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USE OF MEDETOMIDINE HYDROCHLORIDE AS SEDATIVE IN CATTLE CALVES

A. B. Kalhoro, M. Tariq, A. B. Kachiwal, R. Rind, D. H. Kalhoro and S. Kalhoro

Faculty of Animal Husbandry and Veterinary Sciences,
Sindh Agriculture University, Tandojam, Pakistan.

ABSTRACT

This study was carried out to compare the sedative and analgesic effects produced by intravenous administration of three different doses of medetomidine (8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1}) in six healthy cattle calves. Various observations were recorded up to 120 minutes. Onset of sedation was observed at 26.00±0.36, 21.00±0.56 and 16.00±0.43 seconds and total duration of sedation was 73.83±0.69, 96.70±0.71 and 117.20±0.60 minutes with 8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1} body weight of medetomidine, respectively. Onset, duration and degree of sedation were different ($P<0.01$) with all three doses. Medetomidine at the dose rate of 8µg kg^{-1} produced moderate sedation in most animals, where as 10µg kg^{-1} and 12µg kg^{-1} produced deep degree of sedation in all animals. Skin analgesia was produced in all animals with higher doses (10µg kg^{-1} and 12µg kg^{-1}) and in only two animals with lower doses (8µg kg^{-1}). Its onset was at 13.00±2.753, 6.25±0.75 and 2.33±0.21 minutes after administration of medetomidine, while mean total duration was 36.00±7.59, 55.66±5.53 and 93.00±0.57 minutes with 8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1} of medetomidine, respectively which was significantly different ($P<0.01$) with all three doses. Medetomidine produced recumbency in all animals with higher doses (10µg kg^{-1} and 12µg kg^{-1}) and only in two animals with 8µg kg^{-1} body weight. Duration of recumbency was 48.50±10.23, 70.83±2.42 and 100.00±0.57 minutes and standing time was 51.00±10.75, 72.67±2.98 and 102.00±0.57minutes after administration of 8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1} medetomidine, respectively. It was concluded that medetomidine was a very potent sedative for cattle calves. Its dose rate must be carefully calculated based on actual body weight of the animal. At the dose rates studied, medetomidine may be used for sedation in animals requiring diagnostic or minor surgical procedures. It may also be used for pre-anesthetic medication.

Keywords: Medetomidine, sedation, analgesia, dose, cattle, calves.

Corresponding author: amirkalhoro@yahoo.com

INTRODUCTION

The development of new sedatives / analgesics has greatly contributed to the enormous progress made in veterinary medicine and surgery in recent years. These developments have resulted into means of reducing stress, preventing pain and safe and efficient sedation/anaesthesia for carrying out a wide variety of diagnostic and surgical operations in large and small animals. Alpha2 adrenergic agonists and antagonists have a significant role in the development of patient care (Short, 1992). Of these, xylazine, detomidine and medetomidine are frequently used for sedation and pre-anaesthetic medication in veterinary practice.

Medetomidine is a new alpha2-agonist which is about 30 to 40 times as potent as xylazine. It produces immediate and reliable degree of sedation, muscle relaxation and analgesia in a variety of domesticated animals (Lumb and Jones, 1996). Medetomidine is commonly used as sedative but is also used as a pre-anesthetic prior to ketamine, barbiturate, or mask induction with an inhalation anaesthetic (Lumb and Jones, 1996). Combinations with ketamine are more effective than the sedative alone (Hall and Clarke, 2003).

Medetomidine was developed primarily as sedative for use in dogs. However, it has now been experimented in other animals. Some studies have been carried out on sedative, analgesic and physiological effects of medetomidine in horses (Bryant *et al.,* 2004; Muhammad *et al*., 2006), free ranging cattle (Arnemo and Soli, 2005), sheep (Muhammad *et al.,* 1993; Malhi, 2006; Kaka, 2007), goats (Muhammad *et al*., 1989; Memon,1999; Carroll *et al.,* 2005), cats (Golden *et al*., 1996), rabbits (Mangi, 2004), ferrets (Ko and Jones, 1996), buffalo calves (Shahani, 1998; Kalhoro *et al.,* 2000) and in elephants (Sharma *et al.,* 2002). However no comprehensive work has been done on the use of medetomidine in cattle calves (Raekallio *et al.,* 1991; 2008; Rioja *et al*., 2008). Therefore, this study was planned to determine an effective dose rate and sedative and analgesic effects of medetomidine in cattle calves under same experimental conditions.

