

## Cardiovascular Effects of Dexmedetomidine-Ketamine Compared with Thiopental Sodium in Sevoflurane Anesthetized Goats

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### Abstract

The objective of the study is to compare the efficacy and cardiopulmonary effects of dexmedetomidine-ketamine and thiopental sodium in sevoflurane anesthetized in goats. Seven healthy adult female goats with body weight of 35.3±3.82 kg (median±IQ). Each goat received both anesthetics in a randomized cross-over design, with at least 2 weeks intervals. Anesthesia was induced with intravenous dexmedetomidine (2 mg/kg) and ketamine (10 mg/kg) or thiopental sodium (19.3±3.42 mg/kg) (mean±SD) and maintained with sevoflurane for 2 hours. Arterial blood pressure, heart rate (HR), respiratory rate (RR) and arterial blood gases were monitored. Induction of anesthesia was smooth in all goats. Mean recovery times were significantly longer in thiopental sodium group (P<0.05). Side effects were less common in dexmedetomidine-ketamine group (DKS) than thiopental sodium group (TS). Recovery was uneventful in both groups. Although the mean arterial blood pressures (MAP) were decreased in both groups (P<0.05), the prolonged decrease was recorded in DKS group. The temperature was decreased in both groups in time (P<0.05). Changes in blood oxygenation were significantly higher in DKS group at 15 and 120 minutes compared to TS group (P<0.05). Dexmedetomidine-ketamine provides better anesthesia when compare with thiopental sodium as an induction agent before sevoflurane anesthesia in goats.

**Keywords:** Anesthesia, goat, recovery, side effects.

### INTRODUCTION

The  $\alpha_2$ -adrenoceptor agonists are widely used as a sedatives, analgesics and anesthetic drugs in veterinary medicine (Riebold 2007). Dexmedetomidine is one of the two optical enantiomers of medetomidine (Kastner et al., 2001) and its use has become increasingly popular in veterinary medicine especially in dogs and cats (Pascocoe et al., 2006; Monteiro et al., 2009). However, its anesthetic, recovery and side effects in goats has not been investigated except very few studies (Lawrence et al., 1997; Kutter et al., 2006).

The combination of  $\alpha_2$ -adrenoceptor agonists and ketamine is mostly preferable anesthesia in small ruminants (Lin et al., 1997; Kastner et al., 2001; Jud et al., 2010). Rapid onset and short duration of action are the advantages of  $\alpha_2$ -adrenoceptor agonists and ketamine or thiopental sodium, however repetitious or long-term infusion often results in a prolonged recovery; therefore inhalation anesthesia is frequently used for long term procedures (Lin et al., 1997; Kastner et al., 2005; Prassinis et al., 2005; Mohamadnia et al., 2008).

Thiopental sodium is also popular anesthetics in small ruminants (Lin et al., 1997; Prassinis et al., 2005). Thiopental sodium provides short duration of acting time in goats. It has been used as an induction agent to provide an adequate depth of anesthesia for intubation prior to inhalation anesthesia in goats. The previously reported anesthetic studies on small ruminants were especially on sheep, there are not so many studies reported on goat anesthesia (Prassinis et al., 2005; Karşlı et al., 2019).

The aim of this study was to compare the efficacy and cardiopulmonary effects of dexmedetomidine-ketamine and thiopental sodium in sevoflurane anesthetized goats.

### MATERIALS AND METHODS

The study was approved by the Animal Research Local Ethics Committee of Kırıkkale University. Seven adult non-pregnant female Angora goats were used in this study. The goats were healthy, based on physical examination and complete blood count. The age of the goats ranged between 3-6 years and weight between 31.6-42 kg. Each goat received both anesthetic protocols randomly, with at least two week intervals. Food and water were withheld for 16 and 6 hours, respectively. The sample size of the study was calculated with the G\*Power (ver. 3.1.9.2, Franz Faul, Universität Kiel, Germany) statistical analysis. The required sample size for 80% power,  $\alpha = 0.05$  type I error,  $\beta = 0.147$  and sample size was calculated as 21.

