

COMPARATIVE EFFECTS OF DETOMIDINE AND XYLAZINE AS SEDATIVE AND ANALGESIC AGENTS IN SMALL RUMINANTS

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ABSTRACT

The study was carried out on 60 healthy rams and male goats presented for castration in the Surgery Clinics, Department of Clinical Medicine and Surgery, University of Veterinary and Animal Sciences, Lahore. The weight of the animals ranged between 25 and 50 kg and ages between 3 and 6 months. The animals were divided into three groups A, B and C, with 20 animals in each group. In group A, castration was performed under detomidine sedation injected at a dose rate of 50 µg/kg body weight intramuscularly. In group B, xylazine was administered at a dose rate of 200 µg/kg body weight intramuscularly. In group C, castration was performed without the use of any sedative agent. However, animals of group C were given normal saline (placebo). Before surgical manipulation, physical examination of each animal was conducted to ascertain the normal health status. From the study it was concluded that detomidine and xylazine produced similar sedative effects but the analgesia was considerably better with the former.

Key words: Rams, male goats, detomidine, xylazine, castration.

INTRODUCTION

Sheep and goat rearing has been a major source of living for an average person. The population of sheep and goats in Punjab is about 3.64 and 9.35 million heads, respectively (Anonymous, 2000). These animals are of particular importance as they contribute in the shape of meat, milk, wool and hides. In addition, these species provide manure to enrich the soil (Davidlee and Swanson, 1996).

Prevention and treatment of various problems are mandatory to obtain maximum milk and mutton production from these animals. More often, these animals suffer from some surgical problems, requiring regional and local anaesthesia for the cure. The development of new sedatives and analgesics in recent years has solved the problems to handle the complicated surgical problems in these species. Detomidine (Domosedan) is a new synthetic alpha-2 adrenoceptor agonist with sedative and analgesic properties. Its chemical name is 4-(2,3-dimethylphenyl)methyl-1,11-imidazole hydrochloride. It is an imidazole derivative and has been developed as a sedative and analgesic for animals (Vainio, 1983). Xylazine hydrochloride is also alpha-2 adrenoceptor agonist with similar properties like detomidine (Clarke and Hall, 1969).

As little work has been done on the use of detomidine in sheep and goats, therefore the present project was designed to compare the sedative and

analgesic effects of detomidine and xylazine in these species.

MATERIALS AND METHODS

Animals

The study was conducted on 60 normal healthy rams and male goats presented for castration in the Surgery Clinics, Department of Clinical Medicine and Surgery, University of Veterinary and Animal Sciences, Lahore. The weight of the animals ranged between 25 and 50 kg and ages between 3 and 6 months.

A pre-anaesthetic examination of each animal was carried out before castration. Physical examination of the animal was carried out to ascertain the normal health status. For this purpose, temperature, pulse rate and respiration rate of each animal were recorded.

Experimental protocols

The animals were divided into three groups, A, B and C, each comprising of 20 animals. In group A, castration was performed under detomidine sedation using detomidine hydrochloride (Domosedan; Orion Corporation Farnos, Finland) at a dose rate of 50 µg/kg IM. In group B, castration was performed under xylazine sedation using xylazine hydrochloride (Xylaz; Farvet, Holland) at a dose rate of 200 µg/kg body weight IM. In group C, castration was performed without the use of any sedative agent, however, the animals were given normal saline (placebo).

The castration procedure was adopted as a painful stimulus to evaluate the degree of analgesia. In all the animals of groups A, B and C, the castration was performed with Burdizoo's castrator 30 minutes after the injection.

Evaluation of clinical parameters

Temperature, pulse rate, respiration, blood pressure and body reflexes were recorded at zero minute and subsequently at an interval of 15 minutes, till the animals regained their normal posture.

Evaluation of sedation and analgesia

The total period of sedation from its appearance to termination was recorded at an interval of 15 minutes till recovery. The onset of analgesia and its maximum duration were measured by toe pinch test and inflicting pain on various parts of the body. The degree of analgesia was evaluated on the basis of movement of the legs, stretching of muscles and bellowing at the time of castration. Analgesia was graded from 0-6; No sedation/analgesia 0, mild sedation/analgesia 1-2, moderate sedation/analgesia 3-4, deep sedation/analgesia 5-6.

