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Research Article

Use of Three Different Combinations for Spinal Anaesthesia on Clinical and Haematological Parameters in Goats

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ABSTRACT

The aim of this study was to evaluate effectively of the combination of ketamine HCl -xylazine HCl, ketamine HCl -medetomidine HCl and bupivacain-morphine for spinal anaesthesia on clinical and haematological parameters in three groups (each group had 6 goats). Each goat in groups was given a dose of the drugs combination: Group 1; ketamine HCl at 2.5mg/kg and xylazine HCl at 0.05mg/ kg, group 2; ketamine HCl at 2.5 mg/kg and medetomidine HCl at 0.01 mg/kg, group 3; bupivacain at 2 ml and morhine 0.5 ml. The drugs were injected epidurally into the lumbosacral subarachnoid space.

Begining of the skin analgesia and total duration of skin analgesia and duration of recumbency were measured timely. Rectal temperature (RT), heart rate (HR) and respiratory rate (RR) were intervaly recorded at pre-anesthesia and 30^{th}, 60^{th}, 90^{th}, 120^{th} minutes intervals. Pre-injection blood samples were obtained and repeated at 30^{th}, 60^{th}, 90^{th}, 120^{th} minutes intervals during anaesthesia and at 24 hours into the tubes with EDTA and than analyzed. The evaluated parameters were venous blood pH, blood gases (PaCO2, PaO2, etCO2, s02), Na, Cl, hematocrit (HCT), haemoglobin (HGB), bicarbonate (HCO3a, HCO3s). The onset of analgesia was 1.24 ±0.35 min. in (group 1, 1.08±0.22 min. in group 2) and 0.92±0.32 min. in group 3, respectively. Duration of the skin analgesia were 48±8.4 min. in group 1, 50±6.4 min. in group 2, and 55±9.6 min. in group 3, respectively. Duration of recumbency 80-200 min. in all groups. RT did not show any significant change. HR depression significantly ($P<0.05$) in all combination groups and RR decression were recorded in groups 1 and 2. PaO_2 decreased significantly all groups. $PaCO_2$ increased significantly in groups 1 and 2. Serum electrolytes did not show any significant difference. The values were returned to normal at 24th hours in all groups. As a conclusion, The ketamine-xylazine, ketamine-medetomidine and bupivacain-morphine for spinal anaesthesia can be safely used in goats as it caused transient clinical and haemetological alterations.

Key words: Goat, Xylazine, Medetomidine, Ketamine, Bupivacain, Morphine, Spinal anesthesia

INTRODUCTION

The spinal anesthesia, intrathecal injections, where the injectate actually enters the cerebrospinal fluid surrounding the spinal cord, is less commonly performed than epidural injections (Dugdale, 2011). The lumbosacral space in small ruminants can be examined by palpating the space caudal to the spinal process of the sixth lumbar vertebrae between the tuber coxae. Typically, an 18 or 20-gauge, 4-5-cm needle is sufficient equipmant for goats. Perineal, abdominal and extremity operations can be performed under spinal anesthesia (Lin, 2014). Spinal anesthesia, in contrast to general anesthesia, has many benefits including a decrease in postoperative nausea and vomiting, intraoperative and postoperative pain control, decreased opioid requirements, as well as less urinary retention, and a quicker return to mental alertness in human (Harriett, 2016). Density is a major determinant of the distribution, duration, and degree of the clinical block achieved in spinal anesthesia with local anesthetics. Many local anaesthetic solutions (lidocaine 1%, bupivacaine 0.5% and ropivacaine 1%) are slightly hypobaric (less dense than cerebro spinal fluid). Special hyperbaric local anaesthetic and opioid solutions (usually containing glucose) are available for intrathecal injections (Kinjavdekar *et al*., 2000). Morphine and methadone tend to be hypobaric, but when diluted in normal saline or glucose solutions, may become isoor hyperbaric respectively. It has been reported that intractable pain refractory to systemic analgesic administration was successfully controlled with epidural morphine (Novello and Platt, 2006).

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Epidural analgesia produced by xylazine or bupivacaine has been used to effectively reduce post operative pain in goats (Pathak, 1999). Bupivacaine, has been used in for preemptive, and post operative analgesia and for laparotomy in goats (Pathak *et al*., 2002). Xylazine HCl is α2 receptor agonists used in veterinary practice (Singh *et al*., 20005, Moulvi *et al*., 2011). It has also been shown to produce increased duration of analgesia on epidural administration in comparison to conventional local anaesthetics such as lidocaine (Dugdale, 2011). However, cardiopulmonary depression remains the greatest disadvantage when it is used epidurally or spinally (Jean *et al*., 1990). Ketamine HCl is a phencyclidine congener (Dugdale, 2011) and has been used for spinal anesthesia in goats (Aithal *et al*., 1996; Gomez *et al*., 1998; DeRossi *et al*., 2003, DeRossi *et al*., 2005; Kinjavdekar *et al*., 2007).

