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EPIDURAL ADMINISTRATION OF ROMIFIDINE FOR SURGICAL ANALGESIA OF BUFFALOES UNDERGOING STANDING FLANK AND UDDER SURGERY.

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ABSTRACT

The aim of the present study was to evaluate the efficacy of romifidine as epidural analgesic for standing flank and udder surgery in buffaloes. For this purpose, romifidine was administered at dose 50 µg kg-1 via epidural space in 20 female buffaloes had to undergo flank and udder surgery. Buffaloes were examined for time to onset of analgesia, anatomic extent of analgesia, all systemic reactions to the drug and the total procedure time. Moreover, heart rates, rectal temperature, respiratory rates, feces and urine production as well as the degree of analgesia, sedation and ataxia were recorded at different intervals before (baseline) and after administration. In all animals, epidural injection of romifidine induced a significant decrease in the heart rate. However rectal temperature and respiratory rate didn't show any significant changes. There was a significant increase of analgesic effect with time progress. For all animals, the peak analgesic period was extended from 15-240 minutes post- administration of romifidine. Ten minutes after epidural

administration, all buffaloes began to show signs of systemic sedation (mild sedation, score = 1). Maximal sedative effect occurred between 30 and 180 minutes after epidural administration of romifidine. All buffaloes developed moderate ataxia (score 2) 15-20 minutes following epidural administration of romifidine and it lasted for up to 240 minutes. All these results provide evidence for a potential cost-effective intra- and postoperative method of analgesia for abdominal and udder surgery in buffaloes, while allowing the patients to remain standing. Therefore, romifidine might be promising as an analgesic agent for buffaloes even for major abdominal surgery.

Keywords: Romifidine; Epidural analgesia; Buffaloes.

INTRODUCTION

Currently, various local anesthetic techniques for providing anesthesia in standing bovine undergoing flank and udder surgery have been described ***(Skarda 1993)***. Each of these techniques has various advantageous and disadvantages, but the ideal technique would be one that provides complete anesthesia of the flank and the udder following injection of a small volume of anesthetic and is not associated with any adverse effects ***(Lee and Yamada 2005).*** Depending on the site of injection, different types of epidural analgesia are distinguished. In segmental epidural analgesia the local analgesic is injected into the thoracolumbar (T13-L1) or first lumbar (L1-L2) intervertebral space. This provides analgesia of the flank useful for surgeries, such as caesarean section, rumenotomy, or laparotomy ***(Skarda and Muir 1979)***. This technique is difficult to be performed and the reported complications were ataxia or recumbency due to inadvertent subarachnoid injection ***(Skarda 1996).*** The lumbosacral (L6-S1) epidural analgesia is easier to be performed ***(Lewis et al. 1999)***.

According to ***Seiferle (1992),*** the spinal cord reaches as far as the first sacral vertebra. Therefore, the risk of damaging the spinal cord during segmental or lumbosacral epidural anaesthesia does exist ***(Skarda 1996)***. For this reason these techniques are not widely established in cattle practice. On the contrary, caudal epidural analgesia is routinely used in bovine for a variety of surgical and obstetrical procedures and may be described as ˝high˝ or ˝low˝ ***(Benson and Thurmon 1981)***. Both techniques employ the injection of a volume of local anesthetic solution into the sacrococcygeal (S5-Co1) or first coccygeal (Co1-Co2) intervertebral space. High caudal epidural analgesia involves the administration of relatively large volume of local analgesic to provide analgesia to the more cranial body regions and is used for performing hind limb and udder surgery ***(Turner and McIlwraith 1982)***. Low caudal epidural analgesia is more frequently used than high epidural technique and differs only in the volume of local analgesic solution injected. This technique produce analgesia restricted to the tail, anus, vulva and perineal area without compromising the motor function of the pelvic limbs ***(Caron and LeBlanc; 1989).***

Several local anesthetic drugs are used to produce epidural anesthesia, such as lidocaine, bupivacaine, ropivacaine, and mepivacaine **(*Skarda 1996).*** Epidural analgesia is obtained also with opioid agonists, alpha$_2$-adrenergic agonists, and ketamine ***(Natalini and Driessen 2007).***