Statistical analysis

Mean values (\pm SD) for various parameters in each group were computed. The data on sedation and analgesia were subjected to statistical analysis using unpaired "t" test (Steel and Torrie, 1982).

RESULTS

Evaluation of clinical parameters

Temperature

Detomidine treated animals remained in hypothermic stage longer than the xylazine treated group. Majority of the animals of group A showed gradual decline in temperature upto 105 minutes post injection, which later on started elevating from 120 minutes. In group B, hypothermia was observed almost in all animals post injection. But unlike group A, an improvement in temperature was noted in a shorter time. Most of the animals of this group showed gradual rise in temperature. In group C, maximum rise of temperature was observed 15 minutes post operation, then gradual reversal occurred and the temperature became almost normal 120 minutes post-injection (Table 1).

Pulse rate

Decrease in pulse rate and pressure was seen in animals of group A upto 45 minutes, followed by gradual decline upto 105 minutes, Subsequently, the

pulse rate increased till the last observation recorded at 180 minutes. Animals of group B also exhibited decrease in pulse rate soon after the administration of the drug. However, in group C peak elevation was noticed 15 minutes after operation i.e. at 45 minutes post-injection (Table 2).

Respiration rate

Decrease in respiration rate was observed in both the test groups. In group A, majority of the animals showed reversal in respiration rates at 120 minutes post injection. In group B, an improvement in respiration rate was noticed in a shorter time i.e. from 75 minutes onward, whereas group C showed marked increase on first observation recorded 15 minutes after the operation, followed by gradual decline in respiration rate towards normality (Table 3).

Blood pressure

In groups A and B, decrease in blood pressure was observed following the administration of drugs. But the difference existed between the duration of decline in blood pressure. Most of the animals of group A exhibited gradual decline at 15 minutes, followed by gradual increase towards normality from 120 minutes onward. The decline in blood pressure persisted upto 45 minutes and then gradual improvement was observed in group B. However, in group C, sudden rise was observed 15 minutes after operation, followed by gradual improvement towards normality (Table 4).

Evaluation of various body reflexes

Position of eyeball

In animals of group A, rotation of the eyeball was observed at 15 minutes post injection, at 60-90 minutes all the animals showed complete rotation, while at 165 minutes all the animals became normal. In animals of group B, slight rotation was observed at 15 minutes post injection, complete rotation at 45 minutes and normality occurred at 90 minutes post injection. However, no such change was observed in animals of group C (Table 5).

Palpebral reflex

In group A, complete absence of palpebral reflexes was observed in most of the animals upto 120 minutes, and upto 135 minutes in a few animals, after the administration of the drug. In group B, palpebral reflexes were seen at 0 minute and 15 minutes post injection, after which they started disappearing and were absent at 45 minutes which later started appearing at 60 minutes and by 90 minutes all the animals were normal. In group C, palpebral reflexes remained unchanged (Table 5).

Table 1: Mean (\pm SD) values of temperature ($^{\circ}$ F) before and after administration of sedative agents in rams and male goats (n=20)

Group	Time in minutes												
	0	15	30	45	60	75	90	105	120	135	150	165	180
A	103.36 \pm 0.67	103.14 \pm 0.64	103.01 \pm 0.68	102.55 \pm 0.99	102.22 \pm 1.02	101.96 \pm 1.01	101.63 \pm 1.05	101.33 \pm 0.99	101.39 \pm 1.15	101.77 \pm 1.21	102.20 \pm 0.90	102.55 \pm 0.71	102.69 \pm 0.61
B	103.06 \pm 0.64	102.46 \pm 0.62	101.69 \pm 0.76	101.06 \pm 0.93	100.79 \pm 1.17	101.11 \pm 1.05	101.60 \pm 0.88	102.05 \pm 0.71	102.28 \pm 0.60	102.59 \pm 0.57	102.71 \pm 0.49	102.84 \pm 0.49	102.97 \pm 0.54
C	102.84 \pm 0.54	102.84 \pm 0.54	102.87 \pm 0.58	103.37 \pm 0.50	103.29 \pm 0.52	103.16 \pm 0.52	103.04 \pm 0.54	102.92 \pm 0.54	102.87 \pm 0.54	102.84 \pm 0.54	102.84 \pm 0.54	102.84 \pm 0.54	102.84 \pm 0.54

