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Research Article

Effects of Ketamine-Medetomidine and Ketamine-Medetomidine-Morphine Anaesthesia on Haematological and Clinical Parameters in Goats

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ABSTRACT

The effects of the combination of ketamine (5mg/kg i.m.)–medetomidine (0.015mg/kg i.m.) and ketamine (5mg/kg i.m.)–medetomidine (0.01mg/kg i.m.)-morphine (0.3 mg/kg i.v.) anesthesia on clinical and hematological parameters were evaluated in twelve goats. Onset of skin analgesia and total duration of skin analgesia and duration of recumbency were measured. Rectal temperature (RT), heart rate (HR) and respiratory rate (RR) were recorded pre anesthesia and 15, 30, 60, 90 minutes intervals. Pre injection blood samples were obtained and at 15, 30, 60, 90 minutes interval during anesthesia in EDTA bottles and later analyzed.
Group 1: onset of skin analgesia 18.62±4.18 min, duration skin analgesia 50.66±3.40 duration of recumbency 108±12. Group 2: onset of skin analgesia 19.62±3.18 min, duration skin analgesia 48.66±4.40 duration of recumbency 102±11.The ketamine-medetomidine combination produced a significant decrease in HR and RR values from 30 to 60 minutes compared with baseline value. PaCO2 increased significantly at 30, 60, 90 mins and PaO2 decreased significantly at 30, 60, 90 mins compared with baseline value. Cl, HCT, WBC, LYM, HGB, MCHC decreased significantly and others were no significant differences compared with baseline values. The ketamine-medetomidine-morphine combination produced a significant decrease in HR and RR same as first group. PaCO2 increased significantly at 15 minute and PaO2 increased significantly at 15, 30 and decreased 60, 90 mins compared with baseline value. Cl, HCT, WBC, LYM, MID, HGB, decreased and MCHC increased significantly differences compared with baseline values. The both of combination produced effective anesthesia and immobilization in goats. The clinical findings of this study, as hypoxemia and bradycardia were important records that may prevent from the use of the combinations in critical and cardiovascular compromised patients.

Key words: Ketamine, Medetomidine, Morphine, Anesthesia, Goat

INTRODUCTION

Ketamine produces profound analgesia without muscle relaxation that is characterized by catatonic and amnesia with or without actual loss of consciousness (Hall and Clarke, 1991). Medetomidine is a very potent, efficacious and selective agonist for α2 adrenoreceptors in the central and peripheral nervous system (Lumb and Jones, 1996).It is α2 to α1 receptor selectivity binding ratio is very high, compared to xylazine (Virtanen *et al.,* 1988). Medetomidine induces sedation and analgesia and in high doses has anesthetic properties (Kalhoro *et al.,* 2000, Memon 1999, Shahani 1998). Medetomidine has been used in sheep, goat and cattle; i.v. doses of 10 to 20 µg/kg. (Mohammad *et al.,* 1993., Pawde *et al.,* 1996, Muge *et al.,* 1996, Celly *et al.,* 1999, Kalhoro *et al.,* 2000, Moolchand *et al.,* 2014). Medetomidine-ketamine combinations have been found to provide excellent immobilization and relaxation in a wide range of species of animals (Hall and Clarke, 1991). Ketamine can be used for anesthesia in sheep and goats but may be cause convulsions. The surgical anesthesia and muscle relaxation is poor, but may be improved by sedatives such as diazepam, xylazine and detomidine (Durgun *et al.,* 1990, Afshar 2005). The most frequently used anesthetic combinations in goats are ketamine-xylazine, ketamine-medetomidine and tiletamine-zolazepam (Lumb and Jones, 1996). For anesthesia in the goat, medetomidine (Mohammad *et al.,* 1989) or a combination of drugs has been used (Pawde *et al.,* 1996; Afshar *et al.,* 2005; Mahmood and Mohammad 2008). Recommended doses for anesthesia in the goat: Medetomidine-ketamine combinations used at 15 µg/kg+5 mg/kg (Arnemo, 1993), at 20 µg/kg+5 mg/kg (Gogoi, 2003), 0.001mg/kg+5 mg/kg, Umar and Irefin, 2013).