The aim of this study was to evaluate effectivity of the combination of ketamine HCl -xylazine HCl, ketamine HCl -medetomidine HCl and bupivacain-morphine for spinal anaesthesia on clinical and haematological parameters in goats.

MATERIALS AND METHODS

In total 18 female goats, about 3-4 year-old and 30-50 kg of weight were used. The goats were kept in hospitalisation unite at Animal Hospital of Firat University and had free access to feed and water. The feed and water was withheld for 12 h prior to the start of the experiment. The protocol for the use of animals was approved by the National Institute of Health and the Local Committee on Animal Research. The clinical and haematological parameters were evaluated in three groups (each group n: 6). Group 1: each goat was given a recommended dose of the drugs combination: ketamine HCl (1ml/100mg, Ketasol®, Richter Pharma Ag, Austria) at 2,5mg/kg and xylazine HCl (1ml/23,32 mg, Rompun®, Bayer, Germany) at 0,05mg/ kg. Group 2: ketamine HCl at 2,5mg/kg and medetomidine HCl (1ml/1mg Domitor®, Zoetis, Finland) at 0,01 mg/kg. Group 3: bupivacain (1ml/5mg, Marcaine Spinal, AstraZenaca, Turkey) at 2 ml and morphine (1ml/10mg, Morphine HCL Galen, Turkey) 0.5 ml. The drugs were injected into the lumbosacral subarachnoid space. The animals were restrained in standing position. The lumbosacral region was clipped, shaved and painted with iodine solution for aseptic injection. A 20 gauge, hypodermic needle of length 5 cm was placed into the subarachnoid space at the lumbosacral intervertebral space. The correct position of the needle was ascertained by free flow of CSF from the needle hub. The drug was then injected. Onset of skin analgesia and total duration of skin analgesia and duration of recumbency were measured. Onset of analgesia was recorded in the sacral and perineal region using a pin prick method. Onset of analgesia was considered as the time from injection of the drug to the loss of sensation in the perineal, sacral and tail region. Rectal temperature (RT), heart rate (HR) and respiratory rate (RR) were recorded pre anesthesia and 30^{th}, 60^{th}, 90^{th}, and 120^{th} minutes intervals. The respiratory rate was determined by direct observation of the thoracal movements. The HR and rectal temperator (rectal prop and digital thermometry) were recorded by a monitor (Sino-Hero® S80 VET China). Pre injection blood samples were obtained and at 30^{th}, 60^{th}, 90^{th}, and 120^{th} minutes intervals during anaesthesia and 24 hours in EDTA bottles and later by analysed a portable blood gas analyser (Edan® I15 VET China). The parameters evaluated were venous blood pH, blood gases (PaCO2, PaO2, etCO2, s02), Na, Cl, hematocrit (HCT), haemoglobin (HGB), bicarbonate (HCO3a, HCO3s).

RESULTS

The onset of analgesia was respectively 1.24 ±0.35 min (Group 1), 1.08±0.22 (Group 2) and 0.92±0.32 (Group 3). Duration of skin analgesia was respectively 48±8.4 min. (Group 1), 50±6.4 min. (Group 2), and 55±9.6 min. (Group 3). Duration of recumbency 80-200 min. in all the groups. RT did not show any significant change. HR depression significantly ($P<0.05$) in the all combination groups and respiratory rate depression were recorded in groups 1 (Table 1) and 2 (Table 2). PaO2 significant ($P<0.05$) decrease all groups. PaCO2 significant increase in groups 1 and 2. Serum electrolytes did not show any significant change. The values were returned to normalcy by 24 hours in all groups (Table 1, 2, 3).

Table 1: Clinical and haematological parameters of the goats following spinal anesthesia with combination of ketamine HCl and xylazine HCl

