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RESEARCH ARTICLE

Comparative Efficacy of Medetomidine HCl and Lignocaine HCl as Epidural Anesthetic in Buffalo Calves

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ABSTRACT

The efficacy of medetomidine HCl as epidural anesthetic was experimentally assessed in 24 healthy buffalo calves of either sex and body weights ranging from 65-85 kg. The animals were randomly divided into 6 groups A1, A2, A3, A4, B and C (n=4). Medetomidine HCl was used at four different doses 15, 30, 45 and 60 µg/kg BW, respectively in first four groups. Group B animals were administered with lignocaine HCl 2% and normal saline (3mL) was administered epidurally in Group C (control). The onset and duration of analgesia were evaluated after every 15 min, using the pin prick and pinch tests. The onset of skin analgesia was dose dependent, higher and rapid with increase in dose and was earlier in animals of group A than B. Significant change in the duration of analgesia was observed till 40 min post injection ($P<0.05$). The recovery pattern showed a similar trend. The sedation score showed a significant dose dependent effect, becoming more pronounced as the dose of medetomidine HCl was increased in subgroups A1, A2, A3 and A4, respectively. Group B animals showed very mild sedation, while in group C, no sedation was observed at any stage. Thus it was concluded that despite early induction and longer duration of analgesia, medetomidine HCl at these doses is suitable for standing surgeries of hindquarters in buffalo calves. There was ideal onset and duration of analgesia and there was optimal sedation due to effective absorption of drug from injection site.

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INTRODUCTION

Medetomidine HCl (an alpha2-agonist) possesses more potency and economic efficacy than other drugs of this group (Kamine *et al.,* 2012; Morgaz *et al*., 2013). Medetomidine HCl has been used at limited level in cattle calves as anesthetic (Singh *et al*., 2009). Local anesthetics such as lidocaine, mepivacaine and xylocaine are routinely applied as epidural anesthesia in buffaloes (Singh *et al*., 2005).

Epidural alpha-2 agonists induce analgesia by stimulation of alpha-2 adrenergic receptors in dorsal horn of spinal cord. Epidural medetomidine HCl has been used to produce caudal analgesia in cattle (Pathak *et al*., 2012) and goats (Mpanduji *et al*., 2000). The attributes of medetomidine HCl having a lipophilic tendency, rapid elimination, prolonged duration of action and decreased disruption of motor function make it a preferable agent for standing surgical procedures in cattle and buffaloes (Singh *et al.,* 2009; Kalhoro *et al*., 2010). Sedation, cardiopulmonary depression and delayed onset of analgesia are prominent features of medetomidine (Singh *et al*., 2005). The objectives of present study were to determine an ideal dose rate of medetomidine HCl by epidural route for standing surgery of perineal region and to compare effects of medetomidine HCl at variable doses with lignocaine as ideal local anesthetic in buffaloes as these drugs have already been used for spinal analgesia in buffalo calves (Pathak *et al*., 2012). The efficacy of two drugs was determined on the basis of parameters; including onset time of analgesia, intensity/duration of analgesia, degree of ataxia/sedation, change in heart, respiratory rate and rectal temperature.

MATERIALS AND METHODS

Clinically healthy 6 to 10 months old buffalo calves (n=24), weighing 65 to 85 kg were randomly divided into six groups (n=4, each). Groups A1, A2, A3 and A4 were injected medetomidine HCl (15, 30, 45 and 60 µg/kg BW) whereas group B and C by lignocaine (2%) and Normal saline (control) using epidural route. Skin over first intercoccygeal space was clipped, surgically scrubbed and injection was made using a 20-G, 4-cm long hypodermic needle slowly over a period of 10-15 seconds. The needle was inserted at an angle of 45°, directed interiorly and ventrally to a depth of about 2 cm (Singh *et al*., 2009). Clinical parameters evaluated were analgesia, sedation and recovery.