Caudal epidural analgesia using local anesthetics is produced by inhibition of conduction of impulses of sensory nerves located in the cauda equina ***(Levy 1974).*** Local anesthetics show little discrimination among fibers blocking sensory, sympathetic, and motor fibers. Depending upon the placement and volume of local anesthetic, both sensory and motor neural fibers may be affected ***(Turner and McIlwraith 1982).***

Occasionally, the loss of sensory and motor function is desired to facilitate completion of any procedure. Frequently, however, it would be advantageous to block the sensory fibers without affecting motor function, thereby allowing the animal to remain standing ***(Zaugg and Nussbaum 1990).***

It has been shown in a number of species that opioids and alpha-adrenergic agents produce selective caudal epidural analgesia, by activating specific spinal receptors ***(Cousins and Mather 1984; Yaksh 1985; Fierheller et al. 2004; Kinjavdekar et al 2007; Ishii et al 2008).*** Stimulation of these spinal receptors results in inhibition of rostral transmission of nociceptive (pain) impulses. Therefore a potential advantage of such agents is the production of selective sensory blockade, without the unfavorable depression of motor or autonomic neurons. Romifidine is an amino`-imidazolidine derivative, selective alpha 2-adrenoceptor agonist drug ***(Adams 2001)***. It has been administrated IV, IM, and epidurally in horses ***(England et al. 1992; Gasthuys et al. 1996; Kerr et al. 1996),*** dogs ***(England et al. 1996; Lemke, 1999), cats (Selmi et al. 2004),*** cattle ***(Prado et al. 1999; Fierheller et al. 2004)***, sheep (**Celly et al. 1997**) and goat ***(Aithal et al. 2001; Amarpal et al. 2002; Kinjavdekar et al. 2006)***, and it has been shown to have systemic and analgesic effects similar to other alpha-2 agonists. In cattle, romifidine appears to have similar effects as xylazine, although it may provide more rapid onset and greater duration of analgesia ***(Massone et al. 1993)***. To the best of the authors' knowledge, the use of romifidine for epidural analgesia in buffaloe has not been described. Therefore, the objective of this study was to evaluate the effectiveness and usefulness of romifidine as an epidural analgesic in buffaloes for surgical procedures cranial to the perineal region.

MATERIALS AND METHODS

Twenty mature female buffaloes at 1.5 to 7 years of age (5.92 ± 2.15) and weighed 330 - 470 kg (402.57 ± 74.27) were used in this study. All animals under investigation were admitted to both Universities of Kafr-Elsheikh and Cairo Veterinary Medicine Teaching Hospitals and underwent standing flank or teat surgical procedures. All buffaloes considered healthy on the basis of results of physical examination. Each animal had a complete physical examination prior to and at the end of the study, as well as being continually monitored throughout the study. Romifidine (Sedivet, 10 mg/ml, Boehringer Ingelheim, Vetmedica GmbH, Germany) was administrated epidurally in each buffalo.

Each animal was restrained in standing position in a stanchion, the hair over the epidural injections site was clipped, and the site was surgically prepared. Each animal received 50 μg $kg^{-1}$of romifidine (romifidine dosages were diluted in sterile saline to a final volume of 20 ml) injected directly into the epidural space between the first and second coccygeal vertebrae (the first intercoccygeal pace), using 18 gauge, 4 – cm hypodermic needle. The needle was inserted at an angle of 45˚ to the skin surface, directed anteriorly and venterally to a depth of 2 cm. Correct needle placement was verified by detecting negative pressure with the hanging drop technique **(Skarda 1986)** and negligible resistance to injection. Following placement of the needle, the solution was administered into the epidural space by slow injection. The time of administration was noted, and the surgery site was clipped and prepared for surgery.

After administration of romifidine, the following parameters were recorded; time to onset of analgesia, anatomic extent of analgesia, all systemic reactions to the drug and the total procedure time. Heart rates, rectal temperature, respiratory rates, feces and urine production as well as the degree of analgesia, sedation and ataxia, were recorded immediately (time 0) pre-administration and at 5, 15, , 30, 45, 60, 90, 120, 180 and 240 minutes and again at 6, 12, 24 and 48 hours after making the epidural injection. At each monitoring time, the occurrence of feces or urine production during the preceding interval was recorded.