MATERIALS AND METHODS

Experimental animals

Six healthy Red Sindhi cattle calves of 8 to 16 months and weighing 56.16 ± 3.902 kg (mean ± SE) were used in this study. The calves were allowed to adapt the surroundings for atleast two weeks before experiment. They were given thorough physical examination and dewormed with Nilzan® (ICI Pakistan). Calves were vaccinated against anthrax, and haemorrhagic septicemia. All the calves were ear tagged with numbers. They were fed maize, wheat straw, cotton seed cake, and wheat bran and allowed ad libitum access to water. A standard clinical examination procedure was followed.

Experimental procedure

Before start of each experiment, the calf was weighed and brought to the surgery hall for the experiment. The hairs over the left and right jugular vein were clipped with an automatic hair clipper and the skin sites were disinfected with an antiseptic (70% alcohol). Medetomidine was administered by intravenous injection through a cannula or disposable syringe in the left jugular vein. The drug was injected slowly. For precise dosage 1ml disposable syringe was used. The dosage was calculated on the basis of animal's body weight as explained in the experimental design.

Experimental design

Each of six calves received 3 different doses of medetomidine: D_1 = 8µg kg^{-1} body weight, D_2 = 10µg kg^{-1} body weight and D_3 = 12µg kg^{-1} body weight. A randomized cross over experimental design was used. At least ten days interval was allowed between two treatments in each animal.

Sedative and analgesic effects

The degree, duration and onset of sedation and analgesia as well as nature and duration of recovery, standing time, onset of recumbency and duration of recumbency in each animal was recorded with each dose. Nature and safety of analgesic effect was checked by deep needle pricking at various body parts.

Grading of sedation

The degree of sedation was graded following Kalhoro *et al*. (2000).

0 = No sedation (animal alert)
1 = Light degree of sedation (slight effect with animal becoming quieter with its head lowered below shoulder but above knees).
2 = Moderate degree of sedation (animal becoming less alert, partial closure of eyelids with its head lowered beyond knees).
3 = Deep degree of sedation (animal becoming ataxic and recumbent).

Other observations

Other clinical features like salivation, regurgitation, snoring, bellowing, urination, defecation, tympany, jugular pulsation, wobbling, staggering and protrusion of tongue were evaluated with each dosage, if any. Palpebral and pedal reflexes, nystagmus, jaw tone and movement of tail were also noted after administration of sedative in each animal.

Statistical analysis of data

Analysis of data was performed by using analysis of variance (ANOVA) and Duncan Multiple Range Test (DMRT).

RESULTS AND DISCUSSION

Onset of sedation

The mean values ± SE for onset of sedation in the calves were 26.00±0.36, 21.00±0.56 and 16.00±0.43 seconds after administration of 8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1} of medetomidine, respectively (Fig.1). The onset of sedation showed difference ($P<0.01$) with all three doses. The onset of sedation was rapid ($P<0.01$) with 12µg kg^{-1} as compared to 8µg kg^{-1} and 10µg kg^{-1}. The onset of sedation was, therefore, dose dependent, with higher doses producing more rapid effect.

