SM and Venkatgiri

Abstract
The study was carried out to evaluate the feasibility of romifidine sedation for ketamine or propofol-isoflurane general anaesthesia for various surgeries in goats. The study was carried out in 12 clinical cases of goats presented for various surgical procedures and were randomly divided into two groups consisting of six goats in each group. The goats of both the groups were premedicated with romifidine hydrochloride (50 µg/kg, IV). After ten minutes the animals of group I and II were induced with ketamine (6 mg/kg, IV) and propofol (6 mg/kg IV) respectively then anaesthesia maintained with isoflurane (1-2%) in both the groups. Physiological observations revealed that heart rate and respiratory rate reduced significantly at 10 minutes after premedication in both the groups. Ketamine was associated with better haemodynamic stability in comparison to propofol however, Propofol induction had advantage of excellent sedation and muscle relaxation.

Keywords: Romifidine, ketamine, propofol, isoflurane, goats

1. Introduction

Alleviation of pain is one of the important criteria of anaesthetic administration. Pain in animals during surgery is able to produce gross movements. Body responses to pain are not only physical, it is also neuroendocrine in nature. In ruminants the use general anaesthesia is usually avoided due to complications like regurgitation, tympany, internal suffocation and hypersalivation. Most of the surgical interventions are carried out under either local analgesia or regional blocks. Caprine are delicate and quite sensitive to pain among the ruminants. Even the minor surgical procedure requires desensitization of the area involved.

Popular injectable anaesthesia used for small animal is the combination of alpha-2-adrenoceptor agonists and ketamine. Alpha-2-adrenoceptor agonists produce sedation, analgesia and muscle relaxation (Haskins *et al.*, 1986 and England *et al.*, 1996) [24, 25]. These agents produce satisfactory sedative effect based on dose administered. Different alpha-2 adrenoceptor agonists *viz*., xylazine, dexmedetomidine, medetomidine have been used as sedative and analgesic in different species of animals. Romifidine is a specific and relatively new alpha-2-adrenergic agonist drug that is mostly administered systemically to bring about sedation and analgesia. These agents produce a dose-dependent sedative effect, evidenced by muscle relaxation, ataxia, palpebral, labial and head ptosis, cardiorespiratory depression, absence or reduction of reaction to external stimuli, diminution of locomotor activity and hypnosis, which occur a few minutes after administration. Ketamine could be used for anaesthesia in sheep and goats however it might cause convulsions. The surgical anaesthesia and muscle relaxation is poor, however it might be improved by sedatives such as diazepam, xylazine and detomidine (Durgun *et al.*, 1990 and Afshar *et al*., 2005) [6, 1]. The most frequently used anaesthetic combinations in goats are ketamine-xylazine, ketamine-medetomidine and tiletamine -zolazepam (Lumb and Jones, 1996) [13]. Pharmacokinetic studies in various species have revealed that propofol has a high volume of distribution, rapid metabolism and rapid clearance when given by repeated doses or continuous intravenous (IV) infusion. The rapid onset and short duration of action, with rapid recoveries make the drug potentially useful in ruminants, in which these features are particularly desirable.

Reports on the use of propofol for induction and maintenance of anaesthesia have indicated its suitability in goats (Nolan and Reid, 1991) [17]. Romifidine has been evaluated for intrathecal use in goat. There is paucity in literature on usage of romifidine with ketamine or propofol for induction and maintenance of anaesthesia with isoflurane.

2. Materials and Methods

2.1 Sources of research animals

The present clinical study was carried out in 12 clinical cases of goats of either sex presented for various surgical procedures at Veterinary College, Bidar. All the goats were randomly divided into two groups consisting of six goats in each group.

2.2 Preanesthetic preparation of animals

All the animals were kept off feed for 12 to 24 hours depending on age of animal and water was withheld for 6-12 hours prior to anaesthesia and surgery. Adequate pre-operative fluid therapy was given to all the animals. The clinical status of the animals was assessed by recording heart rate, respiratory rate and rectal temperature and by estimating haematological and biochemical parameters prior to anaesthesia.

2.3 Procedure of the study

2.3.1 Sedation and induction

The goats in Group-I were premedicated with romifidine hydrochloride at the dose rate of 50 µg/kg body weight intravenously. After ten minutes of romifidine administration, the animals were restrained in lateral recumbency and anaesthesia was induced by administering ketamine at the dose rate of 6 mg/kg body weight intravenously. The animals were maintained under isoflurane anaesthesia. In the Group-II, animals were administered with romifidine hydrochloride at the dose rate of 50 µg/kg body weight intravenously. After ten minutes, the animals were restrained in lateral recumbency and anaesthesia was induced by administering propofol intravenously at the dose rate of 6 mg/kg body weight. The animals were maintained under isoflurane anaesthesia.