### Anesthesia

A 22 G cannula was placed in the auricular artery for monitoring heart rate (HR), arterial blood pressure and obtain samples for blood gas analysis. The pulse oximeter probe was placed on the pinna. Heart rate (HR), respiratory rate (RR), systolic (SAP), diastolic (DAP) and mean (MAP) arterial blood pressures, oxygen saturation (SpO<sub>2</sub>) and oesophageal temperature were recorded (Petaş, KMA 800, Turkey) prior to anesthesia, after induction of anesthesia and 5, 10, 15, 30, 60, 90 and 120 minutes thereafter. A 20 G catheter was inserted into auricular vein

for administration of drugs and IV fluids. Anesthesia induction was performed using dexmedetomidine (Precedex 200, Meditera, USA) (2 mg/kg) and ketamine (Ketazol, Richterpharma, Austria) (10 mg/kg) in dexmedetomidine-ketamine group (DKS) and thiopental sodium (Pental®Sodyum 1g, I.E. Ulagay, Turkey) (15 mg/kg) in thiopental sodium group (TS) via intravenous route. In the TS group, thiopental sodium was administered within 90-120 seconds as an intravenous bolus to induce anaesthesia. Incremental doses were administered until the intubation of the trachea was possible in the thiopental sodium group. Orotracheal intubation was carried out using an intubation tube (size no:8). Immediately after tracheal intubation the nasogastric intubation was performed via the oral route to prevent the ruminal tympany during anaesthesia. Afterwards, the goats were placed in right lateral recumbency and connected to a semi-closed circle rebreathing system (TMS Maxi 2200, Turkey). Anaesthesia was maintained with sevoflurane (Sevorane, Abbott, UK) in oxygen with a fresh gas flow was 2 l/min and the vaporizer (Royal Medical Ltd., Korea) set at 3-5 %. The goats were allowed to breathe spontaneously. Lactated Ringer's solution (Ringesol, Vilsan, Turkey) was administered intravenously at a rate of 4 ml kg<sup>-1</sup> h<sup>-1</sup> throughout anaesthesia by a continuous infusion pump (Volumetric infusion pump, Accumate 2300, Germany). A sedation score and complications during induction were recorded. The degree of sedation was assessed using a 0-2 scale. The sedation scale was adopted from the study of Dziki et al. (2010) (Table 1). Postinduction apnoea was defined as a period of >30 seconds without spontaneous ventilation, and in such cases intermittent positive pressure ventilation was initiated manually until spontaneous respiration restart. To ensure that arterial blood gases values were within the reference ranges, blood of pH, arterial oxygen (PaO<sub>2</sub>) and carbon monoxide (PaCO<sub>2</sub>) were measured by blood gas analyzers (Gastat Mini, Techno Medica, Japan) at 15-minute intervals. Anesthetic depth was assessed by the same person (ZP) by clamping the claw with Kocher forceps for 60 seconds or until purposeful movement occurred. If purposeful movement occurred the maintenance of sevoflurane was increased to 5% for at least 2 minutes, and anesthetic depth was reevaluated. After the anesthetic depth was considered satisfactory, sevoflurane was decreased to 3% and maintained constant. No attempt was performed to prevent the heat loss during anaesthesia.

**Table 1.** The sedation scale of the goats

| Scale |  |
|-------|--|
| 0     | No sedation  |
| 1     | Moderate sedation-the goat assumed sternal recumbency  |
| 2     | Heavy sedation- the goat failed to maintain sternal recumbency and was unable to hold up its head. |

Administration of sevoflurane was discontinued after 120 minutes and the goats allowed to recovery from anaesthesia. The goats were extubated after the swallowing reflex was regained. The time to recovery of swallowing reflex, first head movement, sternal recumbency and ability to stand up were recorded.

#### Statistical analysis

Statistical analyses were performed with commercial software (SPSS Inc., Chicago, IL, USA). The normality

check of the variables was performed by the Shapiro-Wilk test and the data are reported as median and interquartile range (IQR). Within-group differences in HR, SAP, MAP, DAP and temperature were analyzed by Friedman's nonparametric test while the between group differences at each time point and also the differences in recovery periods between groups are compared by using Wilcoxon signed rank test. All differences were considered significant for  $p < 0.05$ .