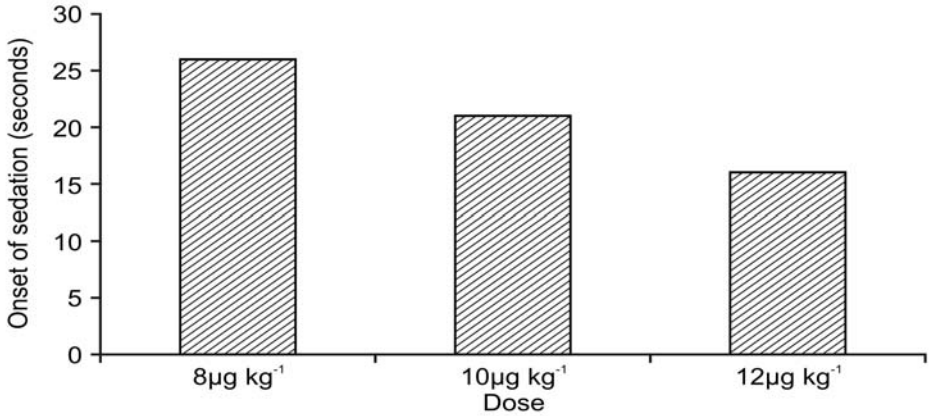

Figure 1. Onset of sedation (seconds) after administration of medetomidine

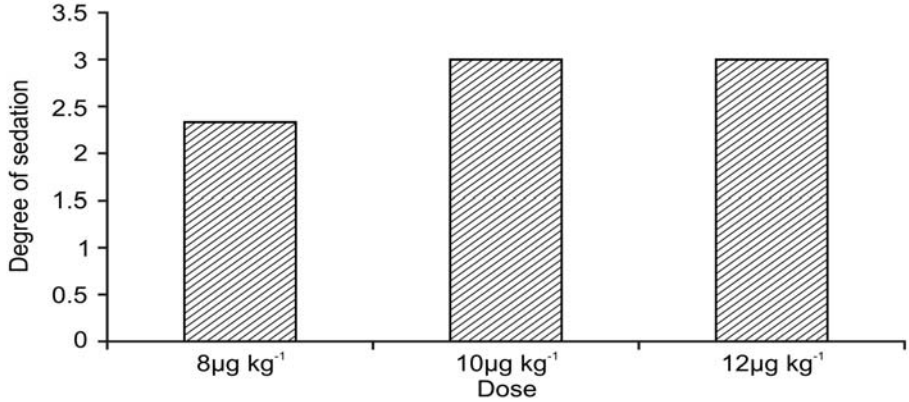

Figure 2. Degree of sedation after administration of medetomidine

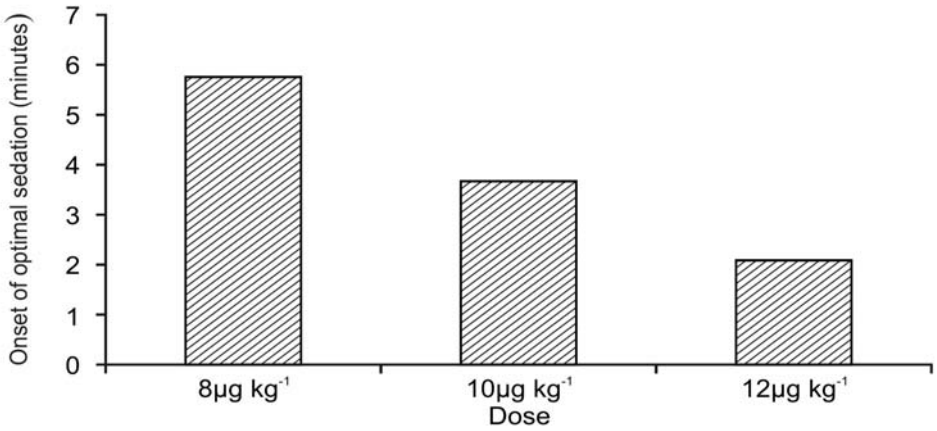

Figure 3. Onset of optimal sedation (minutes) after administration of medtomidine Duration of optimal sedation

Degree of sedation

A dose of 8 µg kg^{-1} body weight resulted in moderate sedation in four animals and deep sedation in two animals. The higher doses of medetomidine (10µg kg^{-1} and 12µg kg^{-1}) produced deep sedation, which was prolonged in case of 12µg kg^{-1} while it was shorter with 10µg kg^{-1} (Fig. 2). These findings are similar to others reported in cattle (Waldridge *et al.,* 1997), buffalo calves (Shahni, 1998), rabbits (Mangi, 2004), goats (Shah, 2008) and in sheep (Malhi, 2006).

Onset of optimal sedation

The mean ± SE values for onset of optimal sedation in the calves were 5.75±0.33, 3.66±0.16 and 2.08±0.20 minutes after administration of 8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1} of medetomidine, respectively (Fig.3). The onset of optimal sedation was different ($P<0.01$) with all three doses. It was rapid ($P<0.01$) with 12µg kg^{-1} as compared to 10µg kg^{-1} and slower with 8µg kg^{-1} as compared to 10µg kg^{-1} of medetomidine. The onset of optimal sedation was thus dose dependent and was more rapid with the higher dose rate.