2.3.2 Maintenance of anaesthesia

The small animal anaesthetic machine[5] (Plate 2) was used to maintain anaesthesia with isoflurane. Semi closed system was used for all animals. The 100% oxygen was given with flow rate set at 2 liters per minute for the first two minutes to increase the fraction of inspired oxygen concentration. The fresh gas flow rate was then reduced to one to two liters per minute based on the size of the animal. Initially isoflurane was given with vaporizer setting at 3%, until downward rotation of eyeball. Later vaporizer setting was reduced to 1-2%. The vaporizer setting was altered during anaesthesia, as and when required to maintain uniform surgical plane of anaesthesia. After completion of surgery, isoflurane vaporizer was closed by setting the vaporizer at 0%. Oxygen (100%) was given until the restoration of swallowing reflex. After reappearance of swallowing reflex, anaesthetic machine was disconnected from endotracheal tube and endotracheal tube was removed after deflating the cuff.

3. Evaluation

To evaluate the efficacy of anaesthetic protocol, the following parameters were recorded before, during and after anaesthesia.

3.1 Physiological observations

Heart rate, respiratory rate and rectal temperature were recorded before premedication (0 minute), 10 minutes after premedication and at 5, 15, 30, 60, 120 minutes and 24 hours after induction of general anaesthesia.

3.2 Heart rate (Beats/min)

Heart rate was recorded by auscultation. The values were expressed in beats/min.

3.3 Respiratory rate (Breaths/min)

Respiratory rate was recorded by observing movement of chest wall and reservoir bag. The values were expressed in breaths/min.

3.4 Rectal temperature (0F)

Rectal temperature was recorded by a clinical thermometer. The values were expressed in ^{0}F.

3.5 Haemodynamic observations

Haemodynamic observations were recorded using vital sign monitor before premedication (0 minute), 10 minutes after premedication and at 5, 15, 30, 60 and 120 minutes after induction of general anaesthesia.

3.6 Mean Arterial Pressure (mm of Hg)

Mean Arterial Pressure was recorded using a non-invasive blood pressure monitor. The blood pressure cuff with an internal pressure sensing bladder was placed around the base of the tail or at forearm to record the mean arterial pressure. The values were expressed in mm of Hg.

3.7 Haemoglobin oxygen saturation (SpO2) (%)

The haemoglobin oxygen saturation (SpO2) was recorded by applying the sensor of the pulse oximeter on the vulva lips or tongue.

3.8 Statistical analysis

The mean and standard error of all parameters were computed as per Snedecor and Cochran (1994) [22]. The variations in clinical, physiological, haemodynamic, haematological and biochemical parameters were compared at different time intervals within the group and between the groups and were analysed using student ‘t’ test by Snedecor and Cochran.

Table 1: Design of the technical programme of the clinical study

Sl. No.	Groups	Number of animals	Surgeries performed	Anaesthetic protocol
1	Group- I	6	Surgical repair of tibial fracture using IILN	Induction: Romifidine [1] (50 µg/kg, IV) Ketamine [2] (6 mg/kg, IV) Maintenance: Isoflurane [3] (1-2%)
			Surgical repair of tibial fracture using Steinmann pinning	
			Oesophageal obstruction- Oesophagotomy	
			Application of fiberglass for fracture of left metatarsal bone.	
			Plating for fracture of right radius and ulna bones	
			k-nailing for left femur bone fracture	
2	Group – II	6	Surgical repair for left teat injury(ablation)	Induction: Romifidine [1] (50 µg/kg, IV) Propofol [4] (6 mg/kg, IV) Maintenance: Isoflurane [3] (1-2%)
			Application of fiberglass for fracture of left metatarsal bone.	
			Plating for fracture of left tibial bone	
			Plating for fracture of left femur bone	
			Castration by open method	
			Application of fiberglass for fracture of left radius and ulna bone	

1. Sedivet (10 mg/mL), Boehringer Ingelheim, Vetmedica, Inc. U.S.A
2. Aneket (50 mg/mL), Neon Laboratories Ltd., Mumbai, India
3. Sosrane, Neon Laboratories Ltd., Mumbai, India
4. Neorof (10 mg/ml), Neon Laboratories Ltd., Mumbai, India

Fig 1: Goat operated for tibial fracture under Romifidine-Ketamine-Isoflurane combination

4. Results

The effects of romifidine is compared with ketamine and propofol for isoflurane general anaesthesia in goats. The results of the study are presented under the following headings.

4.1 Physiological observations

Physiological parameters namely., heart rate (beats/min), respiratory rate (breaths/min) and rectal temperature (^{0}F) were recorded in goats of both the groups before premedication (0 minute), 10 minutes after premedication and at 5, 30, 60 and 120 minutes after induction of general anaesthesia.

4.2 Heart rate (beats/min)

The Mean ± S.E values of heart rate in goats of group I before premedication (0 minute), 10 minutes after premedication and at 5, 30, 60 and 120 minutes after induction of general anaesthesia were 106.33±2.29, 84.00±1.87,99.67±2.17, 93.00±3.12, 95.83±2.95, and 104.00±2.08 respectively. Significant (P≤0.01) decrease in heart rate was observed at 10 minutes after premedication with romifidine and 5 to 60 minutes after ketamine isoflurane anaesthesia. It increased towards the basal value at 120 minutes after administration of ketamine-isoflurane anaesthesia. However, heart rate remained none significantly at a lower level than the basal value at 120 minutes.