#### RESULTS

The induction of anaesthesia was smooth in both groups. The sedation score of the goats after dexmedetomidine-ketamine and thiopental sodium administration was 2. Although all the goats became heavily sedated after IV administration of 2 mg/kg dexmedetomidine, tracheal intubation cannot be performed because of the insufficient relaxation of jaw. Tracheal intubation became possible after 10 mg/kg ketamine administration in the DKS group. Mean effective dose of thiopental sodium for induction of anaesthesia in goats were 19.3±3.42 mg/kg (mean±SD).

In both anaesthesia protocols, induction and recovery were smooth and no side effects were recorded. Excessive regurgitation was observed in a goat in the TS group before tracheal intubation that ruminal content was needed to be aspirated to perform tracheal intubation. The amount of salivation was higher in all goats in the DKS group than the TS group during the anaesthesia period; However, no complication was encountered as a result of tracheal intubation.

Apnoea was recorded in 3 goats after thiopental sodium administration but it resolves spontaneously in 2 minutes after manual ventilation. Neither hypoxemia nor respiratory depression was recorded in both groups.

Recovery from anaesthesia was smooth and uneventful in all cases. Recovery times were shorter in the DKS group than in the TS group (Table 2). The differences between groups were statistically significant ( $p \leq 0.043$ ).

**Table 2.** Recovery times of goats induced with dexmedetomidine-ketamine or thiopental sodium and maintained with sevoflurane. Data are given as median ±IQR.

| Recovery times (minute)     | DKS    | TS          | P value |
|-----------------------------|--------|-------------|---------|
| Time to extubation          | 5±4    | 11±7        | 0.018   |
| Time to first head movement | 14.5±4 | 19.0±38.25  | 0.043   |
| Time to sternal recumbency  | 16.0±7 | 34±56.75    | 0.043   |
| Time to stand up            | 35±17  | 57.5±115.25 | 0.027   |

DKS (Deksmedetomidine-ketamine group), TS (Thiopental sodium group)

Dexmedetomidine caused a decrease in HR. The median baseline HR was 85±16 and it was reduced to 73±41 after dexmedetomidine administration and 69±35 after ketamine administration. In contrast, thiopental sodium caused an increase in HR. The median HR differences were statistically significant between groups at all time points except the baseline and 120. minutes ( $p \leq 0.043$ ). While HR values decreased after induction with ketamine in the DKS group compared to baseline values ( $P = 0.001$ ), it increased in the TS group ( $P = 0.041$ ) (Table 3).

In both groups, respiratory rate (RR) decreased after induction compared to the baseline value ( $P = 0.01$ ), but did not differ from baseline values at the other times

points. Intergroup analyses revealed that TS group had a significantly lower RR values after induction (P=0.01).

There was no statistically significant difference in SPO<sub>2</sub> values between and within groups. (P>0.05) (Table 3).

**Table 3.** Cardiopulmonary measurements and body temperatures of 7 goats anesthetised with dexmedetomidine-ketamine-sevoflurane or thiopental sodium-sevoflurane at intervals.