Table 2: Mean (\pm SD) values of pulse rate before and after administration of sedative agents in rams and male goats (n=20)

Group	Time in minutes												
	0	15	30	45	60	75	90	105	120	135	150	165	180
A	76.8 \pm 13.4	64 \pm 9.3	58.3 \pm 10.2	53.7 \pm 9.4	51.8 \pm 9.1	50 \pm 8.6	48.4 \pm 7.5	46.8 \pm 6.9	47.8 \pm 7.5	52.4 \pm 7.7	56 \pm 8.6	62.1 \pm 9.8	66.6 \pm 9.7
B	75.8 \pm 4.8	66.8 \pm 6.0	62.5 \pm 6.2	58.6 \pm 6.7	56.2 \pm 7.6	56.9 \pm 8.6	59.8 \pm 8.4	63.4 \pm 8.5	66.5 \pm 7.5	69.6 \pm 7.3	71.9 \pm 5.9	74.0 \pm 4.9	74.5 \pm 4.7
C	77.8 \pm 3.1	77.8 \pm 3.1	78.1 \pm 3.4	86.4 \pm 4.9	85.5 \pm 5.1	83.8 \pm 4.7	82.9 \pm 4.6	80.3 \pm 4.3	78.8 \pm 3.7	78.0 \pm 3.2	77.8 \pm 3.1	77.8 \pm 3.1	77.8 \pm 3.1

0 means 15 minutes before administration of drug.

Table 3: Mean (\pm SD) values of respiratory rate before and after administration of sedative agents in rams and male goats (n=20)

Group	Time (minutes)												
	0	15	30	45	60	75	90	105	120	135	150	165	180
A	24.3	21.9	20.4	20.0	20.3	19.8	19.6	19.7	20.1	20.9	21.9	22.6	23.4
	± 5.2	± 4.3	± 4.5	± 5.9	± 6.1	± 5.6	± 4.9	± 4.4	± 3.5	± 3.1	± 3.2	± 3.3	± 4.1
B	24.2	20.1	17.3	15.8	15.1	15.7	17.25	18.75	20.2	21.6	22.5	22.95	23.65
	± 6.2	± 7.9	± 4.5	± 4.2	± 3.7	± 4.7	± 3.5	± 3.8	± 3.4	± 4.9	± 4.3	± 2.6	± 4.3
C	21.60	21.60	21.60	27.10	26.35	25.50	24.40	23.80	22.65	21.80	21.60	21.60	21.60
	± 2.0	± 2.0	± 2.5	± 2.7	± 2.0	± 2.3	± 2.1	± 2.0	± 2.2	± 2.2	± 2.0	± 2.0	± 2.0

Table 4: Mean (\pm SD) values of blood pressure before and after administration of sedative agents in rams in rams and male goats (n=20)