In addition to watching for pain (nociceptive) response during the surgical procedure, also the onset, depth and margins of analgesia was qualitatively assessed by observing the animal's response to skin pinpricks with an 18 gauge hypodermic needle. The sedative and analgesic effect was evaluated and recorded blindly on visual analogue scale by single clinician at the same time points. The buffalo's eyes were covered at the time of stimulation to avoid any visually provoked response. The wounds created by the skin pricks were cleaned and then treated with a topical antiseptic solution. Depth of analgesia was graded on a score system from 0 to 3 as described in horses by **Jöchle and Hamm (1986)**; 0, no analgesia (strong response to noxious stimulus, such as kicking); 1, mild analgesia (moderate response, such as turning the head toward the site of stimulation); 2, moderate analgesia (very weak and occasional response); 3, complete analgesia (no response to noxious stimulus). The time of onset and score and duration of analgesia were recorded for 240 minutes post-administration. Time to onset of surgical analgesia was taken as the time from injection to the time when the animal failed to respond to pinpricks along the incision site. Total procedure time was the time from epidural administration to the

completion of surgery. Epidural (surgical) analgesia was assessed to be poor if the animal responded to pinprick or incision in a violent manner, or demonstrated signs of distress. Analgesia was assessed to be adequate if there was minimal response to incision, i.e., switching feet, lifting hind leg, or turning head to see the incision site. The analgesia was assessed to be good if the animal showed no response to surgical stimulations.

Sedative effect of romifidine was assessed subjectively on a scale 1 to 5 (Table 1). The time of onset and score of sedation were recorded immediately after drug administration. The duration (minutes) of sedation was determined as the time from start of sedation effect to return to score of zero. Sedation was considered to be acceptable if the buffalo developed a low head carriage, ptyalism, and decreased reaction to external stimuli, but showed no signs of ataxia (sedation score = 1).

Table (1): Sedation scoring system for buffaloes receiving romifidine (50 µg kg^{-1}).

Score	Criteria	Subjective assessment
0	No sedation	Buffalo appears unchanged from normal attitude (normal frequency and velocity of movement, head and neck carriage, eye alertness, lid apposition, tongue position, postural tone, stance)
1	Mild sedation	Buffalo appears slightly changed from normal attitude (slightly decreased frequency and velocity of movement, lower head carriage, deviation of the neck, reduced eye alertness, ptosis of upper lid, hanging or protrusion of the tongue out of the mouth, slight base-wide stance, slightly relaxed postural tone, ptyalism)
2	Moderate sedation	Buffalo appears moderately changed from normal attitude (moderately decreased frequency and velocity of movement, obvious head ptosis, increased base-wide stance, appearance of crossed legs, buckled knees and/or fetlocks, more relaxed postural tone, swaying of the hind legs)
3	Deep sedation	Markedly decreased frequency and velocity of movement, marked ptosis of the head and upper eyelid, markedly deviation of the neck, greatly reduced eye alertness, extreme protrusion of the tongue out of the mouth, markedly increased base-wide stance, increased occurrence and severity of crossed legs, buckled knees and/or fetlocks, pronounced loss of postural tone, attempts to lie down but aroused with stimulation)

The degree of ataxia was assessed by the degree of resistance to lateral push on the pelvis, observing the position of animal's hind limbs, how much the animal swayed and leaned against the stanchion, the extent of knuckling or flexion of fetlock (metatarsophalangeal) joints and the animal attempt to lie down (Table 2).

Table (2): Scoring system used for description of ataxia after epidural administration of romifidine in buffaloes (50 µg kg^{-1}).

Score	Criteria	Resistance to push	Fetlock flexion	Swaying and leaning	Attempt to lie down
0	No ataxia	Strong	None	None	None
1	Slight ataxia	Normal	None	Slight	None
2	Moderate ataxia	Decreased	Intermittent	Occasional	attempt to lie down but easily coaxed up
3	Significant ataxia	Weak	Often	Often	attempt to lie down but difficulty coaxed up
4	Sever ataxia	Almost absent	Constant	Constant	Go down and could not be Coaxed up

Statistical analysis- Data analyses were carried out using statistical software program (SPSS for windows Version 15.01, USA). The results are presented as means ± SD. One-way repeated measures ANOVA was used to determine significant differences between values at different time points. Sphericity assumption and Wilks, Lambda were examined for significance. When a significant difference was found, Bonferroni post-hoc multiple comparison test was performed for further evaluation. Differences were considered significant when $P < 0.05$.