Time period from injection to the loss of sensation was considered as onset of analgesia. Depth of analgesia was evaluated on the basis of presence/absence of perineal and inguinal reflexes, tongue protrusion, flexion of upper parts of hind limbs and loss of tail movement. The analgesia was judged by scoring system. Duration of analgesia was based on the time from onset of analgesia to full return of sensation. The average time for duration of analgesia was observed by continuously pricking at perineal area at intervals of 30 seconds until the animals showed a pin-prick response. Evaluation of sedation was carried out on the basis of onset, duration and recovery by observing the presence or absence of reflexes including head down, saliva drooling, jaw tone, palpebral reflex and gait in-coordination. Depth of sedation was calculated by scoring system. The data obtained on the above mentioned parameters was analyzed statistically using one way ANOVA (SPSS Inc. USA). Duncan's multiple range test (DMRT) was used to analyze the results at a significance level of $P<0.05$.

RESULTS

Analgesia: Analgesia was assessed on the basis of onset, duration and recovery. The onset of analgesia in Group A was dose dependent, higher, rapid and statistically significant ($P<0.05$) as compared with Group B. The mean values for onset of skin analgesia in A1 (15 µg/kg) were 3.17±0.17 min, A2 (30 µg/kg) 2.75±0.12 min, A3 (45 µg/kg) 2.77±0.15 min, A4 (60 µg/kg) 2.35±0.12 min as compared to 3.30±0.18 min in Group B. In group C, no analgesia was observed at any stage. Statistically, onset of analgesia showed significant difference in Groups A and B, when compared with Group C.

The duration of analgesia showed dose-dependent pattern and increased with increasing dose of medetomidine HCl. Statistical analysis showed that duration of skin analgesia was significantly different ($P<0.05$) among the four subgroups and subgroup A4 depicted the longest duration of skin analgesia (57.50±1.2 min). In group B, the duration of analgesia was 34.62±1.7 min, while in group C no signs of analgesia were observed at any stage.

The recovery pattern also showed a similar trend as subgroup A4 showed the longest recovery time (59.25±1.7 min), while recovery time of subgroup A1 was 45.50±1.2 min longer than that for Group B (35.82±1.8 min). The four subgroups of A and Group B showed significant differences with each other as well as with group C (Table 1).

Sedation: Sedation was evaluated on the basis of onset, duration and recovery. All of the treated and control groups showed highly significant differences with each other. Onset of sedation was dose-dependent in Group A. The shortest time for onset of sedation was observed in subgroup A4 (2.85±0.12 min), followed by group A3 (4.50±0.57 min), group A2 (5.50±0.57 min) and group A1 (6.50±0.57 min). In group B, mild sedation was observed and its onset was relatively delayed (7.37±0.54 min). Group C depicted no sedation at any stage.

There was significant difference in duration of sedation amongst all groups (A, B and C). The longest sedative duration was observed in group A4 (65.25±0.95 min), followed by A2 (56.50±1.2 min), A3 (55.75±2.5 min) and A1 (46.00±1.8 min). In group B, duration of sedation lasted for 26.75±2.2 min, while, no analgesia observed in group C.

Recovery from sedation was smooth and significantly different among all six groups. Dose-dependent effects of medetomidine HCl in the four subgroups of A were prominent as before and subgroup A4 calves depicted longest time for recovery (67.25±2.0 min). In group B, recovery was attained at an average time of (29.50±1.9 min), which was quite earlier and showed significant difference with group A. It was observed that even the lowest dose of medetomidine HCl as used in subgroup A1, showed longer times of recovery (45.50±1.2 min) as compared to group B. Contrarily, in group C no signs of sedation observed at any stage.