Group		Time (minutes)												
		0	15	30	45	60	75	90	105	120	135	150	165	180
A	Sys.	114	106.5	103.25	99.25	93	90.75	89.50	87.25	93	98.75	104.5	107	109.8
		± 5.0	± 4.9	± 5.4	± 5.9	± 5.5	± 5.4	± 6.3	± 6.4	± 7.3	± 5.8	± 4.3	± 4.1	± 4.1
B	Dia.	72.3	64.50	61.50	58	51.3	49	47.8	45.5	50.8	57.3	62.8	66.3	68
		± 7.0	± 6.3	± 6.3	± 7.0	± 7.0	± 5.5	± 4.4	± 4.8	± 6.9	± 6.0	± 5.0	± 7.2	± 6.8
C	Sys.	116.25	105.25	98.50	91.25	92.25	97.00	102	104.5	107	111	113	114.75	115
		± 9.2	± 9.0	± 7.1	± 4.8	± 8.2	± 9.5	± 8.5	± 8.1	± 8.3	± 8.5	± 8.6	± 8.3	± 8.4
D	Dia.	74.8	63.8	57	49.8	50.8	55	61	63	65.5	69.5	71.5	73.3	73.5
		± 10.6	± 9.7	± 7.7	± 5.5	± 8.8	± 8.9	± 8.7	± 8.2	± 8.6	± 9.2	± 9.6	± 9.6	± 9.7
E	Sys.	118.75	118.75	118.75	128	127	125	123.4	121.75	119.5	118.8	118.8	118.8	118.8
		± 6.3	± 6.3	± 6.3	± 6.8	± 6.8	± 6.1	± 6.1	± 5.7	± 6.0	± 6.3	± 6.3	± 6.3	± 6.3
F	Dia.	78.8	78.8	78.8	86.8	87.0	85.3	83.8	82	80.3	78.8	78.8	78.8	78.8
		± 6.3	± 6.3	± 6.3	± 7.7	± 6.8	± 6.0	± 6.3	± 5.2	± 5.7	± 6.3	± 6.3	± 6.3	± 6.3

Table 5: Reflexes (position of eye ball, palpebral reflex, jaw tone, reflexes and response to stimuli, and postural variation) before and after the administration of sedative agents

Reflexes	Time In minutes												
	0	15	30	45	60	75	90	105	120	135	150	165	180
A	-	19+	13+ 7++	4+ 16++	20++	20++	20++	5+ 15++	12+ 8++	17+ 1++	8+	-	-
B	-	19+	7+ 13++	1+ 19++	9+ 11++	14+ 1++	4+	1+	-	-	-	-	-
C	-	-	-	-	-	-	-	-	-	-	-	-	-
A	+	+	2+	-	-	-	-	1+	6+	15+	+	+	+
B	+	+	8+	-	5+	13+	+	+	+	+	+	+	+
C	+	+	+	+	+	+	+	+	+	+	+	+	+
A	+	+	2+	-	-	-	-	1+	5+	14+	19+	+	+
B	+	+	3+	1+	6+	13+	+	+	+	+	+	+	+
C	+	+	+	+	+	+	+	+	+	+	+	+	+
A	+	+	1+	-	-	-	-	1+	4+	14+	+	+	+
B	+	+	4+	-	5+	13+	+	+	+	+	+	+	+
C	+	+	+	+	+	+	+	+	+	+	+	+	+
A	-	19++ 1+	19++ 1+	++	++	++	++	19++ 1+	11++ 9+	4++ 16+	15+	6+	1+
B	-	19+ 1-	4+ 16++	++	7+ 13++	14+ 5++	12+	4+	-	-	-	-	-
C	-	-	-	-	-	-	-	-	-	-	-	-	-

Reflexes with (*) and (+) sign indicate the normal reflex whereas (-) indicates the effect of sedative agent. In other reflexes without (*), (-)sign indicate the normal reflex whereas the (+) sign indicates the intensity of the effect of the sedative agent.

Table 6: Mean reflexes (coordination, sedation depth, salivation and sedation quality) befor and after the administration of sedative agents.

Reflexes	Time In minutes													
	0	15	30	45	60	75	90	105	120	135	150	165	180	
Coordination (stable/ Ataxic)	A	-	+	+	+	+	+	+	+	+	+	13+	6+	2+
	B	-	+	+	+	+	+	17+	8+	2+	-	-	-	-
	C	-	-	-	+	+	+	+	18+	15+	8+	5+	-	-
Sedation depth (shallow/ Deep)	A	-	18++ 2+	18++ 2+	19++ 1+	19++ 1+	19++ 1+	++	19++ 1+	13++ 7+	3++ 17+	15+	4+	-
	B	-	+	4+ 16++	++	8+ 12++	12+ 5++	7+	6+	-	-	-	-	-
	C	-	-	-	-	-	-	-	-	-	-	-	-	-
Salivation	A	-	18+ 2++	18+ 2++	10+ 9++	2+ 16++	2+ 8++	9++ 11+++	2+ 13++	6+ 11++	14+ 4++	13+ 2++	2+	-
	B	-	6+	14+ 5++	10+ 9++	11+ 6++	7+ 1+++	6+	-	-	-	-	-	-
	C	-	-	-	-	-	-	-	-	-	-	-	-	-
Sedation quality	A	-	19+	19+	+	+	+	+	19+	14+	7+	1+	-	-
	B	-	-	16+	+	13+	5+	-	-	-	-	-	-	-
	C	-	-	-	-	-	-	-	-	-	-	-	-	-