RESULTS

In all animals, the tail and perineal area become desensitized to a skin prick within five minutes after epidural injection of romifidine. Also, flaccidity of the tail was observed in all buffaloes under investigation. The needle prick analgesia test was sufficient and demonstrated when dermatomes were blocked after epidural administration of romifidine. The most cranial level of spinal nerve analgesia was estimated to be about thoracic segments T1 and T2. In all animals, the anatomic level of anesthesia ascended at least to the thoracic segment T4 (Table 3).

Table (3): The evaluation of buffaloes given epidural injection of romifidine (50µg kg^{-1}) to induce surgical analgesia while standing.

Procedure performed	Start of surgical analgesia (min.)*	Length of procedure (min.)	Cranial extent of analgesia**
Rumenotomy and application of ruminal canula (n = 9)	13.0 ± 2.20	90 ± 9.35	T_1(6/9) T_2 (2/9) T_3 (1/9)
cesarean section (n = 5)	13.0 ± 2.73	130 ±15.81	T_1 (4/5) T_2 (1/5)
Teat surgery (n = 6)	11.67 ± 2.58	39.17 ± 14.29	T_1(4/6) T_4 (2/6)

*Time from romifidine injection to surgical analgesia, or to maximum area of desensitization.

**Spinal nerve segments innervating anatomic areas that were desensitized to a skin prick

As shown in figure 1, epidural injection of romifidine induced a significant decrease in the heart rate (Wilks, Lambda, $P < 0.01$; Bonferroni test, $P < 0.05$). Thus the lowest heart rate was recorded at 45 minutes post-administration. However, respiratory rate and rectal temperature didn't show any significant changes. Frequent urination commencing about 60-90 minutes after administration of romifidine was observed during this study. The frequency of urination showed significant increase ($P < 0.01$) in all buffaloes (range 3-5 times).

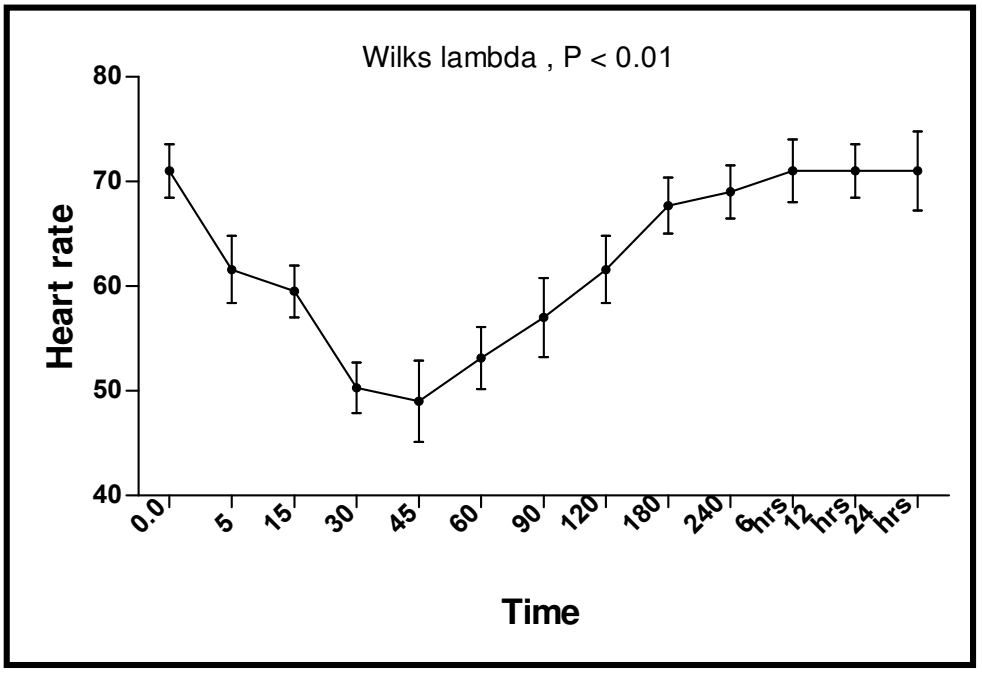

Fig. (1): Heart rate in buffalo pre- and post administration of epidural romifidine at 50 µg kg^{-1}. Note that the lowest heart rate at 45 minutes post –administraion.