|                  |            | Time (minute) |                       |                        |                          |                          |                        |                        |                       |                       |                         |
|------------------|------------|---------------|-----------------------|------------------------|--------------------------|--------------------------|------------------------|------------------------|-----------------------|-----------------------|-------------------------|
| Variable         | Unit       | Group         | Baseline              | Postinduction          | 5                        | 10                       | 15                     | 30                     | 60                    | 90                    | 120                     |
| HR               | Beat/min   | DKS           | 85±16 <sup>a</sup>    | 69±35 <sup>bc</sup>    | 61±14 <sup>b</sup>       | 69±15 <sup>c</sup>       | 71±16 <sup>c</sup>     | 71±10 <sup>c</sup>     | 69±27 <sup>c</sup>    | 69±10 <sup>c</sup>    | 86±24 <sup>ac</sup>     |
|                  | Beat/min   | TS            | 79±18 <sup>ab</sup>   | 100±15 <sup>ab,A</sup> | 102±11 <sup>a,A</sup>    | 94±9 <sup>b,A</sup>      | 94±9 <sup>ab,A</sup>   | 93±10 <sup>ab,A</sup>  | 90±21 <sup>ab,A</sup> | 89±15 <sup>a,A</sup>  | 93±12 <sup>ab</sup>     |
| RR               | Breath/min | DKS           | 24±10 <sup>a</sup>    | 24±0 <sup>b</sup>      | 18±4 <sup>b</sup>        | 24±6 <sup>ab</sup>       | 24±10 <sup>ab</sup>    | 19±20 <sup>ab</sup>    | 19±14 <sup>ab</sup>   | 18±18 <sup>ab</sup>   | 28±2 <sup>ab</sup>      |
|                  | Breath/min | TS            | 24±6 <sup>a</sup>     | 20±8 <sup>b,A</sup>    | 22±6 <sup>ab</sup>       | 24±7 <sup>ab</sup>       | 24±4 <sup>ab</sup>     | 24±4 <sup>ab</sup>     | 25±1 <sup>ab</sup>    | 24±8 <sup>ab</sup>    | 20±7 <sup>ab</sup>      |
| SpO <sub>2</sub> | %          | DKS           | 98±1                  | 98±1                   | 98±4                     | 98±5                     | 100±3                  | 98±2                   | 100±2                 | 98±3                  | 98±3                    |
|                  | %          | TS            | 99±1                  | 99±2                   | 98±3                     | 100±3                    | 97±7                   | 99±3                   | 99±3                  | 98±2                  | 98±3                    |
| SAP              | mmHg       | DKS           | 107±12 <sup>a</sup>   | 94±41 <sup>abc</sup>   | 92±14 <sup>b</sup>       | 86±10 <sup>bc</sup>      | 77±11 <sup>bc</sup>    | 74±20 <sup>ce</sup>    | 68±26 <sup>bc</sup>   | 69±22 <sup>de</sup>   | 81±31 <sup>bc</sup>     |
|                  | mmHg       | TS            | 115±21 <sup>a</sup>   | 112±35 <sup>b</sup>    | 93±37 <sup>c</sup>       | 83±45 <sup>bc</sup>      | 87±38 <sup>bc</sup>    | 91±18 <sup>bc</sup>    | 96±16 <sup>b</sup>    | 96±17 <sup>bc,A</sup> | 97±8 <sup>bc</sup>      |
| DAP              | mmHg       | DKS           | 65±11 <sup>a</sup>    | 64±35 <sup>abc</sup>   | 57±11 <sup>bc</sup>      | 54±22 <sup>bc</sup>      | 43±20 <sup>cf</sup>    | 46±9 <sup>def</sup>    | 45±12 <sup>defg</sup> | 42±11 <sup>df</sup>   | 47±27 <sup>abc</sup>    |
|                  | mmHg       | TS            | 71±26 <sup>a</sup>    | 65±31 <sup>b</sup>     | 63±17 <sup>b</sup>       | 53±25 <sup>b</sup>       | 55±29 <sup>b</sup>     | 67±20 <sup>b,A</sup>   | 66±21 <sup>b,A</sup>  | 66±21 <sup>b,A</sup>  | 70±10 <sup>b</sup>      |
| MAP              | mmHg       | DKS           | 82±14 <sup>a</sup>    | 78±37 <sup>ab</sup>    | 66±13 <sup>bd</sup>      | 60±23 <sup>bcd</sup>     | 56±18 <sup>ce</sup>    | 60±9 <sup>dc</sup>     | 50±21 <sup>dc</sup>   | 57±13 <sup>cd</sup>   | 60±25 <sup>abc</sup>    |
|                  | mmHg       | TS            | 90±27 <sup>a</sup>    | 79±29 <sup>b</sup>     | 76±28 <sup>c</sup>       | 66±30 <sup>c</sup>       | 66±26 <sup>ce</sup>    | 76±20 <sup>bc,A</sup>  | 80±16 <sup>bc,A</sup> | 80±19 <sup>bc,A</sup> | 83±9 <sup>bc,A</sup>    |
| Temp.            | °C         | DKS           | 39.5±0.6 <sup>a</sup> | 39.5±0.7 <sup>bd</sup> | 39.5±0.7 <sup>ab</sup>   | 39.4±0.7 <sup>dc</sup>   | 39.4±0.6 <sup>ce</sup> | 39.2±0.6 <sup>ef</sup> | 39.2±0.9 <sup>f</sup> | 39.0±1 <sup>f</sup>   | 38.5±1.2 <sup>g</sup>   |
|                  | °C         | TS            | 39.0±0.4 <sup>a</sup> | 39.0±0.4 <sup>ab</sup> | 38.8±0.6 <sup>ab,A</sup> | 38.8±0.8 <sup>bc,A</sup> | 38.7±1 <sup>cd,A</sup> | 38.7±1 <sup>d,A</sup>  | 38.3±1 <sup>e,A</sup> | 38.2±1 <sup>f,A</sup> | 38.1±0.8 <sup>g,A</sup> |