The mean ± SE values for duration of optimal sedation in the calves were 46.83±2.00, 60.83±3.60 and 97.00±0.57 minutes after administration of 8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1} of medetomidine respectively (Fig.4.). The duration of optimal sedation was dose dependent. It increased with increasing dose of medetomidine. The duration of optimal sedation was different ($P<0.01$) with all three doses.

Total duration of sedation

The mean ± SE values for total duration of sedation in the calves were 73.83±0.69, 96.70±0.71 and 117.20±0.60 minutes after administration of 8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1} body weight of medetomidine, respectively (Fig.5). The total duration of sedation was dose dependent. It increased with the use of higher dose of medetomidine. The total duration of sedation was different among treatments. The total duration of sedation was longer ($P<0.01$) with dose of 10µg kg^{-1} and 12µg kg^{-1} body weight as compared to 8µg kg^{-1} body weight.

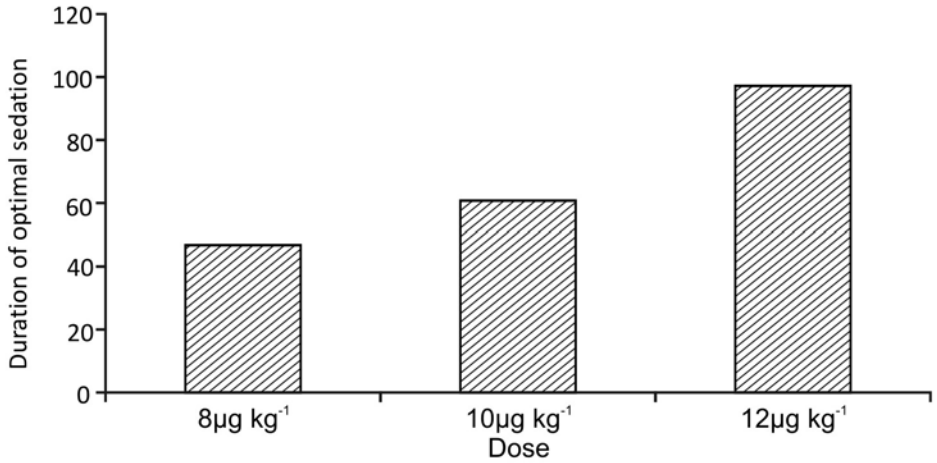

Figure 4. Duration of optimal sedation (minutes) after administration of medetomidine

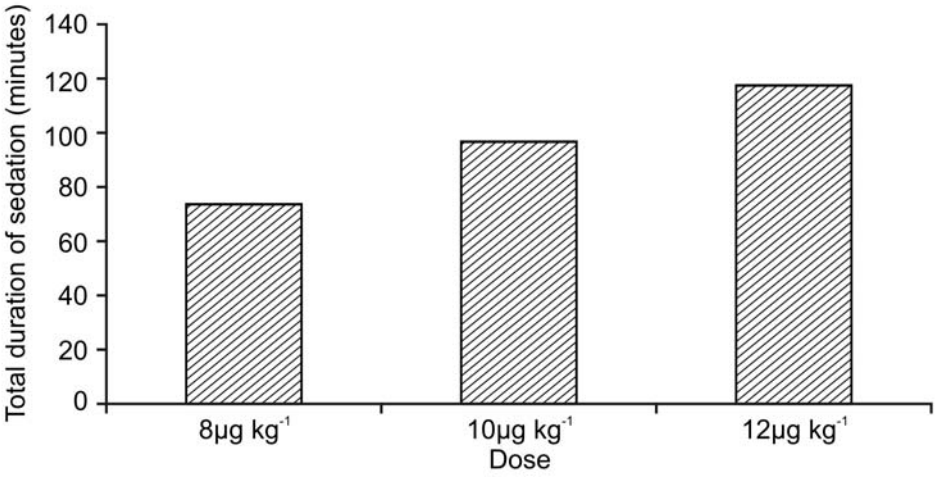

Figure 5. Total duration of sedation (minutes) after administration of medetomidine

Onset of recumbency

The mean ± SE values for onset of recumbency were 6.25±1.31, 3.50±0.18 and 1.50±0.18 minutes after administration of 8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1} body weight of medetomidine, respectively (Fig.6). The data suggested that the time for onset of recumbency was directly related with the dosage of drug. Increasing the dosage resulted in quick recumbency. Onset of recumbency was different ($P<0.05$) among treatments.

