

## SEDATIVE AND ANALGESIC EFFECTS OF DETOMIDINE HYDROCHLORIDE IN GOATS

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### ABSTRACT

The sedative and analgesic effects of three dose rates of detomidine (40, 50 and 60µg/kg body weight) were studied in six goats. Moderate to deep sedation occurred after administration of 40µg/kg of detomidine as compared to deep sedation produced by 50 and 60µg/kg of detomidine. The degree, onset and duration of sedation and onset and duration of maximum sedation were all dose dependent. Skin analgesia and recumbency were produced in all animals with higher doses (50 and 60µg/kg) and in three animals with lower dose (40µg/kg). Duration of recumbency was  $22.66 \pm 1.45$ ,  $35.16 \pm 1.68$  and  $55.66 \pm 1.64$  minutes after administration of 40, 50 and 60µg/kg of detomidine, respectively.

**Key words:** Goat, detomidine, sedation, dose response, analgesia.

### INTRODUCTION

Pakistan has a large number of different categories of livestock, among which goats play an important role in its economy. Goat population of Pakistan is estimated as 49.7 million heads (Anonymous, 1998). Goat has a particular importance in livestock due to its unique qualities, such as high fertility, short kidding interval, good quality mutton, milk and hairs (Mackenzie, 1967). The important role of goat is the production of high quality protein for human consumption. Animal protein supplies essential amino acids which are necessary for body building in human being. In addition, goat provides considerable manure to enrich the soil.

Prevention and treatment of diseases in goat is very essential to obtain maximum milk and mutton production for human consumption. Most clinical and surgical procedures can be performed on goats under regional and local anaesthesia after proper sedation. The development of new sedatives and analgesics in recent years has greatly contributed to success of many and even complicated surgical procedures in goats. Detomidine HCl (Dormosedan) is a new synthetic  $\alpha_2$ -adrenoreceptor agonist with sedative and analgesic properties (Anonymous, 1996). It is an imidazole derivative and has been developed as a sedative/analgesic for animals. Initially, detomidine was developed to use as a sedative and analgesic in horses and cattle (Hall and Clarke, 1991; Thurmon *et al.* 1992). It has also been used in laboratory animals (Hall and Clarke, 1991). Very little work has been done on the use of detomidine in goats. Therefore, this

research work was planned to determine the sedative/analgesic effects of detomidine in goats.

### MATERIALS AND METHODS

#### Animals and treatments

Six female Pateri goats with mean age of 15.33 months and body weight between 12.66 and 33.2kg were used in this study. The goats were purchased locally from Tandojam market. They were physically healthy. Goats were kept at Indoor Patient Ward, Department of Surgery and Obstetrics, Sindh Agriculture University Tandojam during the experiment. Detomidine (Dormosedan, Farnos Group Ltd, Turku, Finland) was injected to all goats intravenously with 1ml disposable syringe. The goats received three treatments of 40, 50 and 60 µg/kg body weight at 10 days intervals.

#### Post-treatment monitoring

The onset of sedation, onset of maximum sedation, duration of maximum sedation, total duration of sedation and degree of sedation for each treatment were recorded. Degree of sedation was quantified as, 0 = for no sedation; goat appeared alert; 1 = for light sedation; goat closed the upper eye lids, was unaware of surroundings with head lowered but still above the shoulder level; 2 = for medium sedation; goat closed the upper eye lids, was unaware of surroundings with the head below the shoulder level; 3 = for deep sedation, goat closed the upper eye lids, unaware of surroundings and was recumbent. The analgesic effect was recorded by recognizing the response of deep muscular pin pricking. The other clinical features like



onset of recumbency, duration of recumbency, standing time, salivation, frequent urination, defecation, snoring, tympany, palpebral and pedal reflexes, drooping of head and animal behaviour occurred after administration of detomidine, if any, were also recorded.

#### Statistical analysis

The data obtained were analysed using one way analysis of variance (ANOVA) and Turkey-Kramer multiple comparison test (Steel and Torrie, 1984).