The Mean ± S.E values of heart rate in goats of group II before premedication (0 minute), 10 minutes after premedication and at 5, 30, 60 and120 minutes after induction of

General anaesthesia were 106.00±2.43, 85.66±1.20, 90.16±2.27, 83.50±1.58, 87.83±3.03, and 101.83±2.15 respectively. Heart rate decreased significantly (P≤0.01) at 10 minutes after premedication with romifidine and at 5 to 60 minutes after induction with propofol-isoflurane anaesthesia. It increased towards the basal value at 120 minutes after induction of general anaesthesia.

Comparison between the groups revealed that, significant (P≤0.05) decrease in heart rate was seen at 5 and 30 minutes after induction in goats with propofol than that of goats with ketamine. No significant changes were observed at 60 and 120 minutes after administration of ketamine or propofol-isoflurane anaesthesia. However, heart rate was found to be non-significantly low in romifidine-propofol-isoflurane combination than that of romifidine-ketamine-isoflurane combination.

4.2.1 Respiratory rate (breaths/min)

The Mean ± S.E values of respiratory rate before premedication (0 minute), 10 minutes after premedication and at5, 30, 60 and 120 minutes after induction of general anaesthesia in goats of group I were 26.83±1.01, 22.33 ± 0.66, 24.00±0.57, 18.50±0.61, 18.33±1.45 and 25.66±0.80 respectively. The corresponding values in goats of group II were 28.16±1.13, 22.83±0.98, 20.33±1.11, 17.33±0.91, 17.16±1.68 and 26.16±0.70 respectively.

In goats of both groups I and II, significant (P≤0.01) decrease in respiratory rate was seen at 10 minutes after premedication with romifidine. It continued to decrease and was significantly (p<0.01) at a lower level from 5 to 60 minutes after induction of general anaesthesia in both the groups. At 120 minutes, it started increasing and it was almost nearer to the basal value. Comparison between the groups revealed significant (P≤0.05) decrease at 5 minutes and no significant

decrease at 30, 60 minutes after induction with propofol than with ketamine.

4.2.2 Rectal temperature (0F)

The Mean ± S.E values of rectal temperature before premedication (0 minute), 10 minutes after premedication and at 5, 30, 60 and 120 minutes after induction of general anaesthesia in goats of group I were 102.50±0.76, 101.13±0.72, 101.70±0.76, 99.68±0.54, 99.53±0.74 and 102.20±0.39 respectively. The corresponding values in goats of Group II were 103.28±0.30, 102.50±0.27, 102.43±0.32, 100.01±0.68, 101.43±0.54 and 102.93±0.22 respectively.

In goats of both groups I and II, significant ($P \leq 0.05$) reduction in rectal temperature was observed from 30 to 60 minutes after administration of ketamine or propofol-isoflurane anaesthesia. At 120 minutes after anaesthesia, it was regaining to normal level. Comparison between the groups showed no significant difference with respect to temperature at all intervals of study.

Table 1: Mean ± S.E of physiological parameters at different intervals in goats of groups I and II

Sl. No.	Parameter	Time Intervals		Group I	Group II
1	Heart Rate (beats / minute)	Before premedication	0 min	106.33±2.29	106.00±2.43
		After premedication	10 min	84.00±1.87**	85.66±1.20**
		After ketamine or propofol- isoflurane	5 min	99.67±2.17*[a]	90.16±2.27**[b]
			30 min	94.00±3.12**[a]	83.50±1.58**[b]
			60 min	95.83±2.95**	87.83±3.03**
			120 min	104.00±2.08	101.83±2.15
2	Respiratory Rate (breaths / minute)	Before premedication	0 min	26.83±1.01	28.16±1.13
		After premedication	10 min	22.33±0.66**	22.83±0.98**
		After ketamine or propofol- isoflurane	5 min	24.00±0.57**[a]	20.33±1.11**[b]
			30 min	18.50±0.61**	17.33±0.91**
			60 min	18.33±1.45**	17.16±1.68**
			120 min	25.66±0.80	26.16±0.70
3	Rectal Temperature (0F)	Before premedication	0 min	102.50±0.76	103.28±0.30
		After premedication	10 min	101.10±0.76	102.50±0.27
		After ketamine or propofol- isoflurane	5 min	101.70±0.76	102.43±0.32
			30 min	99.68±0.54*[a]	100.01±0.68*[b]
			60 min	99.53±0.74	101.43±0.54
			120 min	102.20±0.39	102.93±0.22

Means bearing superscript* differ significantly ($P \leq 0.05$) from interval 'before' within the group
Means bearing superscript** differ significantly ($P \leq 0.01$) from interval 'before' within the group
Means bearing superscript a, b differ significantly ($P \leq 0.05$) between the groups at corresponding intervals

