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Evaluation of experimental subarachnoid analgesia with a combination of detomidine and ropivacaine for flank analgesia in cows

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The aim of this study was to evaluate the analgesic efficacy of subarachnoid application of a low dose of detomidine combined with a low-dose of ropivacaine for flank analgesia in cows. Fifteen non-pregnant adult cows of the Swiss Brown breed, weighing an average of 350 kg, were used. After applying local anaesthesia to the subcutaneous tissues in the area where the catheter was to be administered, a Tuohy needle was inserted into the subarachnoid space at the T13-L1 or L1-L2 region and a combination of detomidine (0.015 mg/kg)-ropivacaine (0.02 mg/kg) HCl was administered at a speed of 0.5 mL/min with a spinal catheter. Flank analgesia started within 1 min after the anaesthetic combinations was injected, the effective duration of the anaesthesia was 104 min on average and the anaesthesia had spread to the T12 and the L5 level. No statistically significant difference was found with regard to cardiopulmonary, haematological or haemodynamic parameters as measured before and during anaesthesia. A relatively small amount of detomidine HCl and ropivacaine HCl is sufficient to achieve safe and rapid analgesia in the left flank.

Key words: subarachnoid analgesia, detomidine, ropivacaine, cattle

Introduction

Due to the side effects of general anaesthesia in cows, it is usually preferable to carry out abdominal surgery with the animal standing (LEVIS et al., 1999; FIERHELLER

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et al., 2004; LEE and YAMATA, 2005; LEE et al., 2006). Usually, techniques such as infiltration (line block or L block), paravertebral, epidural and subarachnoid anaesthesia have been specified for these operations (FIERHELLER et al., 2004; CAULKETT et al., 1993; DeROSSI et al., 2003; SEYREK-INTAS et al., 2001; HIRAOKA et al., 2007). Lumbar segmental epidurals or lumbar segmental subarachnoid anaesthesia are used successfully for abdominal analgesia in cows and other species (CAULKETT et al., 1993; SINGH et al., 2005; SKARDA et al., 1989; OZAYDIN and KILIC, 2003; LEE et al., 2004; KILIC et al., 2008; KACAR et al., 2007; KILIC et al., 2009; OZAYDIN et al., 2006; KILIC et al., 2006). Segmental subarachnoid analgesia is administered through the thoracolumbar (T13-L1) or lumbar (L1-L2) intervertebral space (HIRAOKA et al., 2007; SKARDA et al., 1989; LEE et al., 2004). Local anaesthetics are usually used for these procedures and for postoperative analgesia (OZAYDIN and KILIC, 2003). However, because local anaesthetics cause both sensory and motor blockage, ataxia can develop in the hind legs, causing the animal to lie down (LEE and YAMATA, 2005; CAULKETT et al., 1993; DeROSSI et al., 2003; SEYREK-INTAS et al., 2001; KAMILOGLU et al., 2005).

A needle at least approximately 8 cm long is needed to enter the subarachnoid space. The distance from the skin to the epidural space has been reported to be 71-90 mm (80 mm on average) (LEE et al., 2006).

Although authors have known about spinal and intrathecal anaesthesia for a long time, newly discovered anaesthetic agents that provide ideal analgesia have attracted much attention. However, ropivacaine HCl is still quite popular for spinal administration (WILLE, 2004). Ropivacaine HCl, a new long-acting local anaesthetic, entered clinical practice for treating humans in 1996 and has been used in many experimental studies (WILLE, 2004; KINJAVDEKAR et al., 2007; YAYLA and KILIC, 2010). All local anaesthetics have direct or indirect cardiorespiratory side effects. Although ropivacaine HCl's cardiorespiratory side effects include hypotension, arrhythmia and bradycardia, these side effects are much more subdued than with other local anaesthetics widely used for spinal anaesthesia, such as mepivacaine and bupivacaine HCl (WILLE, 2004; YAYLA and KILIC, 2010).