## RESULTS

#### Onset of sedation

The mean values for onset of sedation were  $335 \pm 16.27$ ,  $210 \pm 10.95$  and  $60 \pm 6.70$  seconds after administration of 40, 50 and 60  $\mu\text{g}/\text{kg}$  detomidine, respectively (Table-1). The onset of sedation was dose dependent with higher doses producing more rapid effect. The dose rate of 60  $\mu\text{g}/\text{kg}$  produced maximum sedation within 1 minute as compared to 3.5 and 5.58 minutes with 50 and 40  $\mu\text{g}/\text{kg}$ , respectively.

Analysis of variance showed that the onset of sedation was significantly different ( $P < 0.01$ ) with all three doses. Further analysis showed that the onset of sedation was significantly rapid ( $P < 0.01$ ) with 60  $\mu\text{g}/\text{kg}$  as compared to 50 and 40  $\mu\text{g}/\text{kg}$  of detomidine. There was significant difference ( $P < 0.01$ ) in onset of sedation within 50 and 40  $\mu\text{g}/\text{kg}$  of detomidine.

#### Onset of maximum sedation

The mean values for onset of maximum sedation were  $21.33 \pm 1.15$ ,  $16.83 \pm 0.79$  and  $7.83 \pm 0.47$  minutes after administration of 40, 50 and 60  $\mu\text{g}/\text{kg}$  detomidine, respectively (Table-2). It was dose dependent. The onset of maximum sedation was more rapid with the increasing dose rate. Analysis of variance showed that the onset of maximum sedation was significantly different ( $P < 0.01$ ) with all doses. Further analysis showed that the onset of maximum sedation was significantly rapid ( $P < 0.01$ ) with 60  $\mu\text{g}/\text{kg}$  as compared to 40 and 50  $\mu\text{g}/\text{kg}$ . There was significant difference at ( $P < 0.05$ ) in onset of maximum sedation between 40  $\mu\text{g}/\text{kg}$  and 50  $\mu\text{g}/\text{kg}$  of detomidine.

#### Duration of maximum sedation

The mean values for duration of maximum sedation were  $21 \pm 2.08$ ,  $32.33 \pm 0.84$  and  $51.33 \pm 1.33$  minutes after administration of 40, 50 and 60  $\mu\text{g}/\text{kg}$  detomidine, respectively (Table-3). The duration of maximum sedation was dose dependent and was increased with increasing dose of detomidine. The dose rate of 40  $\mu\text{g}/\text{kg}$  produced the duration of maximum sedation in 3 animals (No. 1, 2 and 6). Whereas, higher doses (50  $\mu\text{g}/\text{kg}$  and 60

$\mu\text{g}/\text{kg}$ ) produced the maximum sedation in all animals. Analysis of variance showed that the duration of maximum sedation was significantly different ( $P < 0.01$ ) with all three doses. Further analysis showed that the duration of maximum sedation was significantly longer ( $P < 0.01$ ) with 60  $\mu\text{g}/\text{kg}$  as compared to 50 and 40  $\mu\text{g}/\text{kg}$ . There was significant difference ( $P < 0.01$ ) in the duration of maximum sedation between 40  $\mu\text{g}/\text{kg}$  and 50  $\mu\text{g}/\text{kg}$  of detomidine.

#### Total duration of sedation

The mean values for total duration of sedation were  $68.83 \pm 2.13$ ,  $87.33 \pm 1.83$  and  $105.16 \pm 1.51$  minutes after administration of 40, 50 and 60  $\mu\text{g}/\text{kg}$  detomidine, respectively (Table-4). Total duration of sedation was dose dependent with higher doses resulting in longer duration. Analysis of variance showed that the total duration of sedation was significantly different in three doses of detomidine. Further analysis showed that total duration of sedation was significantly longer ( $P < 0.01$ ) with 60  $\mu\text{g}/\text{kg}$  as compared to 40 and 50  $\mu\text{g}/\text{kg}$ . There was significant difference ( $P < 0.01$ ) in total duration of sedation between 40 and 50  $\mu\text{g}/\text{kg}$  of detomidine.