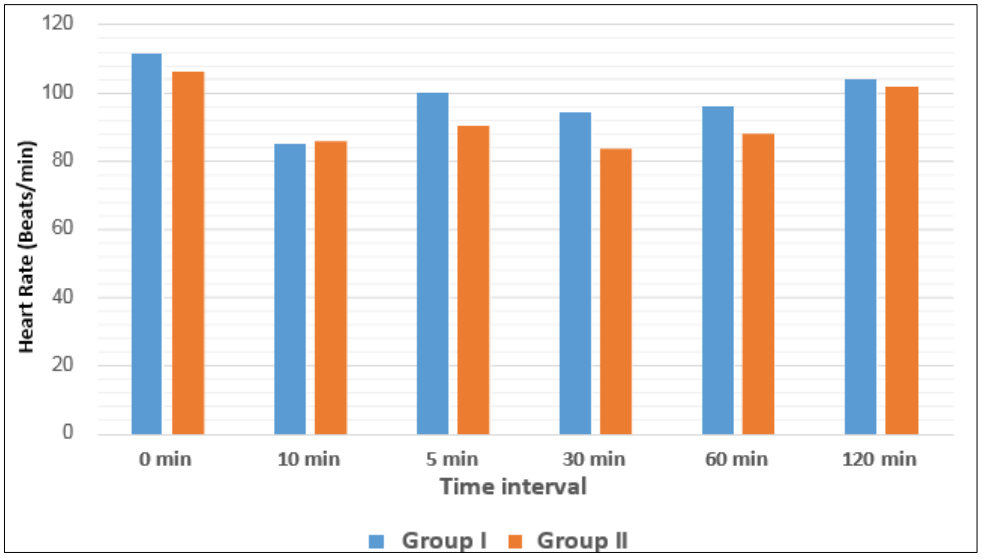

Fig. 1: Mean ±S.E of heart rate (beats/minute) at different intervals in goats of groups I and II

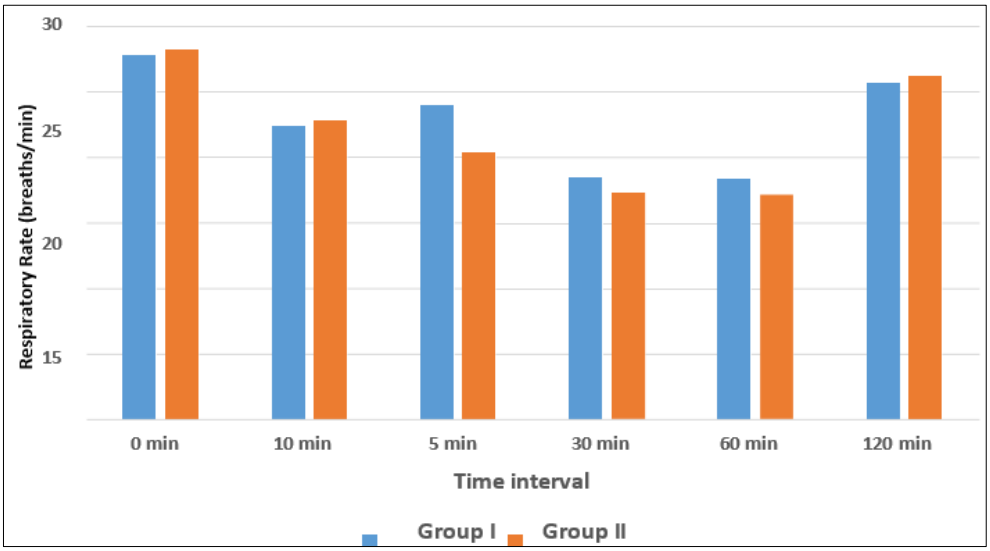

Fig 2: Mean ±S.E of respiratory rate (breaths/minute) at different intervals in goats of groups I and II