<sup>a,b,c,d,e,f,g</sup>Significant change with time within same group denominated by different letters in the same line are significant (P<0.05). <sup>A</sup> Differences between the groups denominated by different letters in the same column are significant (P<0.05). Data are presented as median±iqr. DKS (Deksmedetomidine-ketamine group), TS (Thiopental sodium group), HR (Heart rate), RR (respiratory rate), SpO<sub>2</sub> (Blood oxygen saturation), SAP (Systolic arterial blood pressure), DAP (Diastolic arterial blood pressure), MAP (Mean arterial blood pressure).

Significant differences were found within groups between the SAP, MAP, DAP values during anesthesia period with respect to baseline values (P<0.05). The blood pressure difference between groups was statistically significant at 90. min in SAP, at 30., 60., 90. min in DAP and at 15., 30., 60., 90. and 120. min in MAP (P<0.05) (Table 3).

Rectal temperatures were decreased in both groups until the end of the study. In the same time intervals between the groups and within the group, statistically significant differences were found in rectal body

temperatures after induction and maintenance of anesthesia in both groups (P <0.05) (Table 3).

Significant differences were found between the groups with respect to post-induction Ph value, 30-minute PaCO<sub>2</sub>, and 15 minute and 120 minute PaO<sub>2</sub> levels. There were significant differences between baseline and at 15, 30 and 120 minutes Ph levels in the TS group. In the DKS group, significant differences existed between the baseline and at the other time points PaCO<sub>2</sub> levels (P<0.05). Both groups showed significant differences between the baseline PaO<sub>2</sub> levels and PaO<sub>2</sub> levels at the other time points (P<0.05) (Table 4).

**Table 4.** Blood gases results of goats induced with dexmedetomidine-ketamine or thiopental sodium and maintained with sevoflurane.

|                   |       | Time (min) |                        |                          |                          |                          |                          |
|-------------------|-------|------------|------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Values            | Group | Baseline   | After induction        | 15                       | 30                       | 60                       | 120                      |
| PH                | TS    | 7.46±0.04  | 7.39±0.08              | 7.29±0.07 <sup>*</sup>   | 7.29±0.07 <sup>*</sup>   | 7.36±0.12                | 7.38±0.10 <sup>*</sup>   |
|                   | DKS   | 7.44±0.06  | 7.34±0.07 <sup>†</sup> | 7.32±0.10 <sup>*</sup>   | 7.37±0.07                | 7.38±0.27                | 7.39±0.18                |
| PaCO <sub>2</sub> | TS    | 47.7±10.9  | 46.5±11.3              | 49.4±16.6                | 54.6±9.0                 | 49.1±13.1                | 56.8±21.3                |
|                   | DKS   | 37.0±6.1   | 53.1±10.2 <sup>*</sup> | 47.2±16.0 <sup>*</sup>   | 44.7±5.6 <sup>†</sup>    | 51.8±19.2                | 50.0±15.7 <sup>*</sup>   |
| PaO <sub>2</sub>  | TS    | 84.1±22.4  | 61.6±103.8             | 175.6±146.2              | 216.5±189.1 <sup>*</sup> | 277.1±208.6 <sup>*</sup> | 291.6±149.2 <sup>*</sup> |
|                   | DKS   | 111.0±41.5 | 52.0±67.1              | 368.4±266.7 <sup>†</sup> | 333.4±169.2 <sup>*</sup> | 321.0±118.2 <sup>*</sup> | 460.0±278.1 <sup>†</sup> |