Since they are safe, comfortable and easy to use, α_2 adrenergic receptor agonists are still currently used with local anaesthetic agents for sacrococcygeal/lumbosacral and epidural/spinal administration (LEVIS et al., 1999; FIERHELLER et al., 2004; CAULKETT et al., 1993; SINGH et al., 2005; KAMILOGLU et al., 2005; LEE et al., 2003). Like xylazine HCl, medetomidine HCl and detomidine HCl, α_2 adrenergic receptor agonists are widely used in intramuscular and intravenous form in horses and cattle to provide sedation, muscle relaxation and analgesia, but they always present the risk of cardiorespiratory depression, reduction in ruminal activity, aspiration and diuresis, depending on the dose administered (KAMILOGLU et al., 2005; LEE et al., 2003). When these drugs are used for

spinal anaesthesia, their analgesic effect is caused by activating the α_2 adrenergic receptors found on the dorsal root of the spinal cord (FIERHELLER et al., 2004; CAULKETT et al., 1993; KAMILOGLU et al., 2005; LEE et al., 2003).

Detomidine HCl is 10 times more powerful than xylazine HCl and it has a lower cardiorespiratory effect. Although it provides deeper and longer sedation and analgesia than that provided by xylazine HCl (HALL et al., 2001; TAYLOR and CLARKE, 1999), it has been reported that detomidine HCl provides less analgesia than xylazine HCl after the administration of an epidural in mares (SKARDA and MUIR, 1996).

The goal of this study was to evaluate the clinical effects and certain hemodynamic and haematological effects of subarachnoid anaesthesia, consisting of a combination of detomidine HCl and ropivacaine HCl injected through the T13-L1 or L1-L2 space for surgery in the paralumbar fossa region in cows.

Materials and methods

The present study was carried out on 15 adult cows of the Swiss brown breed weighing an average of 350 kg. after approval by the ethical committee of Kafkas University (April 25, 2008, No:013), Kars, Turkey. After shaving the area where the catheter was to be administered and ensuring asepsis/antisepsis, local anaesthesia (5 mL Adokain® 50 mL vial, Sanovel) was administered to the subcutaneous tissue, after which a Tuohy needle (Perican epidural needle 18G - 80 mm. Braun, Germany) was inserted into the subarachnoid space via T13-L1 or L1-L2, a spinal catheter (Perifix filter set, Braun, Germany) was inserted into the subarachnoid space through the needle, and then the needle was removed. Through the catheter that was affixed, a combination of detomidine HCl (Domosedan® 5 mL vial, Pfizer, Turkey) at a dose of 0.015 mg/kg and ropivacaine HCl (Naropin® 10 mL amp., AstraZeneca, Germany) at a dose of 0.02 mg/kg was injected with a drip at a rate of 0.5 mL/min.

The sedation was determined to be positive on the basis of the closing of the eyelids and the movements of the head and tail, while the start time and duration of the analgesia was determined with deep pin-pricks to the thorax, paralumbar fossa, inguinal area, hind legs, perineum and tail once every 5 minutes after the anaesthetic material had been injected.

Before the anaesthesia, at the time of the anaesthesia was administered (minute 0) and during the anaesthesia at 5, 15, 30, 60, 90 and 120 minutes, the following measurements were taken: heart rate, respiration rate, body temperature, arterial blood pressure (ERKA® D-83646 manual blood pressure device), hematocrit and haemoglobin values (MS4e® hemogram device), and ECG (CardEx™ 100 veterinary ECG-MVM). The distance from the skin to the subarachnoid space was measured by the lengths of the colour scales on the needle and catheter.

Statistical evaluation of the data was carried out using the ANOVA method and SPSS 16.0 (SPSS Inc, Chicago, IL, USA).

Results

The findings were evaluated based on clinical (Table 1) and haematological aspects (Tables 2-3).

Table 1. Doses and effect of the drugs used

	Amount of subarachnoid drug			Information about the anaesthesia				
No	Detomidine (Domosedan)	Ropivacaine (Naropin)	Injection location	Start time	Anaesthesia duration (min)	Sedation	Kicking	Movement
1	0.5 mL	1 mL	L1-L2	<1min	90	+	-	+
2	0.5 mL	0.3+0.3 mL	L1-L2	<1min	190	+	-	+
3	0.5 mL	0.7 mL	L1-L2	<1min	75	+	-	+
4	0.3+0.2 mL	0.3+0.5 mL	T13-L1	<1min	75	+	-	+
5	0.5 mL	0.4 mL	L1-L2	<1min	125	+	-	+
6	0.5 mL	0.4 mL	L1-L2	2 min	60	+	-	+
7	0.3 mL	0.5 mL	T13-L1	<1min	60	+	-	+
8	0.3 mL	0.4 mL	T13-L1	<1min	85	+	-	+
9	0.3 mL	0.3 mL	L1-L2	<1min	125	+	-	+
10	0.3 mL	0.5 mL	L1-L2	2 min	95	+	-	+
11	0.3 mL	0.3 mL	T13-L1	<1min	100	+	-	+
12	0.5 mL	1 mL	T13-L1	<1min	180	+	-	+
13	0.4 mL	1 mL	T13-L1	<1min	90	+	-	+
14	0.4 mL	1 mL	L1-L2	<1min	90	+	-	+
15	0.4 mL	0.7 mL	T13-L1	<1min	120	+	-	+