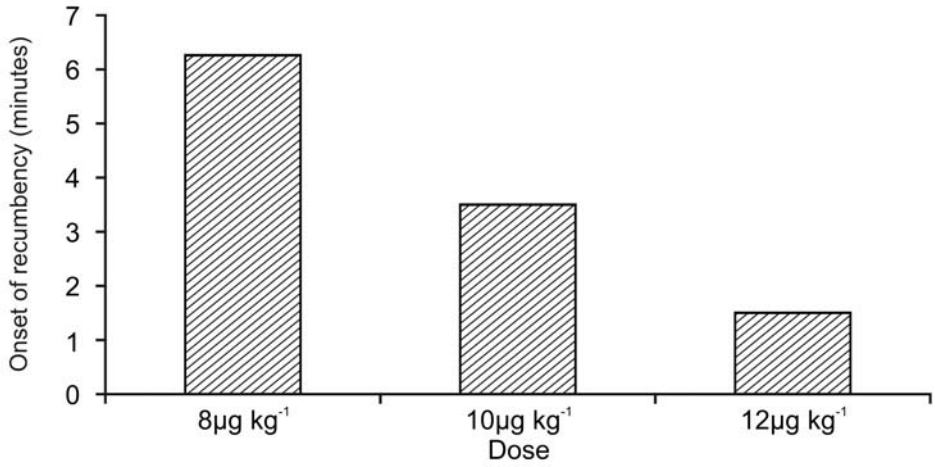

Figure 6. Onset of recumbency (minutes) after administration of medetomidine

Duration of recumbency

The duration (mean ± SE) of recumbency in cow calves was 48.50±10.23, 70.83±2.42 and 100.00±0.57 minutes after administration of 8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1} body weight of medetomidine, respectively (Fig.7). The duration of recumbency was dose dependent and increased with increasing dose of medetomidine. A difference of $P<0.05$ between dose rates of 10 µg kg^{-1} and 8 µg kg^{-1} and 10µg kg^{-1} and 12 µg kg^{-1} body weight was noted.

Standing time

The mean ± SE values for standing time were 51.00±10.75, 72.67±2.98 and 102.00±0.57minutes with 8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1} of medetomidine, respectively (Fig. 8). There was dose dependent effect of medetomidine on standing time. The dose rate of 12µg kg^{-1} resulted in prolonged standing time (102.00±0.57minutes) followed by 10µg kg^{-1} (72.67±2.98 minutes) and 8µg kg^{-1} (51.00±10.75). A difference ($P<0.05$) between 8 µg kg^{-1} and 10µg kg^{-1} ($P<0.01$) between 8µg kg^{-1} and 12 µg kg^{-1} and 10µg kg^{-1} and 12µg kg doses of medetomidine was noted. Onset of recumbency, its duration and standing time

after recumbency were also dose dependent. Higher dose of medetomidine (12µg kg^{-1} body weight) produced more rapid and longer duration of recumbency than 10µg kg^{-1} and 8µg kg^{-1} body weight dose rates.