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The aim of this study is to evaluate the effect of anesthesia using two different combinations of medetomidine and ketamine on hematological and clinical parameters in goats.

MATERIALS AND METHODS

In this study twelve female goats, 3-4 years of age and 32-50 kg of weight were used. The goats were kept at Animal Hospital of Firat University during the experiment. The study period, it is kept under standard managemental conditions. The goats were kept in hospitalisation unite and had free access to feed and water. The feed and water was withheld for 12 h prior to the start of the experiment. Goats were involved in another experimental study in which cranial cruciate ligament repaired with m. peroneus longus and m. tibialis cranialis under general anaesthesia. The study protocol was accepted by the Experimentaly Animal Ethics Committee of the University of Fırat (Acceptance number 2014-02).

The goats were designated casually to two groups. First group (n=6) each goat was given a medetomidine (1ml/1mg Domitor, Zoetis, Finland) at 0.015mg/kg i.m. and ten minutes later ketamine (1ml/100mg, Ketasol, Richter Pharma Ag, Austria) at 5mg/kg body weight i.m. and second group medetomidine at 0.01mg/kg i.m. and ten minutes later ketamine at 5mg/kg body weight i.m. and 0.3 mg/kg morphine i.v. (1ml/10mg, Morphine HCL, Galen, Turkey).

Rectal temperature (RT, °C), and heart (HR, beats/min) and respiratory rates (RR, breaths/min) were recorded pre anesthesia and 15, 30, 60, 90 minutes intervals. The respiratory rate was determined by direct observation of the thoracal movements. The heart rate and rectal temperator (rectal prop and digital thermometry) were recorded by a monitor (Sino-Hero S80 VET China). Onset of skin analgesia and total duration of skin analgesia and duration of recumbency were measured. Pre anesthesia blood samples were taken and at 15, 30, 60, 90 minutes period during anaesthesia in EDTA injectors and later analyzed. The parameters assessed were venous blood pH, blood gases (PaCO2, PaO2), Na, K, Cl, Hematocrit (HCT) by analysed a portable blood gas analyser (Edan I15 VET China). Red blood cells (RBC), white blood cells (WBC), and lymphocytes (LYM), monocytes (MID), granulocytes(GRAN), mean Corpuscular volume (MCV), haemoglobin concentration (HGB), mean corpuscular hemoglobin concentration (MCHC), redcell distribution width - standard deviation (RDW-SD), redcell distribution width - coefficient of variation (RDW-CV) by analysed fully automated hematology equipment (PROKAN, PE 6800-VET, China).

Statistical analysis

The data for parametric or nonparametric observations analyzed using IBM SPSS 22 Statistics program. The data were presented as the mean ± SE. Significance was accepted at $P<0.05$.

Tests of normality of the times obtained throughout anaesthesia were carried out. The non-normal variables were transformed logarithmically and normality was analyzed again. Values regarded as outliers were discarded, care being taken not to exceed the maximum allowed by statistical studies. The factor considered in this model for each variable was the anaesthetic combination used; clinical and haematological values were analyzed.

RESULTS

The ketamine-medetomidine combination: onset of skin analgesia 18.62±4.18 min, duration skin analgesia 50.66±3.40, duration of recumbency 108±12. The ketamine-medetomidine-morphine combination: onset of skin analgesia 19.62±3.18 min, duration skin analgesia 48.66±4.40, duration of recumbency 102±11. Comparison of first and second groups showed no significant difference in onset of skin analgesia, duration skin analgesia and duration of recumbency (Table 1). The clinical symptoms showed for anesthesia duration at Table 2. There was a non-significant lessening in rectal temperature from baseline value of 38.50±1.50 to 37.20±0.60°C after 90 minutes (Group-1) and similarly, there was a non-significant lessening in rectal temperature from baseline value of 38.40±1.30 to 37.18±0.60 °C after 90 minutes (Group-2)

The ketamine-medetomidine combination produced a significant lessening in HR and RR values from 30 to 60 minutes compared with baseline value. PaCO2 enhanced significantly at 30, 60, 90 mins and PaO2 lessening significantly at 30, 60, 90 mins compared with baseline value. Cl, HCT, WBC LYM, HGB, MCHC decreased significantly and others were no significant differences compared with baseline values (Table 3).