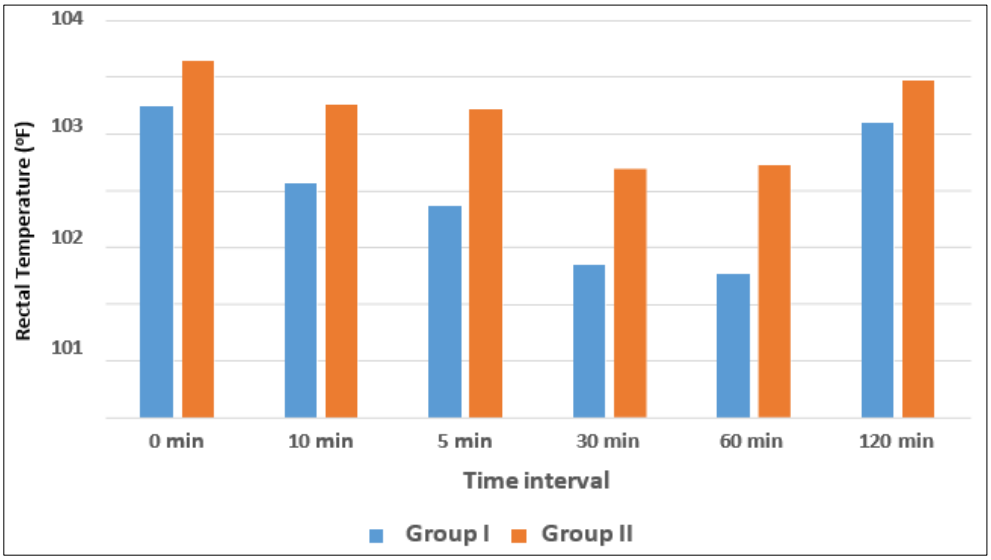

Fig 3: Mean ±S.E of rectal temperature (0F) at different intervals in goats of groups I and II

5. Haemodynamic observations

The haemodynamic observations *viz.*, mean arterial pressure (mm of Hg) and haemoglobin oxygen saturation (%) were estimated in goats of both the groups before premedication (0 minute), 10 minutes after premedication and at 5, 30, 60 and 120 minutes after ketamine or propofol-isoflurane administration.

5.1 Mean Arterial Pressure (mm of Hg)

The Mean ± S.E values of mean arterial pressure before premedication (0 minute), 10 minutes after premedication and at 5, 30, 60 and 120 minutes after induction of general anaesthesia in goats of group I were 118.20±2.72, 98.67±5.22, 100.30±9.62, 101.70±6.31, 99.50±4.99 and 114.16±3.85 respectively. Significant ($P \leq 0.01$) decrease in mean arterial pressure was observed at 10 minutes after premedication with romifidine. It non- significantly increased after ketamine-isoflurane administration. However, MAP was significantly ($P \leq 0.05$) lower at 30 to 60 minutes and non-significantly lower than basal value at 120 minutes.

The Mean ±S.E values of mean arterial pressure before premedication (0 minute), 10 minutes after premedication and at 5, 30, 60 and 120 minutes after induction of general anaesthesia in goats of group II were 117.83±4.49, 99.67±2.15, 92.00±1.71, 84.83±3.17, 87.00±3.86 and 104.00±4.53 respectively. Significant ($P \leq 0.01$) decrease in mean arterial pressure was seen at 10 minutes after romifidine premedication and significantly ($P \leq 0.01$) lower side at 30 to 60 minutes, however it was non-significantly at a lower level at 120 minutes of after administration of propofol-isoflurane anaesthesia.

Comparison between the groups revealed that mean arterial pressure was significantly ($P \leq 0.05$) lower at 60 minutes after administration of general anaesthesia in goats of group II (romifidine-propofol-isoflurane) than in goats of group I (romifidine - ketamine-isoflurane).

5.2 Haemoglobin oxygen saturation (SpO2) (%)

The Mean ±S.E values of haemoglobin oxygen saturation (SpO2) (%) at different intervals in goats of groups I and II are given in Table 11.

The Mean ±S.E values of haemoglobin oxygen saturation before premedication (0 minute), 10 minutes after premedication and at 5,30, 60 and 120 minutes after induction of general anaesthesia in goats of group I were 93.17± 0.30,92.17±0.40, 92.83±0.47, 92.50±0.22, 92.50±0.34 and

93.16±0.47 respectively. The corresponding values in goats of group II were 93.67±0.33, 91.83±1.10, 91.83±1.66, 91.67±0.84, 91.67±0.84 and 93.50±0.42 respectively.

In goats of both groups I and II, non-significant decrease in haemoglobin oxygen saturation was observed at 10 minutes after premedication. It increased towards the normal value once after administration of ketamine-isoflurane anaesthesia. Comparison between the groups showed no significant difference with respect to haemoglobin oxygen saturation at all intervals of study.

Table 2: Mean ± S.E of haemodynamic observations at different intervals in goats of groups I and II

Sl. No.	Parameter	Time Intervals		Group I	Group II
1	Mean Arterial Pressure (mm of Hg)	Before premedication	0 min	118.20±2.72	117.83±4.49
		After premedication	10 min	98.67±5.22**	99.67±2.15**
		After ketamine or propofol - isoflurane	5 min	100.30±9.62	92.00±1.71**
			30 min	101.70±6.31*[a]	84.83±3.17**[b]
			60 min	99.50±4.99**	87.00±3.86**
			120 min	114.16±3.85	104.00±4.53
2	Haemoglobin oxygen saturation (%)	Before premedication	0 min	93.17±0.30	93.67±0.33
		After premedication	10 min	92.17±0.40	91.83±1.10
		After ketamine or propofol - isoflurane	5 min	92.83±0.47	91.83±1.66
			30 min	92.50±0.22	91.67±0.84
			60 min	92.50±0.34	91.67±0.84
			120 min	93.16±0.47	93.50±0.42

Means bearing superscript* differ significantly ($P \leq 0.05$) from interval 'before' within the group Means bearing superscript** differ significantly ($P \leq 0.01$) from interval 'before' within the group Means bearing superscript a, b differ significantly ($P \leq 0.05$) between the groups at corresponding intervals

Physiological observations revealed that heart rate reduced significantly ($P \leq 0.05$) at 10 minutes after premedication in both the groups. Comparison between the groups revealed that, significant ($P \leq 0.05$) decrease in heart rate was seen at 5 and 30 minutes after induction in goats with propofol than that of goats with ketamine. No significant changes were observed at 60 and 120 minutes after administration of ketamine or propofol- isoflurane anaesthesia. However, heart rate was found to be no significantly low in romifidine-propofol-isoflurane combination than that of romifidine -ketamine -isoflurane combination.