#### Degree of sedation

The mean values for degree of sedation were  $2.33 \pm 0.33$ ,  $3.0 \pm 0.0$  and  $3 \pm 0.00$  after administration of 40, 50, and 60  $\mu\text{g}/\text{kg}$  detomidine, respectively (Table-5). After administration of 40  $\mu\text{g}/\text{kg}$  of detomidine, 3 animals were in deep sedation (Nos. 1, 2 and 6), two were in moderate sedation (Nos. 3, 4) and one in light sedation (No: 5). The degree of sedation was deep in all animals after administration of 50 and 60  $\mu\text{g}/\text{kg}$  of detomidine.

#### Onset of analgesia

The dose rate of 40  $\mu\text{g}/\text{kg}$  produced analgesia in three animals (No. 1, 2 and 6) whereas higher doses (50 and 60  $\mu\text{g}/\text{kg}$ ) produced analgesia in all animals (Table-6). The mean values for onset of analgesia were  $22.66 \pm 1.76$ ,  $17.83 \pm 0.79$  and  $8.83 \pm 0.47$  minutes after administration of 40, 50 and 60  $\mu\text{g}/\text{kg}$  detomidine, respectively. The onset of analgesia was dose dependent and was rapid with increasing dose of detomidine.

#### Duration of analgesia

The mean duration of analgesia was  $10 \pm 1.15$ ,  $19.5 \pm 0.88$  and  $27.16 \pm 1.04$  minutes after administration of 40, 50 and 60  $\mu\text{g}/\text{kg}$  detomidine, respectively (Table-7). The duration of analgesia increased with increasing dose of detomidine. Analysis of variance showed that the duration of analgesia was significantly different in three doses. The duration of analgesia was significantly longer



Table 1. Onset of sedation (seconds) in goats after administration of different doses of detomidine

Animal No.	40 µg/kg	50 µg/kg	60 µg/kg
1	300	180	60
2	360	240	90
3	300	210	60
4	390	240	45
5	360	180	60
6	300	210	45
Mean	335**πππ	210**ΔΔ	60ππΔΔ
S.E	16.27	10.95	6.70

\*\* = Significant, difference at (P<0.01) between values of 40 µg/kg and 50 µg/kg.

πππ = Significant difference at ( P<0.01) between values of 40 µg/kg and 60 µg/kg.

ΔΔ = Significant difference at (P<0.01) between values 50 µg/kg and 60 µg/kg.

Table 2. Onset of maximum sedation (minutes) in goats after administration of different doses of detomidine

Animal No.	40 µg/kg	50 µg/kg	60 µg/kg
1	25	15	7
2	19	17	9
3	-	18	6
4	-	20	8
5	-	16	9
6	20	15	8
Mean	21.33*πππ	16.83*ΔΔ	7.83πππΔΔ
S.E	1.15	0.79	0.47

\* = Significant, difference at (P<0.05) between values of 40 µg/kg and 50 µg/kg.

πππ = Significant difference at ( P<0.01) between values of 40 µg/kg and 60 µg/kg.

ΔΔ = Significant difference at (P<0.01) between values 50 µg/kg and 60 µg/kg.

Table 3. Duration of maximum sedation (minutes) in goats after administration of different doses of detomidine.

Animal No.	40 µg/kg	50 µg/kg	60 µg/kg
1	20	35	47
2	25	30	55
3	---	32	50
4	---	30	49
5	---	33	52
6	18	34	55
Mean	21.**πππ	32.33**ΔΔ	51.33πππΔΔ
S.E	2.08	0.84	1.33

\*\* = Significant, difference at (P<0.01) between values of 40 µg/kg and 50 µg/kg.

πππ = Significant difference at ( P<0.01) between values of 40 µg/kg and 60 µg/kg.

ΔΔ = Significant difference at (P<0.01) between values 50 µg/kg and 60 µg/kg.