Time (mins)	Baseline	30 min.	60 min.	120 min.	24 h
RT	39.1±0.69	38.9±0.64	38.4±0.75	37.7±1.01	39.3±0.64
HR	90.8±13.7	77±8.17*	76.1±14*	72±12.39*	86.1±15*
RR	26.16±6.8	29±16.08	22±13.97*	21.8±4.5*	27.5±9.64
PH	7.17±0.09	7.27±0.05	7.28±0.09	7.31±0.06	7.25±0.07
PaCO2	63.2±16.5	65.5±3.03	73.6±1.8*	73.5±1.9*	63.96±5.5
PaO2	96±34.23	90±53.46*	91±38.9*	92±47.2*	97.1±39.5
Na	134.1±8.3	136.3±3.7	134.5±7.9	136±6.21	136.5±3.2
Cl	118±11.5	116.6±4.5	115.6±10	114.3±4.2	119.6±6.4
HCT	17.6±5.36	13.5±2.8	14.6±2.40	16.6±5.4	15±40
HGB	6.04±1.89	4.61±0.93	4.98±0.74	5.64±1.83	5.15±1.26
HCO3a	24.28±6.3	29.8±3.66	34.26±5.3	36.1±1.56	28.2±4.64
HCO3s	21.1±5.50	26.82±3.6	30.71±6.4	32.25±1.5	25.65±4.6
ctCO2	26.33±6.8	31.83±3.5	36.66±5.3	38.33±2.0	30.66±5.3
sO2(est)	97.83±1.8	97.33±3.3	97±2.75	90±12.55	97.16±4.0
pCO2(T)	64.8±17.6	61.8±2.92	68.9±10.8	71,3±17,9	61.23±5.2
pO2(T)	134±34.56	129±53.1	113.6±40	84±40.70	131.6±39

Values are expressed as mean ± standard deviation; *These values have significant difference ($P<0.05$) from baseline.

Table 2: Clinical and haematological parameters of the goats following spinal anesthesia with combination of ketamine HCl and Medetomidine HCl

Time (mins)	Baseline	30 min.	60 min.	120 min.	24 h
RT	38.91±0.84	39±0.50	38.06±0.58	37.13±0.66	39.31±0.48
HR	71.16±17.04	57.3±13.95*	61.6±22.17*	61.7±13.8*	77±15.47
RR	24.5±12.72	21.33±26.1*	20.83±32.5*	22.3±11.74*	21.16±3.43*
PH	7.282±.021	7.279±0.03	7.326±0.02	7.368±0.01	7.258±0.07
PaCO2	60.3±8.74	67.26±7.22*	68.26±7.62*	62.88±7.49	61.66±6.10
PaO2	97.33±34.58	84.8±39.23*	88.5±31.09*	95.83±42.84	96.83±14.68
Na	137.16±2.13	138.4±2.88	137.16±3.12	139.33±1.75	139±3.16
Cl	117.66±5.88	113±3.09	116±5.29	115.5±2.81	120.33±6.15
HCT	16.83±3.12	15.2±3.56	13.5±2.07	15.83±1.72	15.83±3.06
HGB	5.7±1.00	5.2±1.16	4.53±0.66	5.4 ±0.65	5.41±0.96
HCO3a	27.75±3.14	31.14±5.50	34.96±4.20	35.38±4.11	26.75±3.43
HCO3s	25.31±2.44	28.18±5.22	32.33±3.87	33.11±3.77	24.6±2.97
ctCO2	29.83±3.65	33±5.83	37±4.64	37.33±4.22	28.33±3.72
sO2(est)	91.83±11.1	90.8±5.89	95.33±3.38	97 ±2.75	92.16±3.60
pCO2(T)	57.71±8.37	60.6±4.65	66.02±8.14	59.6±7.85	58.2±6.45
pO2(T)	92.16±33.29	93.6±3.45	92.8±32.06	109±43.85	93.6±5.85

Values are expressed as mean ± standard deviation; *These values have significant difference (P<0.05) from baseline.

Table 3: Clinical and haematological parameters of the goats following spinal anesthesia with combination of bupivacain- Morphine HCl

Time (mins)	Baseline	30 mins	60 mins	120 mins	24 h
RT	39.4 ±0.24	39.35±0.30	39.15±0.32	39.31±0.14	39.08±0.24
HR	90.66±7.86	78±12.26*	77.8±15.95*	75.83±11.6*	76±9.38*
RR	26.33±7.03	34.33±8.68	32.16±6.11	40±17.00	40±5.05
PH	7.266±0.05	7.282±0.07	7.32±0.02	7.328±0.03	7.258±0.07
PaCO2	62.76±10.66	63.58±3.59	62.55±3.04	63.15±4.63	64.66±6.10
PaO2	91±35.07	85.8±14.51*	84.5±26.92*	82.6±16.76*	89.83±14.68
Na	136.5±2.81	135.5±2.58	134.66±2.16	137.16±2.40	138±3.16
Cl	115.5±4.92	115.83±1.47	113.16±3.54	113.5±3.72	116.33±6.15
HCT	15.5±3.08	14.5±2.73	13.5±1.37	15.66±1.36	15.83±3.06
HGB	6.04±1.89	4.9±0.88	4.7±0.55	5.38±0.55	5.98±0.45
HCO3a	24.28±6.32	28.38±5.14	29.6±3.09	29.9±4.11	26.28±3.12
HCO3s	21.1±5.50	26.01±5.01	27.55±2.88	31.3±11.08	22.3±61.58
ctCO2	26.33±6.88	30.16±5.26	31.5±3.27	31.83±4.35	28.48±3.18
sO2(est)	97.83±1.83	83±9.14	93.33±5.46	93.33±4.27	95.63±2.25
pCO2(T)	59.62±3.82	60.21±6.84	61.84±5.47	61.81±9.47	60.22±6.34
pO2(T)	94.33±24.4	92.86±23.2	93.26±28.2	92.46±23.2	93.18±22.4