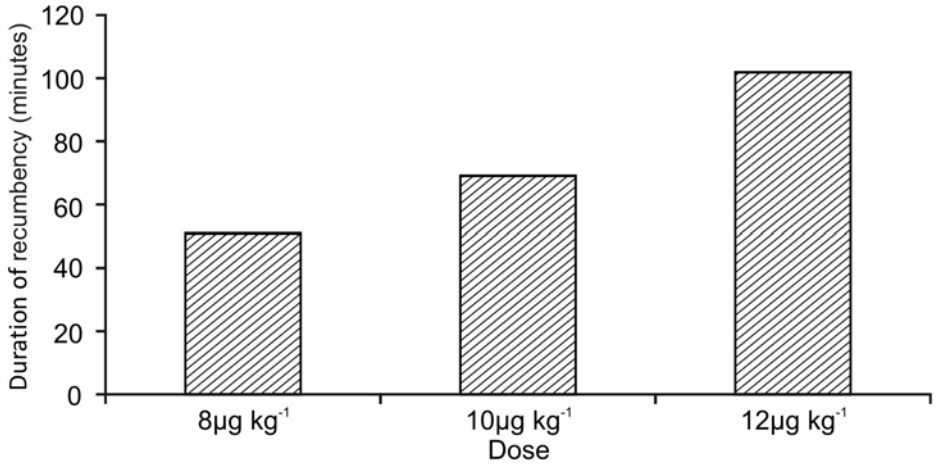

Figure 7. Duration of recumbency (minutes) after administration of medetomidine

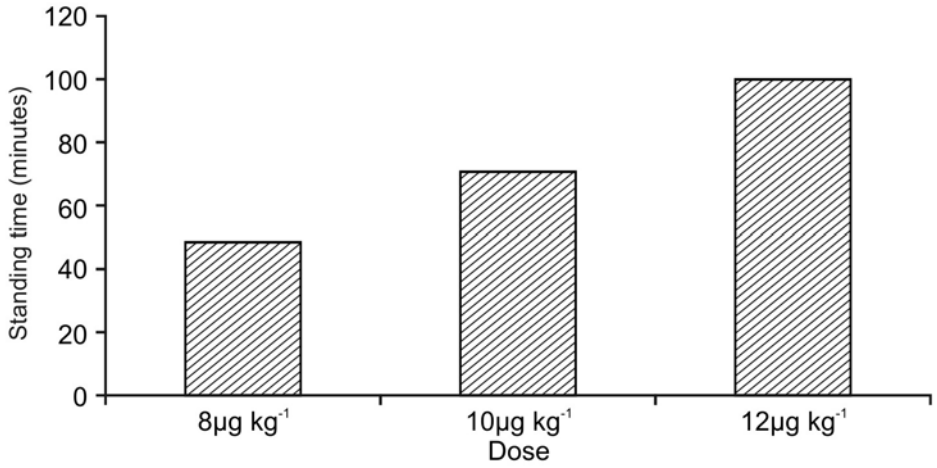

Figure 8. Standing time (minutes) after administration of medetomidine

In the present study, all parameters of sedation showed dose dependent effect. The highest dose (12µg kg^{-1}) of medetomidine resulted in quick onset of sedation which lasted for longer time, while 8µg kg^{-1} had slower effect and took comparatively longer time to sedate experimental calves. Dose dependent sedative effects of medetomidine have been reported in cattle (Waldridge *et al*., 1997), buffalo calves (Shahani, 1998), rabbits (Mangi, 2004), goats (Shah, 2008)

and sheep (Malhi, 2006). However, effective dose rate required for sedation in cattle calves recorded in the present study was slightly higher than sedative doses reported by above workers in other species of animals; but is slightly lower than those used by others in cattle calves (Raekallio *et al.,* 1991; 2008 and Rioja *et al.,* 2008).

Onset of skin analgesia

The mean ± SE values for onset of skin analgesia were 13.00±2.75, 6.25±0.75 and 2.33±0.21 minutes after administration of 8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1} body weight of medetomidine, respectively (Fig. 9). The onset of skin analgesia was dose dependent, with high dose producing more rapid effect. A difference ($P<0.01$) amongst all three doses of medetomidine was noted.