<sup>\*</sup>Differences within same group between baseline and at other time points denominated by different letters in the same line are significant (P<0.05). <sup>†</sup> Differences between the groups denominated by different letters in the same column are significant (P<0.05). Data are presented as median±iqr. DKS (Deksmedetomidine-ketamine group), TS (Thiopental sodium group), pH (Arterial blood pH), PaCO<sub>2</sub> (Arterial carbon dioxide partial pressure), PaO<sub>2</sub> (Arterial oxygen partial pressure)

## DISCUSSION AND CONCLUSION

Sedatives used to tranquilize small ruminants include  $\alpha$ -2-adrenoreceptor agonists such as xylazine, romifidine, detomidine, medetomidine, and dexmedetomidine (Kastner 2006; Riebold 2007). It has been reported that hypoxemia develops after using  $\alpha$ -2-adrenoreceptor

agonists in sheep (Celly et al., 1997), but it has also been reported that this condition occurs only after the use of xylazine in goats (Kumar and Thurmon 1979). Several authors advise against the use of a sedative agent prior to anesthesia induction in sheep and goats due to the risk of regurgitation and delayed post-anesthesia recovery. They

instead recommend the use of a short-acting anesthetic agent that ensures rapid anesthesia induction (Hall et al., 2001; Prassinis et al., 2005; Riebold 2007). Sedation in animals may vary by the administered dose and the temperament of a given animal species (Kastner 2006). It is reported that the use of a combination of  $\alpha_2$ -adrenoceptor agonists and ketamine potentiates the analgesic effect and prolongs anesthesia duration although it also causes respiratory depression in a dose-dependent manner (Hall et al., 2001). The dose of dexmedetomidine in this study was chosen on the basis of the studies of Kutter et al. (2006) and Kastner et al. (2006), and the induction dose of ketamine was the same as in the study of Prassinis et al. (2005). Prassinis et al. (2005) recorded an increase in jaw tone after ketamine induction in 2 of 7 goats and reported difficulty in tracheal intubation. According to the result of this study, the combination of 2  $\mu\text{g}/\text{kg}$  dexmedetomidine with 10  $\text{mg}/\text{kg}$  ketamine provided good muscle relaxation for tracheal intubation and small surgical procedures.

Thiopental sodium is one of the most popular anesthetics used in small ruminants. Smooth and rapid induction of anesthesia was reported after thiopental sodium administration. The dose of thiopental sodium used for induction of anesthesia in the current study was higher than those reported by the studies performed by Hikasa et al. (2002) and Prassinis et al. (2005). In the presented study, although the preplanned dosage of thiopental sodium was 10  $\text{mg}/\text{kg}$ , intubation was not possible with this dosage in goats, which necessitated incremental dosages. Three animals exhibited apnea after induction with thiopental sodium, which may have resulted from a high intravenous dose (Galatos 2011).

Regurgitation is an important complication in small ruminants before tracheal intubation (Riebold 2007; Jud et al., 2010). It commonly occurs during light anesthesia when the cardia relaxes. Maintenance of laryngeal and swallowing reflexes during regurgitation increases the risk of aspiration. With regard to regurgitation, it has been reported that either thiopental sodium or ketamine resulted in regurgitation during the induction and maintenance of anesthesia (Prassinis et al., 2005). Other researchers evaluated the administration of  $\alpha_2$ -adrenoceptor agonists prior to ketamine and reported no regurgitation during induction and anesthesia (Jud et al., 2010). In a previous study (Prassinis et al., 2005), it is reported that laryngeal and swallowing reflexes are maintained during ketamine anesthesia; however, in this study, 2  $\mu\text{g}/\text{kg}$  dexmedetomidine that was intravenously administered prior to 10  $\text{mg}/\text{kg}$  ketamine depressed both reflexes while it provided smooth tracheal intubation without regurgitation. The incidence of regurgitation in this study is lower than that reported by Prassinis et al., (2005) after thiopental sodium administration. It may have been related to an approximately 3 times higher thiopental sodium dose used in our study, which ensures deeper anesthesia, depression of the laryngeal and swallowing reflexes, and facilitated intubation.