Clinical assessment: Medetomidine HCl was observed to induce a dose-dependent hypothermia. When compared with groups B and C, the subgroup A4 depicted the maximum fall in body temperature (101.67±0.29ºF) which was statistically significant ($P<0.05$). Group B calves also showed a slight decline in rectal temperature, however, the difference was non-significant as compared to control group. The pulse rate showed slight, yet significant ($P<0.05$) changes in subgroup A4 (69.00±1.8/min) as compared to groups B and C. The difference between groups B and C was also significant (Table 2). Respiratory rate of calves did not depict dose-dependent

Table 1: Evaluation of analgesia and sedation in buffalo calves after epidural administration of various drugs

Groups	Drugs used	Analgesia Time (min)			Sedation Time (min)		
		Onset	Duration	Recovery	Onset	Duration	Recovery
A1	Med 15µgm/kg	3.17±0.17^{d}	42.50±1.2^{c}	45.50±1.2^{c}	6.50±0.57^{e}	46.00±1.8^{c}	45.50±1.2^{c}
A2	Med 30 µgm/kg	2.75±0.12^{c}	44.00±2.1^{c}	47.50±1.2^{c}	5.50±0.57^{d}	56.50±1.2^{d}	58.50±1.2^{d}
A3	Med 45 µgm/kg	2.77±0.15^{c}	46.75±1.7^{d}	51.75±1.7^{d}	4.50±0.57^{c}	55.75±2.5^{d}	62.50±1.2^{e}
A4	Med 60µgm/kg	2.35±0.12^{b}	57.50±1.2^{e}	59.25±1.7^{e}	2.85±0.12^{b}	65.25±.95^{e}	67.25±2.0^{f}
B	Lignocaine 2%	3.30±0.18^{d}	34.62±1.7^{b}	35.82±1.8^{b}	7.37±0.54^{f}	26.75±2.2^{b}	29.50±1.9^{b}
C	Normal saline	0.00±0.00^{a}	0.00±0.00^{a}	0.00±0.00^{a}	0.00±0.00^{a}	0.00±0.00^{a}	0.00±0.00^{a}

Means carrying same superscripts differed non-significantly ($P>0.05$) and having different superscripts differed significantly ($P<0.05$).

Table 2: Temperature, pulse, respiration and heart rate in animals treated with medetomedine HCl and lignocaine

Groups	Drugs used	Clinical parameters		
		Temperature °F	Pulse beats /min	Respiration /min
A1	Med 15 µgm/kg	102.40±0.43^{b}	68.00±1.8^{a}	22.50±1.2^{a}
A2	Med 30 µgm/kg	102.50±0.25^{b}	75.75±1.7^{bc}	27.50±1.2^{b}
A3	Med 45 µgm/kg	102.35±0.26^{b}	72.75±1.7^{b}	31.50±1.2^{c}
A4	Med 60µgm/kg	101.67±0.29^{a}	69.00±1.8^{a}	27.50±1.2^{b}
B	Lignocaine 2%	102.60±0.31^{b}	72.50±03.6^{b}	29.00±2.4^{bc}
C	Normal saline	102.75±0.31^{b}	76.25±0.95^{c}	29.75±2.3^{bc}

Means carrying same superscripts differed non-significantly (P>0.05) and having different superscripts differed significantly (P<0.05).

effect of medetomidine HCl. However, significant (P<0.05) decline in respiratory rate was noticed in animals of subgroup A1 (22.50±1.2/min), as compared to the groups B and C (Table 2).