Values are expressed as mean ± standard deviation; *These values have significant difference (P<0.05) from baseline.

DISCUSSION

The early onset of analgesia in the medetomidine – ketamine and xylazine- ketamine groups might due to local anaesthetic action of ketamine HCl on the spinal cord (Hustveit *et al.*, 2009). In this study, ketamine HCl in combination with xylazine or medetomidine moderate to complete analgesia of the caudal regio for 55 min. The prolonged duration of analgesia suggested synergistic interaction between ketamine and α2-agonists. Similar findings have been reported after epidural administration of a combination of ketamine and xylazine in goats (Aithal *et al*., 1996; Kinjavdekar *et al*., 2007) and of ketamine and medetomidine in dogs (Kinjavdekar *et al*., 1997).

Subarachnoidally administered local anesthetics and opoid analgesic same as morphine to obtain segmental analgesia in animal have been described (Lin H, 2014). The authors reported that pain was successfully controlled with epidural morphine. Later, in 1994, the epidural morphine in doses from 0.05 to 0.1 mg/kg produced segmentally distributed analgesia in animal. The higher dose producing a faster onset of analgesia, longer duration and cranial spreading.

Spinal anesthesia requires a small mass or volume of drug, virtually devoid of systemic pharmacologic effect to produce profound, reproducible sensory analgesia. In contrast, epidural anesthesia necessitates use of a large mass or volume of local anesthetics that produces pharmacologically active systemic blood levels, which may be associated with side effects and complications. The epidural morphine and detomidine, suggesting that the combination produces profound hindlimb analgesia in horses. In another study, epidural morphine decreased the minimum alveolar concentration (MAC) of halothane. Spinal anesthesia often combines the administration of both opioid and local anesthetic agents. Because morphine is water soluble, it has a slow onset and a long duration of action in the intratechal space. The onset time of 30-60 minutes and a duration time of 18 to 24 hours make morphine a good analgesic choice for surgeries in human (Harris and Gewirtz,2004). The longer duration of analgesia were not recorded significantly in all groups. In this study, combination with morphine and bupivicaine produced analgesia of the caudal region for 50-60 minutes. Similar findings were observed in goats (Aithal *et al*., 1996 and Kinjavdekar *et al*., 2007).

α2-Agonists have been reported to induce prolonged depression of thermoregulation (Ponder and Clarke,1980) and depress the hypothalamic noradrenergic α2-receptors to cause hypothermia (MacDonald *et al*., 1988). In this study, rectal temperature decreased in all groups but did not show any significant change. Aithal and colleagues (1996) reported that, despite its cardiostimulatory actions, ketamine in small doses did not produce any significant change in the hearth rate. However, Kinjavdekar and colleagues (2007) reported that a similar dose of ketamine produced a significant increase in hearth rate in goats.

In the present study HR depression significantly ($P<0.05$) in the all combination groups. α2-agonist have partially the bradycardic effect and ketamine and α2-agonists in the combination groups produced probably a less pronounced decrease in heart rate.

Ketamine HCl alone produced an increase in RR; however, Aithal and colleagues (1996) did not find any significant change in the RR after epidural/intrathecal administration of ketamine in different species. Kinjavdekar and colleagues (2007) reported that respiratory rate depression was found to be delayed. In the present study respiratory rate depression significantly ($P<0.05$) in the group I and II but respiratory rate inreased in group III. This may probably be due to the predominant stimulatory effect of ketamine, which might have balanced the depressive effects of α2-agonists (Kinjavdekar *et al*., 2007).

PaO2 significantly ($P<0.05$) decreased in all groups. PaCO2 significantly increased in groups 1 and 2. Probably due to respiratory rate depression. Serum electrolytes did not show any significant change in all groups after injection of the different drugs. The values were returned to normalcy by 24 hours in all groups.

As this study results, the ketamine-xylazine, ketamine-medetomidine and bupivacain-morphine for spinal anaesthesia can be safely used in goats by veterinary practitioners.

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