It has been reported that small ruminants need to recover early from anesthesia due to the risk of hypoxemia and tympany. Early recovery ensures to minimize the risk of aspiration of the contents resulting from regurgitation. It is reported that the administration of sedatives prior to induction will prolong post-anesthesia recovery (Hall et al., 2001; Prassinis et al., 2005). In a study, induction was achieved by thiopental sodium or ketamine, and it was reported that the goats that were administered thiopental

sodium anesthesia assumed the sternal position and stood up earlier (Prassinis et al., 2005). In the present study, the post-anesthesia recovery time was found to be shorter in the DKS group than that reported by Prassinis et al. (2005). Except for the return of stand-up time, all recovery times in the TS group were similar to the times reported by Prassinis et al. (2005) after thiopental sodium in goats. The longer stand-up times may be related to the high doses we used, suggesting that cumulative effects of the thiopental sodium remained after 120 minutes in goats. The duration and the potency of the anesthetic effect of thiopental sodium are dose-dependent in goats, with higher doses possibly causing prolonged recovery times (Hall et al., 2001; Riebold 2007; Galatos 2011). As compared to the recovery times in the DKS group, it was shorter in this study than those reported by Prassinis et al. (2005) who used the same dose of ketamine with a shorter period of Sevoflurane administration. It may be possible that the goats in the Prassinis et al. (2005) study were under the influence of ketamine during the recovery period after 30-minute sevoflurane administration. To the authors' knowledge, there is no information available as to the pharmacokinetics of ketamine in goats. It was reported that in adult sheep, ketamine has an elimination half-life of 30 minutes (Jud et al., 2010). If the pharmacokinetics of ketamine in goats is similar to sheep, the residual effects of ketamine have a minor influence on recovery after 120 minutes.

In several studies, it has been reported that  $\alpha_2$ -adrenoceptor agonists cause a dose-dependent decrease in HR as a result of two different mechanisms: one of them states that the initial increase in blood pressure induces an increased vagal tone via the baroreceptor reflex with subsequent bradycardia while the second mechanism states that central sympatholysis reduces the positive chronotropic influence on HR (Kastner et al., 2001; Kastner et al., 2005; Kutter et al., 2006; Kastner 2006; Jud et al., 2010). The results of our study may conclude that the decrease in HR could be related to more pronounced central sympatholytic effects of  $\alpha_2$ -adrenoceptors in goats because the initial increase in blood pressure was not recorded in any goat.

When compared with the HR, it was significantly higher in the TS group than the DKS group at all time points except for 120<sup>th</sup> min. The HR was decreased and remained low until 90 minutes. Kutter et al. (2006) compared the effect of dexmedetomidine on HR in sheep and goats and reported that the decrease in HR lasted longer in goats than in sheep. It was emphasized that the decrease in heart rate lasted for 5 minutes in sheep but continued longer than 120 minutes in goats. The longer period in goats was explained by the more sensitive central sedating effects of  $\alpha_2$ -adrenoceptors in goats than in sheep (Kutter et al., 2006; Riebold 2007).

Ketamine is known as a dissociative anesthetic that stimulates cardiovascular function via sympathomimetic effects. Some researchers (Lin et al., 1997; Prassinis et al., 2005) reported an increase in HR and blood pressure after ketamine administration in goats; however, this was not supported by the result of this study. The minimum HR was recorded 5 minutes after ketamine administration in this study. This can be explained by the additional decrease in sympathetic tone as a result of anesthesia depth or the effect of  $\alpha_2$ -adrenoceptors on HR (Hikasa et al., 1998; Kastner et al., 2005). Jud et al. (2010) also reported a decrease in HR with the combination of  $\alpha_2$ -adrenoceptor and ketamine in goats. The increase of HR overtime was

possibly a result of the waning effect of dexmedetomidine and ketamine through the end of the study.

It has been reported that RR is reduced after induction with ketamine and thiopental sodium in goats. It has also been reported that there was no significant difference between the groups in terms of the RR at the same time periods among goats that underwent induction using thiopental sodium and ketamine (Prassinis et al., 2005; Karılı et al., 2019). In a study, it was reported that the respiratory rate of goats that underwent induction with thiopental sodium increased during the period of inhalation anesthesia compared to baseline (Hikasa et al., 2002). In the present study, on the other hand, the RR decreased compared to the baseline level after induction in both groups. This is reflected by a post-induction reduction of PaO<sub>2</sub> level. It is noteworthy that the reduction in fR after induction with thiopental sodium was greater than induction with ketamine. It is thought that this may be related to apnea formation following thiopental sodium induction in goats and thiopental sodium being a respiratory depressing agent (Lin and Pugh 2002).