Table 2. Changes in hemodynamic values

	0	5	15	30	60	90	120	F
S	132 ± 4.47	148 ± 4.94	151 ± 10.69	149 ± 9.11	147 ± 9.36	126 ± 4.36	125 ± 8.33	1.621
D	70 ± 7.78	86.6 ± 6.00	80 ± 12.28	91.4 ± 11.46	78.5 ± 12.48	70 ± 4.94	61.6 ± 8.46	1.358
P	71.5 ± 5.46	58 ± 2.59	57.4 ± 3.53	56.5 ± 5.08	63 ± 6.67	70.6 ± 8.36	67.2 ± 8.26	1.197
R	26 ± 1.73	22.5 ± 0.84	18.5 ± 1.67	21.4 ± 2.44	22.4 ± 1.73	21.4 ± 14.26	21.2 ± 1.75	1.123
T	39.1 ± 0.39	38.9 ± 0.59	39.0 ± 0.40	38.9 ± 0.35	39.0 ± 0.46	38.9 ± 0.45	39.0 ± 0.50	00.213

S: Systolic, D: Diastolic, P: Pulse, R: Respiration, T: Temperature ($P<0.05$)

Table 3. Hematocrit and haemoglobin findings

	0	5	15	30	60	90	120	F
Hb	9.60 ± 1.41	9.49 ± 1.75	9.00 ± 1.36	8.93 ± 1.22	9.21 ± 1.31	9.41 ± 1.29	9.54 ± 1.29	00.404
PCV	31.51 ± 4.47	30.30 ± 5.53	28.99 ± 4.01	29.08 ± 4.18	28.68 ± 4.38	30.09 ± 4.36	30.30 ± 4.78	00.524

Hb: Haemoglobin, PCV: Hematocrit ($P<0.05$)

Clinical findings. Using a scale on the catheter inserted through the Tuohy needle, the distance from the skin to the subarachnoid space was found to be an average of 90 ± 3.13 mm, depending on the size of the animal.

No animal developed ataxia or laid down during in the study. No complications such as increase in salivation or tympany occurred.

The pin-pricks revealed that analgesia suitable for surgery developed in much less than 1 minute and that the period of suitable anaesthesia lasted from 60 to 190 minutes (an average of 104 ± 38.64 minutes). The anaesthesia was determined to cover the region from T12 in the cranial direction to L5 in the caudal direction.

Hemodynamic and haematological findings. Although there was a drop in pulse and respiration rates prior to subarachnoid anaesthesia and at certain times during the anaesthesia, there was no statistically significant change in diastolic or systolic arterial blood pressure.

Body temperature remained at a level that could be considered stable, and no statistically significant difference was found over time ($P<0.05$).

Cardiac rhythm was evaluated on ECG obtained by D_2 lead. Sinus rhythm was observed in all the animals in the study, and no indications of arrhythmia were found.

Haemoglobin values dropped gradually up to 60 minutes, while haematocrit levels decreased until 90 minutes, but this decrease was not found to be statistically significant ($P<0.05$).

Discussion

Techniques such as infiltration (line block or L block), paravertebral, epidural and subarachnoid anaesthesia have usually been specified for paralumbar fossa surgery carried out on cattle without laying them down (FIERHELLER et al., 2004; CAULKETT et al., 1993, DeROSSI et al., 2003; SEYREK-INTAS et al., 2001; HIRAOKA et al., 2007). Although each method has certain advantages and disadvantages, subarachnoid anaesthesia may be the most effective method when administered by a specialist (HIRAOKA et al., 2007).