All buffaloes responded with a score of zero (no analgesia) to noxious stimulation before epidural injection of romifidine. An increased threshold to skin pricks stimulation (complete analgesic effect; pain score 3), was achieved approximately 15 minutes after epidural administration of romifidine (13.00 ± 2.51 minutes) and duration of surgery ranged from 20 to 150 minutes (84.75 ± 36.76 minutes) (Table 4). There was significant increase of analgesic effect with time progress (Wilks, Lambda, $P < 0.01$) (Table 3). For all animals, the peak of the analgesic period extended from 15-240 minutes post- administration of romifidine. In one treated buffalo, the skin around the surgical incision became

somewhat sensitive to suturing after about 100 minutes following romifidine injection. Six hours after epidural administration of romifidine, all treated buffaloes showed a very weak and occasional response to skin pricks stimulation (moderate analgesia; pain score 2). By 12 hours after epidural administration, there were no longer analgesia and all treated buffaloes responded with a score of 0 (no analgesia) to skin pricks stimulation.

Fifteen minutes after epidural administration, all buffaloes began to show signs of systemic sedation (mild sedation, score = 1) (Table 4). No difference in onset was detected between all buffaloes. Maximal sedative effect (moderate sedation, score = 2) occurred between 30 and 180 minutes after epidural administration of romifidine (Wilks, Lambda, $P < 0.05$, post-hoc Bonferroni, $P < 0.05$). All animals remained calm and appeared to be unaware of their surroundings. Dropping (ptosis) of the eyelids and external conchea of the ear, lowering the head carriage, deviation of the neck, protrusion of the tongue from the mouth and ptyalism were recorded. Six and twelve hours after epidural administration of romifidine, all treated buffaloes remained mildly sedated with dropping lower eyelids, a decreased response to external stimuli, and lack of appetite (mild sedation, score = 1). By 24 hours after epidural administration, all buffaloes were no longer sedated and were eating well. All treated buffaloes did not show any clinical evidence of ruminal tympany. Forty-eight hours after epidural administration of romifidine, one buffalo developed a transient watery diarrhea that lasted for approximately 24 hours. This diarrheic buffalo remained bright and alert with a good appetite.

Table (4): Analgesic and sedative scores (Median and range) of epidural romifidine (50µg kg^{-1}) in buffaloes with abdominal and teat surgery.

Time Post-administration (minutes)	Analgesic effect	Sedative effect
Zero	00 ±00 [a]	00 ±00[a]
5	1.4 ± 0.70 [b]	1.0 ± 0.2[b]
15	2.95 ± 0.22 [c]	1.15 ± 1.30[b]
30	2.96 ± 0.23 [c]	2.0 ± 0.0[c]
45	3.00 ± 0.0 [c]	2.0 ± 0.0 [c]
60	3.00 ± 0.0 [c]	2.0 ± 0.0 [c]
90	3.00 ± 0.0 [c]	2.0 ± 0.0 [c]
120	3.0 ± 00 [c]	2.0 ± 0.0 [c]
180	3.00 ± 0.0 [c]	2.0 ± 0.0 [c]
240	2.94 ± 0.50 [c]	1.3 ± 0.43 [b]
360	1.6 ± 0.52 [b]	1.0 ± 0.18 [b]
720	0.0 ± 00 [a]	0.0 ± 0.0 [a]

Values with different superscript letters in the same column are significantly different at $P < 0.05$

All buffaloes developed moderate ataxia (score 2, Table 2) 15-20 minutes following epidural treatment with romifidine and it lasted for up to 240 minutes. All the animals remained standing throughout the observation period. One buffalo became recumbent during suturing of the incision. After 15 minutes, the animal stood without assistance. All buffaloes had poor coordination of the hind limbs when they were walked out of the stanchions, but none of them fell down. By six hours after epidural injection, all buffaloes showed a normal gait.