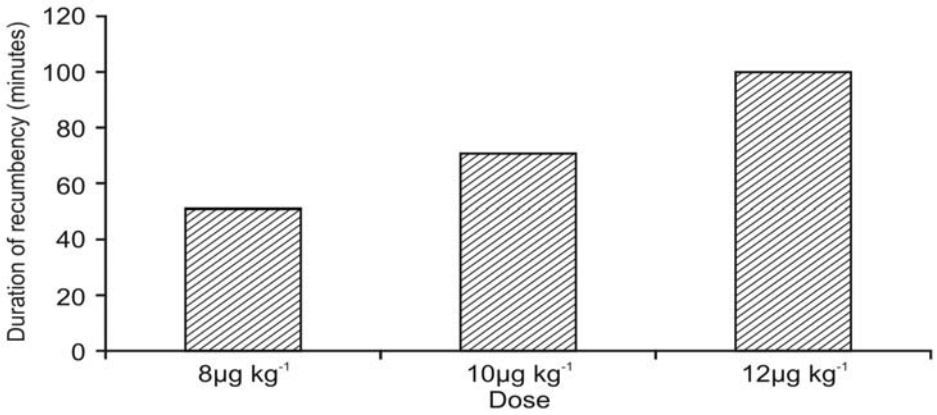

Figure 9. Onset of analgesia (minutes) after administration of medetomidine

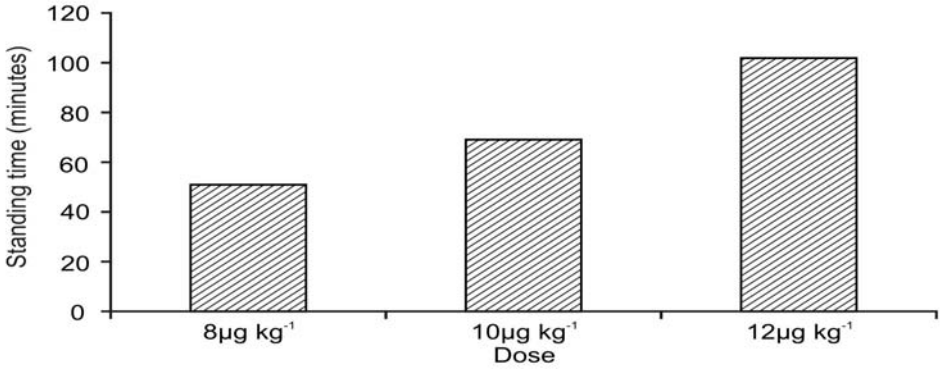

Figure 10. Total duration of skin analgesia (minutes) after administration of Medetomidine

Duration of skin analgesia

The mean ± SE values for duration of skin analgesia were 36.00±7.59, 55.66±5.53 and 93.00±0.57 minutes after administration of 8µg kg^{-1}, 10µg kg^{-1} and 12µg kg^{-1} of medetomidine, respectively (Fig. 10). The duration of skin analgesia was dose dependent which increased with increasing dose of medetomidine. The duration of skin analgesia was different ($P<0.01$) with all three doses. Onset and duration of skin analgesia were both dose dependent. Higher dose of medetomidine (12µg kg^{-1} body weight) produced more rapid and longer duration of skin analgesia than dose rates of 10µg kg^{-1} and 8µg kg^{-1} body weight.

Other observations

A number of observations and side effects were recorded after the use of medetomidine in cattle calves which are described in Table 1.

Table 1. Summary of other observations recorded after administration of medetomidine.

Symptoms	8µg kg body weight	10µg kg^{-1} body weight	12µg kg^{-1} body weight
Salivation	All	All	All
Staggering	All	All	All
Muscle relaxation	Present in 2 animals	Present	Present
Recumbency	Present in 2 animals	All	All
Wobbling	All	All	All
Head dropping	All	All	All
Defaecation	Only in 1animal	No	No
Frequent urination	Present in 4 animals	All	All
Jugular pulsation	Present in 3 animals	All	All
Tail movement	Present in 4 animals	Absent	Absent
Bellowing	Present in 3 animals	Present in 2 animals	Only in 1 animal
Protrusion of tongue	Absent	Present in 3animal	All
Palpebral reflexes	Absent 2 animals	Absent	Absent
Pedal reflexes	Present in 4 animals	Absent	Absent
Skin analgesia	Present in 2 animals	All	All
Tympany	Present in 3 animals	All	All
Lacrimation	Only in 1 animal	Present in 3 animals	Present in 5 animals
Regurgitation	Present in 4 animals	Only in 2 animals	Absent
Nystagmus	Present in 4 animals	Only in 1 animal	Absent
Jaw tone	Present in 3 animals	Present in 2 animals	Absent

Medetomidine produced some side effects such as salivation, increased urination and moderate tympany. These changes do not cause many problems to the animals except salivation. Saliva may enter the respiratory tract in recumbent animals and may cause suffocation. This can be prevented by giving injection of atropine sulphate or by lowering the head of animals. Marked salivation, mild

tympany and increased frequency of urination havealso been reported in cows (Ranheim *et al*., 2000), in goats (Memon, 1999), sheep (Malhi, 1996) and buffalo calves (Kalhoro, 2000).

CONCLUSION

It is concluded that medetomidine is a very potent sedative for cattle calves. Its dose rate must be carefully calculated based on actual body weight of the animal. At the dose rates studied, medetomidine may be used safely for sedation in animals for diagnostic or minor surgical procedures. It may also be used for pre-anesthetic medication.

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