In recent years, epidural or subarachnoid administration of α2 adrenergic receptor agonists, including xylazine HCl, together with local anaesthetics has become more

widespread for caudal analgesia in horses and cattle (CAULKETT et al., 1993, SEYREK-INTAS et al., 2001; HIRAOKA et al., 2007; DeROSSI et al., 2007; YAMASHITA, 2000).

A study carried out by CAULKETT et al. (1993) reported that an analgesic period of 22.6 minutes, sufficient for surgery, was obtained with an L block using lidocaine HCl, that the administration of an epidural with a combination of xylazine HCl and lidocaine HCl administered through the 1st and 2nd coccygeal vertebral space provided sedation, that the analgesia lasted 94.8 minutes but the undesired effect was that the analgesia started late (22.6 minutes) and that the animal lay down due to the development of ataxia (CAULKETT et al., 1993). Similarly, LEE et al. (2005) reported a start time of 10 minutes for sedation with epidural administration of xylazine-lidocaine HCl, but this period was 25 minutes for analgesia in the paralumbar fossa. With regard to undesired effects, it is notable that in all similar studies that used xylazine HCl (LEE et al., 2005; HIRAOKA et al., 2007; LEE et al., 2004), ataxia developed and the animal often lay down. In a study by SKARDA et al. (1989) where procaine HCl was administered through the L1-L2 space, the start time for analgesia was reported to be 10-20 minutes, while the period of effect was found to be 60-105 minutes. This study found that analgesia suitable for surgery on the paralumbar fossa developed in less than 1 minute, this analgesia lasted for an average of 104 minutes and spread to the T12 in the cranial direction and to the L5 in the caudal direction. None of the animals in the study were observed to develop ataxia or lie down because they were unable to stand. Therefore, we think that the choice of both detomidine and ropivacaine HCl as a local anaesthetic offers significant advantages over similar studies, both because they are used as an agent and because they are used at very low doses.

Studies to date have reported that hypotension may develop due to blockage of the sympathetic fibres in the thoracic spinal cord due to the use of local anaesthesia (LEVIS et al., 1999; CAULKETT et al., 1993, SEYREK-INTAS et al., 2001). In a study that administered a lumbosacral epidural using xylazine HCl with lidocaine HCl, it was reported that there was no change in respiratory rate, but that there was a drop in heart rate, diastolic arterial blood pressure and body temperature (LEVIS et al., 1999). Similarly, KAMILOGLU et al. (2005) used a combination of xylazine and lidocaine for epidural analgesia and found that although there was a statistically significant drop in respiratory rate and body temperature, the drop in heart rate was not statistically significant. Although SKARDA et al. (1989) did not find a statistically significant difference in heart and respiratory rate, they reported that there was a drop in diastolic arterial blood pressure. In this study, even though the expected drop in pulse and respiration did occur, it was not statistically significant, in contrast to the other studies. In addition, there was no change, either an increase or a decrease, in body temperature. In this regard, it is possible to say that ropivacaine HCl has much fewer cardiopulmonary side effects than many other local anaesthetics.

In a study that administered a combination of epidural xylazine and lidocaine it was reported that there was no significant difference in hematocrit and haemoglobin concentrations (LEVIS et al., 1999), while another study that administered epidural xylazine-lignocaine concluded that all these values fell (SINGH et al., 2005). A study where subarachnoid detomidine HCl and mepivacaine HCl was administered, via infiltration, found a significant drop in haemoglobin and hematocrit values (SEYREK-INTAS et al., 2001). A study that used epidural ropivacaine HCl reported that no statistically significant difference was found in haemoglobin or hematocrit values (KINJAVDEKAR et al., 2007). In this study, although there was a drop in the hematocrit and haemoglobin concentrations, this drop was not found to be statistically significant, which is similar to other studies that used ropivacaine. This partial drop is inevitable and we think that it will increase depending on the dosage. As a result, it is more advantageous than other anaesthetic agents because it provides effective analgesia even at low doses, but it does not cause significant haematological changes.

In a study that administered epidural xylazine-lidocaine, it was reported that ruminal activity was depressed and that salivation increased, but that no complications were encountered regarding salivation, but heart rate and respiration dropped significantly (SINGH et al., 2005). In this study, no complications were encountered with tympany or salivation. For this reason, these kinds of complications could be avoided by using detomidine HCl instead of xylazine HCl, to which cattle are reported to be very sensitive.