In goats of both groups I and II, significant ($P \leq 0.01$) decrease in respiratory rate was seen at 10 minutes after premedication with romifidine. Comparision between the groups revealed significant ($P \leq 0.05$) decrease at 5 minutes and no significance decrease at 30, 60 minutes after induction with propofol than with ketamine.

A significant ($P \leq 0.05$) reduction in rectal temperature was observed from 30 to 60 minutes after administration of ketamine or propofol-isoflurane an anesthesia in both the groups. At 120 minutes after anaesthesia, it was regaining to normal level. Comparison between the groups showed no significant difference with respect to temperature at all intervals of study.

Haemodynamic observations revealed that Significant ($P \leq 0.01$) decrease in mean arterial pressure was seen at 10 minutes after romifidine premedication in both the groups. Between the groups revealed that mean arterial pressure was significantly ($P \leq 0.05$) lower at 60 minutes after administration of general anaesthesia in goats of group II (romifidine- propofol-isoflurane) than in goats of group I (romifidine-ketamine- isoflurane). Non- significant decrease in haemoglobin oxygen saturation at 10 minutes after premedication was observed in both the groups.

6. Discussion

The heart rate decreased significantly at 10 minutes after premedication in both the groups. The results is in agreement with earlier study by Saxena *et al*. (2001) [20] for romifidine -ketamine anaesthesia in goats, Naylor *et al*. (2005) [16] in foals and Selmi *et al*. (2004) [21] in cats. Kinjavdekar *et al.* (2006**)** [10] reported that the heart rate decreased significantly soon after the administration of romifidine subarachnoidally in goats until the end of the observation period. Inhibition of sympathetic tone due to reduction in nor-epinephrine 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 have been reported as the possible mechanisms by which alpha-2-agonists induce bradycardia (MacDonald and Virtanen, 1992) [26].

In our study comparison between the groups revealed that, significant ($P \leq 0.05$) decrease in heart rate was seen at 5 and 30 minutes after induction in goats with propofol than that of goats with ketamine. No significant changes were observed at 60 and 120 minutes after administration of ketamine or propofol-isoflurane anaesthesia. However, heart rate was found to be no significantly low in romifidine-propofol-isoflurane combination than that of romifidine-ketamine-isoflurane combination. Okwudili *et al.* (2014) [18] reported that heart rate significantly ($p<0.05$) decreased in groups xylzine+ ketamine (group A) and xylazine + propofol (B). The heart rate was significantly ($p<0.05$) lower in group A from 20min to 40min after induction when compared to other groups. However, the heart rate was significantly ($p<0.05$) decreased in groups B and D (xylazine + ketamine + propofol) at 60 min when compared to the control (group A).

Heart rate increased towards the basal value once after administration of ketamine- isoflurane anaesthesia in goats of groups 1. This might be attributed to release of catecholamines from peripheral tissue stores, diminution of frequency response of the carotid sinus baroreceptors, stimulation of sympathetic nervous system by ketamine and/or to an atropine like action on the heart (Traber *et al.*, 1968) [23]. Increase in heart rate was observed after administration of ketamine in dogs, goats (Kumar *et al.*, 1986), horses (Muir *et al*., 1999) [15].

However, heart rate was comparatively on lower side in goats of group II induced with propofol than in goats of group I induced with ketamine. The similar findings were observed during a ketamine based total intravenous anaesthesia, a significantly higher heart rate was reported in a group of dogs

receiving ketamine compared to a group of dogs receiving propofol (Hellebrakers *et al*.,1998). Higher values of heart rate during ketamine infusion in comparision to post sedation values in the present study could be attributed to its sympathomimetic action mediated within CNS, inhibition of catecholamine re-uptake by peripheral sympathetic nerve endings and the subsequent effects of catecholamines on the myocardium.