The ketamine-medetomidine-morphine combination produced a significant lessening in HR and RR same as second group. PaCO2 enhanced significantly at 15 minute and PaO2 increased significantly at 15, 30 and decreased 60, 90 mins compared with baseline value. Cl, HCT, WBC LYM, MID, HGB, decreased and MCHC enhanced significantly differences compared with baseline values (Table 4).

Table 1: Comparison of first and second groups in onset of skin analgesia, duration skin analgesia and duration of recumbency

	Onset skin analgesia (Min)	Duration skin analgesia (Min)	Recovery time (Min)
Group 1 (MK)	18.62±4.18	50.66±3.40	108±12.4
Group 2 (MKM)	19.62±3.12	48.66±4.40	102±11.8

Value are expressed as mean ± SD, n = 6

Table 2: Comparison of first and second groups in clinical sign in anesthesia duration

Clinical signs	Medetomidine and Ketamine	Medetomidine Ketamine and Morphine
Salivation	+	+
Recumbency	+	+
Urination	+	+
Defecation	-	-
Staggering	+	+
Snoring	+	+
Mild Tympany	+	+
Palpebral Reflex	-	-
Tail Movement	+	+
Protrusion of Tongue	-	-
Jaw Tone	-	-

Table 3: Effects of combination of medetomidine and ketamine anesthesia on hematological and clinical parameters in goats

Time (mins)	Baseline	15 mins	30 mins	60 mins	90 mins
RT	38.50±1.50	38.20±0.40	37.60±1.20	37.20±0.80	37.20±0.60
HR	80.34±2.64	78.12±4.32	76.64±4.42*	73.18±3.23*	76.34±2.48
RR	24.30±2.08	23.24±1.34	22.43±2.12*	24.26±2.24	25.48±3.14
PH	7.25± 0.05	7.29± 0.12	7.27±0.05	7.31±0.04	7.33±0.04
PCO2	63.60±10.8	64.44±13.3	76.64±10.2*	70.25±9.28*	70.06±6.90*
PO2	110.66±1.2	109.50±0.6	106.66±2.0*	104.66±1.1*	91.83±3.7*
Na	138.33±3.1	137.2±0.4	139.8±0.6	138.1±1.6	139.8±1.2
K	4.67±0.52	4.53±0.76	4.80±0.31	4.62±0.26	4.07±0.11
Cl	115.33±1.75	112.78±1.6*	111.8±2.14*	112.66±1.6*	110.83±2.7*
HCT	20.00±2.6	15.00±0.4*	18.16±3.2	16.16±1.2*	17.12±4.1
WBC	12.28±2.55	9.30±0.51*	10.60±3.08	10.65±1.45	10.06±3.76
LYM (%)	60.65±2.8	58.16±3.2	56.42±2.2*	53.32±2.6*	51.38±3.6*
MID (%)	20.08±2.4	21.02±3.6	22.03±3.2	21.04±3.6	22.06±3.4
GRAN (%)	19.27±4.2	20.06±3.8	20.08±3.6	21.02±3.2	20.04±2.8
LYM (#)	6.58±3.80	6.84±3.62	5.77±3.75	5.43±4.26*	5.85±3.82
(MID(#)	2.35±0.86	2.24±0.76	2.65±0.66	2.44±0.82	2.26±0.96
GRAN(#)	2.35±0.78	2.20±0.72	2.18±0.82	2.48±0.72	2.66±0.76
RBC	2.51±0.66	2.01±0.74	1.96±0.84	1.84±0.64	1.83±0.68*
HGB	7.18±0.64	6.24±0.72	5.93±0.78*	6.15±0.68	6.02±0.62
MCV	44.42±0.8	44.06±0.6	43.63±0.7	43.55±0.6	43.65±0.6
MCH	30.97±4.4	31.08±4.8	32.42±5.4	34.15±6.2	34.12±5.8*
MCHC	66.7±12.4	69.4±11.8	71.1±13.4*	78.8±12.6*	76.4±12.2*
RDW-SD	19.5±0.8	19.2±0.7	18.9±0.8	18.2±0.5	18.6±0.6
RDW-CV	13.73±0.4	13.62±0.5	13.52±0.4	13.16±0.4	13.22±0.4

Values are expressed as mean ± SD, n = 6; *Values decreased significantly (P<0.05) from baseline.