DISCUSSION

In human and animal anesthesia, epidural and spinal administration of drugs is used to provide surgical anesthesia and/or postoperative analgesia. Alpha-2 adrenoceptor agonists are becoming increasingly popular for providing intraoperative and postoperative analgesia in domestic species ***(Jean et al. 1990; Caulkett et al. 1993a &b; Zaugg and Nussbaum, 1990; Nowrouzian et al. 1991; LeBlanc et al. 1988; Day et al. 1995; Popilskis et al. 1991; Fierheller et al. 2004; Kinjavdekar et al. 2007)***. They resulted in safe and effective analgesia and produced much less depression of motor function than that produced by lidocaine. By raising the injection volume it is possible to extend the anaesthetized area ***(Zaug and Nussbaum 1990; Rehage et al. 1994; Junhold and Schneider 2002).***

The aim of the present study was to assess the sedative and analgesic effect of epidural romifidine for standing flank and udder surgery in buffaloes. Baseline values for all estimated variables were within normal limits for buffaloes. These observations indicate that the buffaloes were healthy and calm at the time of administration of the drug. At the given dose (50µg kg^{-1}), epidural romifidine produced significant decrease in the heart rate (Wilks' Lambda, P = 0.001). Bonferroni post-hoc multiple comparison test showed that the lowest value was at 60 minutes post-administration. This result is in agreement to previous studies in cattle and dogs ***(Massone et al. 1993; Pyppendob and Verstegen2001)***. Bradycardia following administration of alpha-2 adrenoceptor agonist may be due to central stimulation mediated through the vagus nerve ***(Hall et al. 2001)***.

No significant effect on respiratory rates and the rectal temperatures of treated buffaloes was detected after epidural administration of romifidine. However, a significant decrease in the respiratory rate ($P < 0.05$) was reported in cattle and goat after epidural or subarachnoid administration of romifidine ***(Fierheller et al. 2004; Kinjavdekar et al. 2006).***

In horses, perineal sweating is a sign that alpha 2-adrenoceptor agonists had been injected correctly into the epidural space ***(Leblanc et al. 1988)***. In the present study, buffaloes showed no such sweating as evidence of proper injection. Despite that, it was not difficult to correctly place the hypodermic needle for epidural injection of these buffaloes. This was similar to that previously recorded after the use of xylazine in cattle ***(Zaugg and Nussbaum 1990)***.

The dosage of romifidine in buffaloes is not yet well established. When it was given intravenously at a dose rate of 50μg kg^{-1} to buffalo calves, they become recumbent in 15 minutes and the anesthetic period lasted for approximately one hour ***(Shekidef et al. 2007).*** In the present study, a 50μg kg^{-1} dose was used, based on a study in goats in which 50 and 75 μg kg-1 romifidine were administrated in the subarachnoid space ***(Pablo 1993)***. Goats treated with 50 μg kg-1 romifidine had similar levels of analgesia, but with less sedation and cardiovascular depression than did goats treated with 75 μg kg^{-1}. The dose-dependent systemic effects of romifidine have been described in dogs when doses ranging from 5 to 100 μg kg^{-1} were administered IV ***(Pyppendob and Verstegen 2001)***. Systemic effects of romifidine were minimized by using lower doses; however, these effects were comparable when doses greater than 25 μg kg^{-1} were administered, suggesting a possible ceiling effect for

romifidine. In the present study, although the buffaloes did not become recumbent, the degree of sedation documented might have been minimized if a lower dose had been used. Further research is needed to determine a romifidine dose that causes minimal systemic effects while maintaining adequate analgesic effects in buffaloes.

The total volume of the administered solution given epidurally in this study was derived from other epidural studies in cattle and the migration of new methylene blue in the epidural space of cattle, horses, goats, and calves ***(Caulkett et al. 1993a &b; Lee et al. 2001; Hendrickson et al. 1998; Skarda 1996; Lopez et al. 1997; Johnson et al. 1996; Meyer et al. 2007).*** A total volume of 20 ml was decided for each buffalo, in an attempt to standardize the volume for practical use by veterinarians having to estimate doses in the field. By increasing the volume of delivered drug in the epidural space, the cranial extent of migration and analgesia may be increased.