6.1.1 Respiratory rate

In goats of both groups I and II, significant ($P \leq 0.01$) decrease in respiratory rate was seen at 10 minutes after premedication with romifidine, which may be due to direct depression of the respiratory centres by preanesthetic. Kinjavdekar (2006) [10] recorded more prolonged reduction in respiration rate from 5 minute to 75 minutes in goats administered with romifidine and lignocaine subarchnoidally and also reported following systemic administration of romifidine in goats (Saxena *et al*.,2001) [20] and dogs (England *et al*.,1996 and Amarpal *et al*.,2000) [25, 3]. The decrease in respiration rate recorded in the present study conforms to the observation of Celly *et al.* (1997) [5], who also reported a decrease in respiration rate following intravenous administration of romifidine in sheep. It continued to decrease and was significantly ($p<0.01$) at a lower level from 5 to 60 minutes after induction of general anaesthesia in both the groups. At 120 minutes, it started increasing and it was almost nearer to the basal value. Comparison between the groups revealed significant ($P \leq 0.05$) decrease at 5 minutes and non-significant decrease at 30, 60 minutes after induction with propofol than with ketamine. This might be due to some degree of hyperventilation induced by ketamine. Prassinos *et al.* (2005) [19] reported that ketamine caused less induction apnoea and respiratory depression in comparison with propofol in goats. Propofol caused a further decrease in mean respiration rate by depressing central inspiratory drive and ventilatory response to arterial carbon-dioxide response (Singh, 2013) [11].

Reduction in respiratory rate following dexmedetomidine administration was observed in sheep (Monsang, 2011) [27], buffalo calves (Khattri *et al.,* 2013) [11], buffaloes (Singh *et al.,* 2013) [11] and goats (Kumar *et al.,* 2014) [29] which might be due to the inhibition of locus coeruleus neurons through the activation of alpha-2-adrenergic pathway. Singh (2013) [11] opined that ketamine infusion was responsible to cause significant respiratory depression with decrease in all measures of ventilation in buffaloes. Hikasa *et al.* (2000) [32] reported significant decrease in respiratory rate throughout the study period after atropine- thiopental-isoflurane anaesthesia in sheep. Apnoea has been reported in goats after propofol administration while ketamine alone or ketamine + xylazine caused apnoea in goat .Propofol alone or with xylazine induced respiratory depression in dogs. The respiration rate decreased below the pre-induction level following propofol injection but, thereafter, it increased above the post-induction level.

6.1.2 Rectal temperature

In our study in goats of both groups I and II, significant ($P \leq 0.05$) reduction in rectal temperature was observed from 30 to 60 minutes after administration of ketamine or propofol-isoflurane anaesthesia. The decreased temperature might be due to generalized sedation, decreased metabolic rate, muscle relaxation and central nervous system depression (Khattri *et al.,* 2013) [11]. At 120 minutes after anaesthesia, it was regaining to normal level. Alpha-2-agonists have been reported to induce prolonged depression of thermoregulation.

Comparison between the groups showed no significant difference with respect to temperature at all intervals of study. Malik *et al.* (2012) also recorded significant decrease in rectal temperature in water buffaloes administered ketamine from 40 minutes up to the end of observation period. Ok wudili *et al.* (2014) [18] also recorded significant decrease in rectal temperature in group of goats administered xylazine /propofol from 10 minutes to 40 minutes after induction when compared to xylazie/ketamine. Decreased temperature might also be due to decreased skeletal muscle tone, shivering threshold, vasodilation and impairment of thermoregulatory centre. Decrease in rectal temperature was observed after dexmedetomidine administration in dogs. Buffalo calves (Khattri *et al.,* 2013) [11], buffaloes (Singh *et al.,* 2013) [11] and goats (Kumar *et al.,* 2014) [9]. Chitale *et al.* (1998) observed decrease in rectal temperature in atropinized goats following diazepam- ketamine or romifidine-ketamine anaesthesia. Kumandas and Elma (2015) [34] observed significant decrease in temperature at 5 to 60 minutes of propofol-isoflurane anaesthesia when compared with propofol-sevoflurane anaesthesia in goats. Haskins *et al.* (1985) [9] and Muir *et al.* (1999) [15] reported increase in body temperature after ketamine administration in dogs and horses respectively.

6.2 Haemodynamic observations

6.2.1 Mean arterial pressure

In our study Significant ($P \leq 0.01$) decrease in mean arterial pressure was observed at 10 minutes after premedication with romifidine in both the groups. However, it increased after ketamine-isoflurane administration in group I, which might be due to selective positive inotropic influence of ketamine on heart muscles or reflex organic autonomic nervous system changes. However, it was below the base line value at all the intervals of study. The decrease in the mean arterial pressure was more significant at 10 minutes after premedication and 30, 60 minutes after general anaesthesia in goats of both groups. Romifidine produced a significant reduction in the mean arterial pressure (MAP), similar to other alpha-2-adrenoceptors agonists used in goats (Kinjavdekar *et al.,* 1999). The alpha-2-adrenoceptors agonists produce a biphasic effect on arterial blood pressure, with an initial transient increase, coincident with a reflex-mediated decrease in heart rate, followed by a long-lasting hypotension and bradycardia. Biphasic pattern in MAP characterised by initial hypertension has been reported by Celly *et al.* (1997) [5] after intravenous administration of romifidine in sheep. Hypotension has also been reported following the systemic administration of romifidine in goats Saxena *et al.* (2001) [20]. Similar effects on MAP have been observed after the subarachnoid administration of lidocaine and xylazine/medetomidine, and romifidine and ketamine in goats ((Kinjavdekar *et al*.,1998). In our study we recorded significant decrease in MAP at 60 minutes after induction with propofol.