Table 4: Effects of combination of ketamine, medetomidine, and morphine anesthesia on hematological and clinical parameters in goats

Time (mins)	Baseline	15 mins	30 mins	60 mins	90 mins
RT	38.40±1.30	38.25±0.30	37.80±1.10	37.30±0.70	37.18±0.60
HR	80.32±2.44	79.12±3.42	76.84±3.72*	74.16±3.42*	75.44±2.62
RR	24.60±2.16	23.14±1.32	22.13±2.12*	24.36±2.62	25.36±3.22
PH	7.21± 0.15	7.28± 0.14	7.31±0.08	7.34±0.03	7.35±0.03
pCO2	62.68±9.80	68.42±12.2*	63.74±9.22	62.24±9.26	60.16±9.20
PO2	121.08±10.4	129.50±10.6*	128.66±9.0*	115.82±10.2*	113.68±9.6*
Na	136.24±3.2	135.6±1.8	136.4±0.8	135.7 ±1.8	135.4 ±1.6
K	4.62±0.58	4.63±0.72	4.72±0.45	4.72±0.28	4.46±0.27
Cl	113.5±1.82	112.64±1.2*	111.4±2.11	112.30±1.4	111.72±1.7
HCT	19.42±3.4	15.22±3.2*	15.18±3.3*	15.52±3.1*	17.26±3.2
WBC	13.00±2.16	10.06±2.4*	10.45±2.8*	10.62±2.4*	12.27±3.6
LYM (%)	55.45 ±3.6	55.35±3.4	54.13±2.3	50.01±2.8*	48.05±3.5*
MID (%)	20.37±5.4	15.77±4.6*	18.42±3.8	20.07±3.5	19.83±3.7
GRAN (%)	24.18±4.6	28.08±4.7	27.45±4.6	29.83±4.3	31.76±4.8*
LYM (#)	7.33±3.20	5.88±2.22	5.67±2.35	5.35±4.26*	5.95±3.82
(MID(#)	2.57±0.82	1.64±0.86*	1.92±0.68	1.95±0.72	2.12±0.84
GRAN(#)	3.10±0.72	3.13±0.68	2.88±0.86	3.28±0.82	4.26±0.77
RBC	2.93±0.62	2.26±0.64	2.21±0.74	2.22±0.62	2.35±0.60
HGB	8.12±0.84	6.75±0.73	6.58±0.72*	6.75±0.60	6.90±0.64
MCV	44.53±0.7	44.06±0.8	44.13±0.6	44.03±0.6	44.12±0.8
MCH	30.12±3.4	32.18±4.2	32.37±4.4	32.82±4.2	31.75±4.8
MCHC	68.6±10.4	74.1±10.8*	74.5±11.4*	75.8±12.2*	73.4±11.2*
RDW-SD	20.4±0.9	19.5±0.8	19.5±0.7	19.5±0.8	18.8±0.8
RDW-CV	14.32±0.6	13.82±0.5	13.78±0.6	13.83±0.5	13.35±0.6

Values are expressed as mean ± SD, n = 6; *Values decreased significantly (P<0.05) from baseline.

DISCUSSION

Medetomidine produced dose dependent levels of sedation in goats (Kalhoro and Memon, 2011). Light, moderate and deep sedation were produced with 4, 5 and 6 µg/kg medetomidine, respectively (Kalhoro *et al.,* 2000, Memon *et al.,* 1999). Similar inspections have been described with medetomidine in calves (Kalhoro *et al.,* 2000, Kilic N, 2008). Medetomidine (6 µg/kg) produced light to medium sedation in sheep which may be useful for physical and radiologic examination, biopsy, and for pre-anaesthetic medication (Moolchand *et al.,* 2014). Ketamine-medetomidine combinations have been found to provide excellent immobilization and relaxation in a wide range of species of animals (Hall and Clarke, 1991). Recommended doses for surgical anaesthesia in the goat: Medetomidine-ketamine combinations used at 20 µg/kg+5 mg/kg (Gogoi *et al.,* 2003), at 15 µg/kg+5 mg/kg (Arnemo and Soli, 1993), 0,001mg/kg+5 mg/kg, (Umar and Irefin, 2013).