Analgesia is an important quality of alpha-2 agonists ***(England and Clarke 1996).*** These substances act on both pre-and postsynaptic alpha-2 receptors, in the central nervous system, which decrease interneuronal transmission of norepinephrine and promote sedative and analgesic effects ***(Hall et al. 2001).*** Results in the study reported here suggest that epidural administration of romifidine provides significant analgesia of flank and udder regions, which was adequate for all required surgeries. Maximal effects were present at 15 minutes and gradually decreased to baseline levels after about 6 hours. As the buffaloes were only evaluated at 6, 12 and 24 hours postepidural administration, the exact duration of analgesia remains speculative. The onset of action of analgesia in this study appears to correlate well with studies on the epidural administration of romifidine in cattle ***(Massone et al. 1993; Fierheller et al. 2004).***

Whether the degree of analgesia produced in this study was due to local effects on the spinal cord or systemic sedation is difficult to evaluate. It has been shown that the effects of epidural versus IM administration of detomidine in cattle induce comparable degrees of analgesia. One theory for the analgesic effects observed was that IM detomidine acted on supraspinal α2-adrenergic receptors in the brain, while epidural detomidine had its effects locally in the spinal cord ***(Prado et al. 1999)***. However, the total volume of drug administered epidurally may not have been sufficient to achieve cranial migration of drug to the caudal lumbar and sacral spinal cord segments, thus the epidural effects in this study may also be attributable to systemic absorption and central effects in the CNS.

It was expected that epidural romifidine would produce spinal analgesia, similar to xylazine in cattle. In one study, 0.05 mg kg-1 body weight epidural xylazine produce 75-180 minutes of perineal analgesia ***(Caron and LeBlanc 1989).*** The more prolonged time of effect in our study can be explained by the fact that romifidine has longer duration of action than xylazine ***(Hall et al. 2001)***.

The prolonged duration of epidural analgesia using romifidine was not without disadvantage. Systemic absorption of the romifidine is likely, as treated buffaloes often showed signs of sedation. Dosages that did not result in sedation inconsistently produced epidural analgesia. Measurement of blood concentrations of romifidine or its metabolites were not conducted in this study. A second disadvantage of epidural romifidine is the somewhat delayed onset of analgesia compared to local anesthetic drugs as lidocaine. This disadvantage may be avoided with the simultaneous use of lidocaine and romifidine, but this combination was

not investigated in this study. However, for buffaloes in the present study, scrubbing, disinfecting, and draping of the surgical site were performed immediately after epidural administrationof romifidine (during the initial period before the onset of analgesia). Thus, surgery was begun approximately 15-20 minutes after epidural injection.

The sedative effects of romifidine at different doses and routes of administration have been studied in different animals ***((England et al. 1992 & 1996; Gasthuys et al. 1996; Kerr et al. 1996; Lemke 1999; Selmi et al. 2004; Prado et al. 1999; Fierheller et al. 2004; Celly et al. 1997; Aithal et al. 2001; Kinjavdekar et al. 2002; Kinjavdekar et al. 2006)***: however, there is no reported study on the use of romifidine for epidural analgesia in buffaloes. Our study indicated that romifidine is capable of producing systemic sedation (mild sedation, score=1). Onset of sedation started soon (10 minutes) after epidural injection of romifidine. No difference in onset was detected between all buffaloes. Our findings describing the sedation qualities of romifidine in buffaloes are similar to those reported for cattle and goats after epidural administration of romifidine and xylazine ***(Caron and LeBlanc 1989; Zaugg and Nussbaum 1990; Fierheller et al. 2004; Kinjavdekar et al. 2006).*** Sedation occurs following the absorption of epidurally administr-ated drugs into the vascular system ***(Gomez de Segura et al. 1998; Robinson and Natalini 2002)*** or transfer from the cerebral spinal fluid ***(Pedraz et al. 1991).*** Slow systemic absorption from the epidural space explains why romifidine produced mild sedation and did not produce recumbency, as would be expected if the same dose was used IV.

Ataxia was commonly observed in horses and cattle following epidural injection of xylazine and was attributed to the local anesthetic

properties of such analgesic agent ***(Leblanc et al. 1988; Caron and Leblanc 1989).*** A similar mechanism may have been responsible for the ataxia observed in this study. The combined systemic effects of muscle relaxation and sedation could be responsible for the ataxia observed in our study. High doses of alpha 2-adrenoceptor agonists have been shown to produce hind limb flaccidity in rats ***(Yaksh 1985)***. Ataxia may be less problematic with the availability of more selective alpha 2-adrenoceptor agonists.