However, in contrast Carroll *et al.* (1998)[30] had reported increase in SAP (systemic arterial pressure) and MAP after inducing anaesthesia with propofol in goats and observed an increasing trend towards end over 90 minutes observation period. Aithal *et al.* (2001) [2] recorded a significant increase in central venous pressure in goats administered romifidine (50 µg/kg) and romifidine (50 µg/kg) –ketamine (2.5 mg/kg) combination in trathecally. Mean arterial pressure was reduced in both groups, however it was more markedly

reduced in romifidine alone group. A decrease in blood pressure after propofol administration has been reported in goats and has been associated with arterial and venous vasodilatation and decreased contractility of the heart. A decrease in arterial pressure after propofol administration was commonly reported in domestic animals and was found associated with arterial and venous vasodilatation and decreased contractility of the heart (Robinson *et al*., 1997) [31] Afshar *et al.* (2005) [1] reported that MAP decreased none significantly ($p<0.01$) at 5 minutes and significantly at 15-60 minutes after induction of xylazine and ketamine anaesthesia at 0.20 mg/kg, IM and 10 mg/kg, IV respectively in goats.

A dose dependent decrease in systemic blood pressure was observed under isoflurane anaesthesia in goats (Hikasa *et al.*, 1998 and Kumandas and Elma, 2015) [32, 34].

6.2.2 Haemoglobin oxygen saturation

The haemoglobin oxygen saturation decreased non-significantly at 10 minutes after premedication in both the groups. It increased towards the normal value once after administration of ketamine or propofol-isoflurane anaesthesia and no significant difference was seen between the groups at all the intervals of study. Luna *et al*. (2000) [14] reported haemoglobin O2 saturation was lower at 90 minutes in the dogs treated with romifidine/ketamine. However, Selmi *et al.* (2004) [21] reported haemoglobin saturation was not different over time in any given dose of romifidine in their study (100, 200, and 400 µg /kg or xylazine 1 mg kg) 1) and mean SpO2 values were >94% at all times in cats. Mohamadnia *et al.* (2008) reported no significant changes regarding SpO2 values after ketamine-isoflurane anaesthesia in sheep. Khattri *et al.* (2013) [11] reported significant decrease in SpO2 at 15 and 20 min and a highly significant decrease in SpO2 from 30 to 60 min of observation following dexmedetomidine - propofol anaesthesia in buffalo calves. Kumar *et al.* (2014) [9] reported that SPO2 values were no significantly higher at most of the intervals after dexmedetomidine-ketamine anaesthesia in goats. Fayyaz *et al.* (2009) [28] observed that isoflurane anaesthesia resulted in more haemodynamic depression when compared with diazepam-propofol or diazepam-ketamine anaesthesia in dogs. This decrease in the SpO2 levels in the present study might be due to the decrease in the respiratory rate, which occurred as a result of respiratory depression at anaesthetic dosages. The changes in SpO2 during propofol or ketamine- isoflurane anaesthesia could be adjusted easily by changing anaesthetic settings.

7 Conclusion

Physiological observations revealed that heart rate reduced significantly ($P\leq0.05$) at 10 minutes after premedication in both the groups. Comparison between the groups revealed that, significant ($P\leq0.05$) decrease in heart rate was seen at 5 and 30 minutes after induction in goats with propofol than that of goats with ketamine. No significant changes were observed at 60 and 120 minutes after administration of ketamine or propofol- isoflurane anaesthesia. However, heart rate was found to be non-significantly low in romifidine-propofol-isoflurane combination than that of romifidine-ketamine -isoflurane combination.

In goats of both groups I and II, significant ($P\leq0.01$) decrease in respiratory rate was seen at 10 minutes after premedication with romifidine. Comparision between the groups revealed significant ($P\leq0.05$) decrease at 5 minutes and no significance decrease at 30, 60 minutes after induction with propofol than with ketamine.

A significant ($P\leq0.05$) reduction in rectal temperature was observed from 30 to 60 minutes after administration of ketamine or propofol-isoflurane anaesthesiai in both the groups. At 120minutes after anaesthesia, it was regaining to normal level. Comparison between the groups showed no significant difference with respect to temperature at all intervals of study.

Haemodynamic observations revealed that Significant ($P\leq0.01$) decrease in mean arterial pressure was seen at 10 minutes after romifidine premedication in both the groups. Between the groups revealed that mean arterial pressure was significantly ($P\leq0.05$) lower at 60 minutes after administration of general anaesthesia in goats of group II (romifidine- propofol-isoflurane) than in goats of group I (romifidine-ketamine- isoflurane). Non- significant decrease in haemoglobin oxygen saturation at 10 minutes after premedication was observed in both the groups.

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