In this study medetomidine at 0,015 mg/kg and ketamine 5 mg/kg and other group (medetomidine at 0,01mg/kg and ketamine at 5mg/kg body weight i.m. and 0,3 mg/kg morphine i.v.) were found to produce deep

analgesia and sedation allowing surgical operations as repaired cruciate ligament by transposition tendons recorded by the authors. Therefore, these doses and drug combinations rate were selected for detailed study.

Medetomidine has been widely used in combination with ketamine and other drugs to prolong recumbency (Hall and Clarke, 1991). This study recovery time 90-150 minutes in group-1 and 90-130 minutes in group-2. The other clinical symptoms showed for anestesia duration same as Salivation, Recumbency, Urination, Defecation both groups (Table-2). Reduction in rectal temperature may be attributed to used of medetomidine as reported in Shami kids by Mohammed *et al*., 1991, in goats (Memon, 1999, Gogio *et al.,* 2003) and in calves by Shahani, 1998. This study rectal temperature similary were fall both groups.

Medetomidine-ketamine combinations has the usual marked cardiovascular effects (bradycardia, reduced cardiac output and arterial hypertension) (Lumb and Jones1996). MacDonald and Virtanen, 1992, reported that Medetomidine induced bradycardia. A similar fall in pulse rate has been reported by Sinclair 2003, in small animal. Medetomidine (15 µg/kg i.m.) lowered the pulse rate goats (Memon, 1999). In most animals medetomidine slows respiration (Clarke and England, 1989). Goats and sheep can both react with acute decreases in arterial oxygenation after the administration of an α2-agonist (Kutter *et al.,* 2006). Umar and Irefin, 2013, Afshar *et al.,* 2005 also recorded decreased heart rate, rectal temperature and blood pressure during medetomidine-ketamine anaesthesia in goats. This study ketamine-medetomidine and morphine combination produced a significant decrease fall pulse rate and respiratory rate goats in both groups. It is thought that the centrally stimulating effects of ketamine counteract the depressive effects of alpha2 agonist compounds. There is less depression of the ventilatory response to CO2 which *P*aCO2 does not rise to an excessive level group 2. *P*aO2 significant decrease both groups. Decrease in haematological parameters reported after Medetomidine (15 µg/kg i.m.) administrationin goats. Medetomidine induced fall in Hb, PCV and TLC but Serum electrolytes remained unaltered (Pawde *et al.*, 1996). Medetomidine (15 µg/kg i.m.) and ketamine (5mg/kg) administrationin goats, decreases in haemoglobin, packed cell volume, total erythrocyte count and total leukocyte count were not significant (Arnemo and Soli 1993). The medetomidine (0.01mg/kg) and ketamine (5mg/kg) combination produced decreases in PCV, Hb and neutrophils (Umar and Wakil 2013). In this study Cl, HCT, WBC LYM, HGB, MCHC decreased significantly and others were no significant differences compared with baseline values in Groups-1. Cl, HCT, WBC LYM, MID, HGB, decreased and MCHC inreased significantly differences compared with baseline values in Groups-2.

Probably, other factors not considered in our study, such as season, nutrition and environmental temperature, may affect some of these variables.

Conclusions

Ketamine-medetomidine and ketamine-medeto-midine-morphine produced effective anesthesia in goats. The results of this study suggest that both groups produce adequate anaesthesia for surgical procedures in goats for about 50 min. Changes found in haematological variables suggest minor differences in the different anesthetic combinations used. But according to clinical findings of this study, as well as hypoxemia and bradycardia were important records that may prevent from the use of the combinations in critical and cardiovascular compromised patients.

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