Excessive salivation was recorded in this study. Similarly, cattle given romifidine had obvious increases in salivation ***(Fierheller et al. 2004)***. The marked increase in urine production after administration of alpha-2 agonists thought to be through inhibition of antidiuretic hormone release and hyperglycemia ***(Hall et al. 2001).***

Although, it was proved that alpha-2 agonists (xylazine, detomidine and romifidine) exert a marked pressure increase in the mare uterus ***(Schatzmann et al. 1994),*** it has not yet been established whether romifidine is safe for use in pregnant buffaloes or other animal species.

The economic factors associated with analgesic administration of romifidine in food animals must be taken in consideration. The cost of romifidine for epidural administration was double the cost of lidocaine required for a local nerve block of the flank region (EGP 45 versus EGP 22). Although the romifidine is expensive, the benefits of sedation and postoperative analgesia may outweigh the difference in price. Comparing the cost of epidural analgesia with the cost of nonsteroidal anti-inflammatory drugs labeled for use in cattle, a significant economic benefit is apparent with the use of epidural analgesics.

CONCLUSIONS

The present study showed that the clinical use of epidural romifidine can be indicated when long-term moderate analgesia is desired. Epidural administration of romifidine provides adequate analgesia for abdominal and udder surgery in buffalo, while allowing the patients to remain standing. The side effects of epidurally administrated romifidine were acceptable and had a little influence on the procedures or on recovery. Therefore, romifidine might be promising as an analgesic agent for buffaloes even for major abdominal surgery. Although a dosage of 50µg kg^{-1} was efficient and safe, further studies were needed to be done onto spinal toxicity; withdrawal times, systemic effects, and potential adverse using different doses before recommending the safely clinical use of romifidine.

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حقن عقار الروميفيدين فوق الام الجافية فى الجاموس لاحداث تخدير جراحى يمكن من اجراء جراحات منطقة الخاصرة والضرع فى وضعية الوقوف

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لقد كان الغرض من هذه الدراسة هو تقييم قدرة عقار الروميفيدين كعقار يمكن حقنة فوق الام الجافية لإجراء جراحات منطقة الخاصرة والضرع فى وضعية الوقوف فى الجاموس.

استخدم عدد عشرون من انثى الجاموس تم اجراء جراحات لهم فى منطقة الخاصرة والضرع .تم حقن عقار الروميفيدين بجرعة مقدارها 50 ميكروجرام/كجم في الفراغ فوق آلام الجافية بين أول وثاني فقرة عصعصية فى كل الحيوانات وهى تامة الإفاقة وفى وضعية الوقوف.

تم تسجيل البيانات الخاصة ببدء الإحساس بفقد الألم ، حدود منطقة فقد الإحساس بالألم ، التأثيرات العامة للعقار، والوقت المستغرق لإجراء الجراحة لكل حيوان علاوة على ذلك تم قياس النبض والتنفس ودرجة حرارة الجسم ، كمية إخراج البول والبراز بالإضافة إلى ذلك تم تحديد درجة فقد الإحساس بالألم ، السكون والاتزان على فترات زمنية قبل وبعد الحقن.

وقد أظهرت الدراسة أن حقن عقار الروميفيدين قد احدث انخفاض معنوي في ضربات القلب مع أنه لم يحدث أي تأثير على درجة الحرارة والتنفس. كما كان هناك زيادة معنوية فى درجة فقد الإحساس بالألم مع مرور الوقت والتي وصلت إلى أعلى معدلاتها في الفترة ما بين 15 و 240 دقيقة بعد الحقن. وقد بدأت كل الحيوانات في إظهار علامات السكون العام بعد مرور عشرة دقائق من الحقن (سكون معتدل من الدرجة الأولى) وكان أعلى تأثير للسكون فى الفترة ما بين 30–180 دقيقة بعد الحقن وأيضا أظهرت كل الحيوانات درجة متوسطة من فقد الاتزان بعد حوالى 15–20 دقيقة من الحقن والتي استمرت إلى 240 دقيقة بعد الحقن. من كل هذه النتائج يتضح أنه يمكن استخدام هذه الطريقة كطريقة آمنة وغير مكلفة لإحداث تخدير جراحي لمنطقة الخاصرة والضرع يمكن من إجراء الجراحات في هذه المناطق في وضعية الوقوف. كما أن استخدام عقار الروميفيدين في هذه الدراسة يشير أنه يمكن استخدامه لإجراء جراحات البطن الكبرى في الجاموس.