There are similarities between the previous studies and this study when dealing with the effects of thiopental sodium on blood pressures in goats (Prassinis et al., 2005). It was reported by one study that the MAP value in goats was significantly reduced compared to its baseline level for 80 minutes after dexmedetomidine administration (Kutter et al., 2006). The mean arterial blood pressure in this study was lower than the mean arterial blood pressure reported by Kastner et al. (2005) who used sevoflurane with dexmedetomidine in sheep. The combination of dexmedetomidine with ketamine for induction may be the reason for lower blood pressure since ketamine causes a decrease in blood pressure in goats (Prassinis et al., 2005). In the present study, blood pressure decreased significantly after thiopental sodium administration and remained low by the end of the study. Although all values were lower than the beginning values, they were within the clinically acceptable limits throughout the study. The decrease in blood pressure was more in the DKS group than the TS group. It is thought that this situation may be related to the central vasodilatory effect of peripheral postsynaptic  $\alpha_2$ -receptors in the subsequent period. However, lower arterial pressure in the subsequent periods of anesthesia in the ketamine group is thought to be possibly related to anesthesia depth and a longer anesthesia period when ketamine is used with dexmedetomidine (Hughan et al., 2001; Kutter et al., 2006).

In a study on dogs, blood pH levels decreased after the administration of thiopental sodium and diazepam-ketamine while blood PaCO<sub>2</sub> and PaO<sub>2</sub> levels significantly increased after induction (Enouri et al., 2008). A study on goats revealed a decrease in blood Ph level but a significant increase in blood PaCO<sub>2</sub> and PaO<sub>2</sub> levels after induction with ketamine and thiopental sodium. Similar statistically significant increases were reported in the thiopental sodium and ketamine groups (Prassinis et al., 2005). A study on sheep demonstrated significantly higher PaO<sub>2</sub> and Ph levels at 70 and 100 minutes compared to baseline after the administration of dexmedetomidine as a pre-anesthetic (Kastner et al., 2001). In line with the above-mentioned studies, the present study also showed a significant decrease in blood Ph level after the induction with thiopental sodium. That decrease occurred within 15 minutes after induction with ketamine and started to rise thereafter. It was noteworthy that blood Ph level decreased

to a greater extent after induction with ketamine compared to thiopental sodium. It was thought that this may be due to the administration of a pre-anesthetic prior to ketamine. A significant rise in PaCO<sub>2</sub> level was noted following ketamine administration, and it maintained its level during the anesthesia period. In the TS group, on the other hand, post-induction PaCO<sub>2</sub> levels showed no difference from the baseline levels. Arterial carbon monoxide levels at 30 minutes were lower in the DKS group, which was thought to show parallelism with the difference between the baseline levels. Arterial oxygen levels significantly increased from baseline beyond 30 minutes after induction in the TS and DKS groups. Arterial oxygen levels were significantly higher at 15 and 120 minutes in the DKS group compared to the TS group, which was thought to be a continuation of the difference between the baseline levels of the two groups.

The results of this study indicate that dexmedetomidine-ketamine or thiopental sodium provide satisfactory induction with a minimum cardiovascular and respiratory depressant effect in spontaneously ventilating goats. In addition, dexmedetomidine-ketamine is recommended instead of thiopental sodium as an induction agent when rapid recovery is desired in goats. Our study concluded that dexmedetomidine-ketamine is superior to thiopental sodium as an induction agent in goats.

#### Conflict of Interest

The authors declare that they have no competing interests.

#### Authorship contributions

Concept: B.K., A.K., Z.P., Design: B.K., A.K., Z.P., Data Collection or Processing: B.K., A.K., Z.P., Analysis or Interpretation: B.K., A.K., Z.P., Literature Search: B.K., A.K., Z.P., Writing: B.K., A.K., Z.P.

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