**Table 4. Total duration of sedation (minutes) in goats after administration of different doses of detomidine**

Animal No.	40 µg/kg	50 µg/kg	60 µg/kg
1	60	90	108
2	70	80	102
3	75	84	100
4	72	88	105
5	70	92	106
6	66	90	110
Mean	68.83**πππ	87.33**ΔΔ	105.16πππΔΔ
S.E	2.13	1.83	1.51

\*\* = Significant, difference at (P<0.01) between values of 40 µg/kg and 50 µg/kg.

πππ = Significant difference at ( P<0.01) between values of 40 µg/kg and 60 µg/kg.

ΔΔ = Significant difference at (P<0.01) between values 50 µg/kg and 60 µg/kg.

**Table 5. Degree of sedation in goats after administration of different doses of detomidine**

Animal No.	40 µg/kg	50 µg/kg	60 µg/kg
1	3	3	3
2	3	3	3
3	2	3	3
4	2	3	3
5	1	3	3
6	3	3	3
Mean	2.33	3	3
S.E	0.33	0.00	0.00

1 = Light sedation      2 = Medium sedation      3 = Deep sedation

**Table 6. Onset of analgesia (minutes) in goats after administration of different doses of detomidine.**

Animal No.	40 µg/kg	50 µg/kg	60 µg/kg
1	26	16	8
2	20	18	10
3	-	19	7
4	-	21	9
5	-	17	10
6	22	16	9
Mean	22.66 *πππ	17.83 *ΔΔ	8.83 πππΔΔ
S.E	1.76	0.79	0.47

\* = Significant, difference at (P<0.01) between values of 40 µg/kg and 50 µg/kg.

πππ = Significant difference at ( P<0.01) between values of 40 µg/kg and 60 µg/kg.

ΔΔ = Significant difference at (P<0.01) between values of 50 µg/kg and 60 µg/kg.

**Table 7. Duration of analgesia (minutes) in goats after administration of different doses of detomidine**

Animal No.	40 µg/kg	50 µg/kg	60 µg/kg
1	10	18	28
2	12	20	30
3	-	16	25
4	-	21	24
5	-	22	30
6	8	20	26
Mean	10.**πππ	19.5**ΔΔ	27.16πππΔΔ
S.E	1.15	0.88	1.04

\*\* = Significant, difference at (P<0.01) between values of 40 µg/kg and 50 µg/kg.

πππ = Significant difference at ( P<0.01) between values of 40 µg/kg and 60 µg/kg.

ΔΔ = Significant difference at (P<0.01) between values 50 µg/kg and 60 µg/kg.



( $P < 0.01$ ) with 60  $\mu\text{g}/\text{kg}$  as compared to 40 and 50  $\mu\text{g}/\text{kg}$  of detomidine. There was significant difference in duration of analgesia between 40 and 50  $\mu\text{g}/\text{kg}$  of detomidine.

#### Onset of recumbency

The mean values for the onset of recumbency were  $18 \pm 1.15$ ,  $13.83 \pm 1.01$  and  $5.16 \pm 0.30$  minutes after administration of 40, 50 and 60  $\mu\text{g}/\text{kg}$  detomidine, respectively (Table-8). The onset of recumbency was dose dependent, with higher doses producing more rapid effect. The dose rate of 40  $\mu\text{g}/\text{kg}$  produced recumbency in 50% of animals (No:1, 2 and 6), where as higher doses (50 and 60  $\mu\text{g}/\text{kg}$ ) produced recumbency in all animals. Analysis of variance showed that the onset of recumbency was significantly different in three doses. Further analysis showed that the onset of recumbency was significantly rapid ( $P < 0.01$ ) with 60  $\mu\text{g}/\text{kg}$  as compared to 40 and 50  $\mu\text{g}/\text{kg}$  of detomidine. There was significant difference ( $P < 0.05$ ) in the onset of recumbency between 40 and 50  $\mu\text{g}/\text{kg}$  of detomidine.