DISCUSSION

The analgesia induced in calves of group A (subgroups A1, A2, A3 and A4) was dose dependent, earlier in onset, longer in duration and statistically significant when compared with group B. This was evidenced by the stronger response in animals administered a higher dose in A4 (60 µgm/kg) and vice versa. These results were found to be in accordance with the findings of Singh *et al*. (2005) who reported an early onset and longer duration of analgesia after epidural administration of medetomidine HCl in buffaloes. In group B (lignocaine 2%), earlier onset of analgesia was recorded which is supported by outcome of studies in cows (Singh *et al*., 2005; Bigham *et al.,* 2010) describing similar efficacy of lignocaine in terms of rapid onset and long duration analgesia. Lignocaine and xylazine are being used as epidural anesthesia in calves and dogs (Meyer *et al*., 2009; DeRossi *et al.,* 2011). Medetomidine and ketamine combination is reported to be effective for anesthesia in goats (Kinjavdekar *et al.,* 2007). The duration of skin analgesia depicted a dose-dependent relationship, prolonged with an increasing dose of medetomidine HCl. The difference in duration of analgesia may be due to site of injection (lumbosacral or sacrococcygeal), level of injection (subarachnoid or epidural) and dose rate of drug (Singh *et al*., 2005). In present study, medetomidine HCl produced a very long duration of analgesia at higher doses, its effects were more pronounced when compared to effects produced by lignocaine. Since, medetomidine HCl was injected in the sacrococcygeal space, it was assumed that maximum concentration of drug was present in this area, evidenced by the complete analgesia recorded at tail and perineal region. These results recorded were in agreement with those reported by Lin *et al*. (1998). The experimental units, dose and conditions used were also in accord with present study.

Mild to moderate sedation and ataxia were noticed in present study. Animals appeared tired with dropping of head and eye-lids. Appearance of sedation signs is a common side effect after epidural administration of medetomidine HCl in cows (Amarpal *et al*., 2002; Condino *et al*., 2010). Similar pattern of signs was depicted in goats by sub-arachnoid administration of romifidine (Fierheller *et al*., 2004). From present study findings, it could be hypothesized that sedation was attributable to the supra-spinal effects of xylazine or medetomidine HCl following their systemic absorption from the extra-dural space. Similar reasons for sedation were also presented by Correa-Sales *et al*. (1992) who attributed sedation to sequential events including absorption of drug from subarachnoid space into systemic circulation, reaching to brain and causing decrease in release and turnover of epinephrine in CNS. The onset of sedation in group A was delayed and signs appeared early in subgroup A4. This indicated that analgesic action of the drug was due to its rapid local action rather than general effects. Similar findings have been reported by Aithal *et al*. (1996). Mild sedation was observed in all animals of groups A1, A2, A3 and A4 increased with higher dose of medetomidine HCl. A mild degree of general sedation was recorded in group B which is a common side effect with alpha-2-agonists (Sinclair, 2003).

Heart rate decreased in medetomidine HCl treated group A only, while no such effect observed in group B and C. Similar findings associated with use of medetomidine HCl has been reported in buffaloes (Singh *et al*., 2009), dogs (Vesal *et al*., 1996), cats (Duke *et al*., 1994) and cattle (Lin *et al*., 1998). Alpha-2 agonists are also used in the treatment of arterial hypertension (Mavropoulos *et al.,* 2014). Bradycardia post administration of alpha-2 agonists might be due to inhibition of sympathetic tone from the CNS, inhibition of nor-epinephrine release from sympathetic nerve terminals, vagal stimulation due to vasoconstriction and a direct increase in the release of acetylcholine from parasy-mpathetic nerves in the heart (Gargiulo *et al*., 2012).

In present study, respiratory rate was decreased in medetomidine HCl treated group A, compared to groups B and C which is in accord with findings of Kamine *et al*. (2012). There was not any dose dependent relationship and is in agreement with Malik *et al.* (2011). Group A animals showed a significant decrease in rectal temperature as compared to B. The reason behind this was again attributed to the fall in ambient temperature during course of trial or due to generalized sedation and decreased metabolism (Tanaka *et al.,* 2014). Conclusively, decrease in rectal temperature observed in present study may be caused by sedation, reduced metabolism, muscle relaxation and depression of the CNS. Similar results reported by Kinjavdekar *et al*. (2000) strengthened present study.

Conclusion: From this study it was concluded that epidural injection of medetomidine HCl produced a longer duration of analgesia with more pronounced effects in higher doses, as compared to lignocaine. Medetomidine administration produced complete analgesia of tail, perineum and inguinal region but this analgesia was dose dependent as higher doses produced deeper and longer analgesia. On the other hand local anesthetic (lignocaine) also produced good analgesia but was of short duration.

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