LEE et al. (2005) found the distance between the skin and the subarachnoid space to be 84-93 mm in 8 cows and 85-95 mm in 10 cows, and did not find any statistically significant difference in the effect on analgesia in these two groups. Another study (LEE et al., 2006) reported this distance as 82-91 mm in adult animals and 57-65 mm in young animals, while another source (LEE et al., 2004) gave this figure as 89 mm. HIRAOKA et al. found this distance to be 81-90 mm (SEYREK-INTAS et al., 2001). In this study, this distance was found to be approximately 90 mm. In this regard, our study was similar to other studies. For subsequent studies, we recommend that at least a 90-100 mm Tuohy needle could be used so that the desired area can easily be reached.

DeROSSI et al. (2007) administered butorphanol-lidocaine HCl and reported that they obtained analgesia for 170 minutes in the paralumbar fossa, tail, perineum, hind legs and belly, but that severe ataxia developed in all animals and that they could not remain standing. A significant increase in heart rate was found and it was recorded as tachycardia up to 120 minutes into the procedure. Similarly, an increase in respiratory rate was observed (DeROSSI et al., 2007). A study by KINJAVDEKAR et al. (2007) that used ropivacaine HCl in different doses as a lumbosacral epidural reported that analgesia began in 2-5 minutes in the tail and hind legs, that analgesia remained in effect in the

hind legs for 45 minutes at a low dosage (37.5 mg) and for 75 minutes at a high dosage (75 mg). However, the study reported that this time period was significantly shorter in the paralumbar fossa. In the same study (YAYLA and KILIC, 2010), the spread of analgesia was only limited to the hind legs in the group that used low dose ropivacaine HCl, while in the high dose group, it was reported to spread as far as T9-T10. Ataxia developed in the animals in both groups and lying down in the sternal position was reported as an undesirable effect. In this study, the animals were prevented from lying down by use of ropivacaine HCl at a much lower dose.

A study that used epidural ropivacaine HCl reported that no statistically significant difference was found in ECG readings (YAYLA and KILIC, 2010). In this study, the fact that no pathological issue was observed in ECG readings is consistent with the literature, which indicates that ropivacaine HCl has minimal side effects on the heart.

Although studies report advantages such as rapid effect, minimum distribution and low anaesthetic dose with thoracolumbar subarachnoid anaesthesia, administered via a catheter inserted through the lumbosacral region, they also report disadvantages such as the breaking or folding of the inserted catheter, trauma that may occur to the medulla spinalis, or vascular injury. This study avoided the disadvantages associated with inserting the catheter via a lumbosacral route by administering the catheter to the subarachnoid space using the dorsolumbar route via the L1-L2 space. In addition, a relatively small amount of detomidine HCl and ropivacaine HCl were used to carry out safe anaesthesia in the area of the paralumbar fossa, such that anaesthesia began quickly and continued for a sufficient amount of time for surgery.

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SAŽETAK

Cilj ovoga istraživanja bio je procijeniti učinkovitost analgezije u slabinskom području u krava nakon subarahnoidalne primjene male doze detomidina u kombinaciji s malom dozom ropivakaina. U istraživanju je korišteno 15 negravidnih krava Brown Swiss pasmine, s prosječnom tjelesnom masom od 350 kg. Nakon lokalne anestezije potkožnih tkiva u području oko katetera, uz pomoć Tuohy-eve igle u subarahnoidalni prostor T13-L1 ili L1-L2 primijenjena je kombinacija detomidina (0,015 mg/kg) i ropivakaina (0,02 mg/kg) HCl, u količini od 0,5 mL/min. Analgezija slabinskog područja započela je unutar jedne minute nakon primjene anestetika, a trajanje anestezije prosječno je iznosilo 104 min uz širenje do razine T12 i L5. Vrijednosti srčanoplućnih, hematoloških i hemodinamskih pokazatelja nisu se statistički značajno razlikovale prije i tijekom anestezije. Relativno mala količina detomidina HCl i ropivakaina HCl dostatna je za postizanje sigurne i brze analgezije lijevoga slabinskog područja.

Ključne riječi: subarahnoidalna anestezija, detomidin, ropivakain, govedo