#### Duration of recumbency

The mean values for duration of recumbency were  $22.66 \pm 1.45$ ,  $35.16 \pm 1.68$  and  $55.66 \pm 1.64$  minutes after administration of 40, 50 and 60  $\mu\text{g}/\text{kg}$  detomidine, respectively (Table-9). The duration of recumbency was increased with increasing dose of detomidine and was significantly different with three doses. It was longer ( $P < 0.01$ ) with 60  $\mu\text{g}/\text{kg}$  as compared to 40 and 50  $\mu\text{g}/\text{kg}$ . There was significant difference in the duration of recumbency between 40 and 50  $\mu\text{g}/\text{kg}$  of detomidine.

#### Standing time

The mean values for standing time were  $44.66 \pm 2.33$ ,  $49 \pm 1.50$  and  $60.83 \pm 1.79$  minutes after recumbency at the doses of 40, 50 and 60  $\mu\text{g}/\text{kg}$  detomidine, respectively (Table-10). There was dose dependent effect of detomidine on standing time. Analysis of variance showed that the standing time was significantly different with three doses. Further analysis by Turkey-Kramer multiple comparison test showed that the standing time was significantly longer ( $P < 0.01$ ) with 60  $\mu\text{g}/\text{kg}$  as compared to 40 and 50  $\mu\text{g}/\text{kg}$  detomidine. There was significant difference ( $P < 0.05$ ) in the standing time between 40 and 50  $\mu\text{g}/\text{kg}$  of detomidine.

#### Other observations

Head drooping, salivation, grumbling, snoring, staggering and wobbling were seen in all animals with all three doses used. Palebral and Pedal reflexes were present in three (Nos, 3, 4 and 5) while absent in the remaining three animals (No. 1, 2 and 6) after

administration of 40  $\mu\text{g}/\text{kg}$ , while these reflexes were absent in all animals after administration of 50  $\mu\text{g}/\text{kg}$  and 60  $\mu\text{g}/\text{kg}$  of detomidine. Tympany, muscle relaxation and skin analgesia were seen in three animals (No. 1, 2 and 6) after administration of 40  $\mu\text{g}/\text{kg}$  of detomidine, while in all animals after administration of 50 and 60  $\mu\text{g}/\text{kg}$  of detomidine. Frequent urination was observed in three animals (No. 1, 2 and 6) with dose of 40  $\mu\text{g}/\text{kg}$ , in four animals (No. 1, 2, 3 and 4) with 50  $\mu\text{g}/\text{kg}$  and in all animals with 60  $\mu\text{g}/\text{kg}$  of detomidine. Tail movement was observed in three animals (No. 3, 4 and 5 only) with 40  $\mu\text{g}/\text{kg}$  but was absent in all animals which received 50 and 60  $\mu\text{g}/\text{kg}$  of detomidine. Defecation was observed in three animals (No. 1, 2 and 4) with 50  $\mu\text{g}/\text{kg}$ , in two animals (No. 3 and 6) with 60  $\mu\text{g}/\text{kg}$  but was absent in all animals given the dose of 40  $\mu\text{g}/\text{kg}$  of detomidine.

## DISCUSSION

Some studies on the use of detomidine in goat have been reported in the past (Singh *et al.*, 1991; Clarke *et al.*, 1993; Dilip *et al.*, 1996) but, there has been no comprehensive study on various dose rates carried out in goats. This study was designed to compare safe and effective dose of detomidine for sedation and analgesia after administration of 40, 50 and 60  $\mu\text{g}/\text{kg}$  intravenously in six healthy goats. Onset of sedation and duration of maximum sedation were dose dependent with higher doses producing more rapid effect. Other researchers have also reported related observations of dose dependent duration of maximum sedation in buffaloes (Silva *et al.*, 1991). Total duration of sedation and degree of sedation were also dose dependent in goats after administration of detomidine, 40  $\mu\text{g}/\text{kg}$  produced medium to deep sedation, 50  $\mu\text{g}/\text{kg}$  and 60  $\mu\text{g}/\text{kg}$  produced deep sedation in all goats. Singh *et al.* (1994) have also reported similar observations after administration of detomidine in sheep. The onset and duration of analgesia were also dose dependent. Same was true for the onset of recumbency, duration of recumbency and standing time.

The results of this study demonstrated that intravenous administration of detomidine induced satisfactory and safe sedation and analgesia in goats. Detomidine hydrochloride produced dose dependent sedation, analgesia and side effects such as frequent urination, tympany, tail movement in goats.

A dose rate of 40  $\mu\text{g}/\text{kg}$  of detomidine produced medium to deep sedation and total duration of sedation was 68.83 minutes. This dose rate may be useful for physical examination, handling of difficult animals,



**Table 8. Onset of recumbency (minutes) in goats after administration of different doses of detomidine**

Animal No.	40 µg/kg	50 µg/kg	60 µg/kg
1	20	12	5
2	18	15	6
3	-	14	4
4	-	18	5
5	-	13	6
6	16	11	5
Mean	18*πππ	13.83*ΔΔ	5.16πππΔΔ
S.E	1.15	1.01	0.30

\* = Significant, difference at (P<0.05) between values of 40 µg/kg and 50 µg/kg.

πππ = Significant difference at ( P<0.01) between values of 40 µg/kg and 60 µg/kg.

ΔΔ = Significant difference at (P<0.01) between values 50 µg/kg and 60 µg/kg.

**Table 9. Duration of recumbency (minutes) in goats after administration of different doses of detomidine**

Animal No.	40 µg/kg	50 µg/kg	60 µg/kg
1	23	40	50
2	25	35	59
3	-	28	55
4	-	34	52
5	-	36	58
6	20	38	6
Mean	22.66**πππ	35.16**ΔΔ	55.66πππΔΔ
S.E	1.45	1.68	1.64

\*\* = Significant, difference at (P<0.01) between values of 40 µg/kg and 50 µg/kg.

πππ = Significant difference at ( P<0.01) between values of 40 µg/kg and 60 µg/kg.

ΔΔ = Significant difference at (P<0.01) between values 50 µg/kg and 60 µg/kg.

**Table 10. Standing time (minutes) from recumbency in goats after administration of different doses of detomidine**

Animal No.	40 µg/kg	50 µg/kg	60 µg/kg
1	43	52	55
2	43	50	65
3	-	42	59
4	-	52	57
5	-	49	64
6	36	49	65
Mean	44.66*πππ	49*ΔΔ	60.83πππΔΔ
S.E	2.33	1.50	1.79

\*\* = Significant, difference at (P<0.05) between values of 40 µg/kg and 50 µg/kg.

πππ = Significant difference at ( P<0.01) between values of 40 µg/kg and 60 µg/kg.

ΔΔ = Significant difference at (P<0.01) between values of 50 µg/kg and 60 µg/kg.

biopsy, tagging, radiography, for pre-anesthetic medication, for performing diagnostic procedures, dressing of wounds, drainage of abscess, application of plaster casts, passing of urinary catheters and removal of stitches.

A dose rate of 50  $\mu\text{g}/\text{kg}$  of detomidine produced deep sedation and total duration of sedation was 87.33 minutes. This dose produced good sedation, skin analgesia and staggering with animal's head drooping and lowered to knees. Onset of recumbency occurred immediately and animal went into voluntary recumbency within few minutes.

The dose rate of 60  $\mu\text{g}/\text{kg}$  of detomidine produced immediate and deep sedation, analgesia and lateral recumbency in all goats. Total duration of sedation was 105.16 minutes. The dose rates of 50  $\mu\text{g}/\text{kg}$  and 60  $\mu\text{g}/\text{kg}$  may be used along with local anaesthesia for performing minor surgical operations such as dehorning, tail docking, castration, declawing, reduction and immobilization of fractures etc.

Detomidine also produced other side effects such as salivation, head drooping, frequent urination, snoring, staggering, tympany and rolling of eye balls. These changes do not cause much problems to the animals except salivation and recumbency. 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.

It is concluded that detomidine may be used for control of goats in painful conditions and for minor surgical operations and reduction in physical stress or danger during examination. These results indicate that detomidine is safe and produces satisfactory sedation and analgesia in goats, and the effects are dose dependent.

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