Note: The (-) sign indicate the normal reflex whereas the (+) sign indicates the intensity of the effect of the sedative agent.

Jaw tone

In group A, jaw tone disappeared completely in all the animals at 30 minutes which lasted upto 120 minutes in most of the animals, and upto 135 minutes in a few animals. In group B, jaw tone disappeared in most of the animals at 30 minutes and almost all the animals showed disappearance at 45 minutes, followed by quick appearance at 60 and 75 minutes post injection. The period of disappearance of jaw tone in animals of group B was found comparatively shorter than the animals of group A. However, the jaw tone remained unaffected in group C (Table 5).

Reflexes and responses to stimuli

In animals of group A, responses to stimuli were seen after 15 minutes post injection which almost disappeared later and lasted for a period of 120 minutes post injection. At 135 minutes, the responses to stimuli were observed in most of the animals. In animals of group B, complete absence of response to various stimuli was observed at 45 minutes, followed by quick recovery from 60 minutes, and complete recovery was noticed at 90 minutes post injection. However in group C, no such changes were observed (Table 5).

Postural variations

In group A, all the animals attained sitting posture within 15 minutes post injection which changed to complete recumbency and persisted upto 105 minutes in most of the cases, and up to 120 minutes in a few cases. In group B, sedation was similar to group A, but the recumbency appeared in almost 80% of the animals at 30 minutes, followed by recumbency in all animals. However, the animals of group C did not show any postural variation (Table 5).

Coordination

Most of the animals of group A were found ataxic at 15 minutes and all became ataxic at 30 minute, which persisted upto 135 minutes and became normal at 180 minutes post injection. All of the animals of group B were found ataxic at 15 minutes and recovery started at 90 minutes and at 135 minutes all of the animals were found stable. However, in group C, all the animals became ataxic 15 minutes after operation and remained so upto 90 minutes later, 100% improvement was noticed at 165 minutes (Table 6).

Salivation

In 50% animals of group A, slight salivation was observed at 15 minutes which gradually increased towards moderate and profused salivation upto 90 minutes and in rest of the animals upto 120 minutes post injection. A slight salivation was observed in most

of the animals of group B. It started at 15 minutes which lasted upto 90 minutes post injection. However, no evidence of salivation was seen in animals of group C (Table 6).

Evaluation of sedation

Sedation depth

In group A, sedation depth was shallow at 15 minutes post injection in most of the animals, which later became deep and persisted upto 120 minutes. In group B, sedation was shallow at 15 minutes post injection in some of the animals, which later became deep in all animals at 45 minutes post injection. At 60 minutes the sedation depth was observed as deep in 60% of animals, followed by complete recovery at 120 minutes post injection. In group C, no such changes were observed (Table 6).

Sedation quality

The period of satisfactory sedation was longer in group A, which was observed at 30 minutes in almost all animals and persisted upto 105 minutes post injection. In group B, the period of satisfactory sedation started at 30 minutes post injection in almost 80% animals and by 45 minutes all the animals showed satisfactory sedation. At 60 minutes recovery started, and by 90 minutes post injection, all the animals became normal. However, no evidence of sedation was noticed in group C (Table 6).

Evaluation of analgesia

In most of the animals of group A, the analgesia was graded as deep (degree 5-6) at 30 minutes post injection as no movement of the legs, stretching of muscles and bellowing were observed during castration. In most of the animals of group B, the analgesia was graded as degree 4 (moderate analgesia), in some animals degree 5 and in very few animals degree 6 (deep analgesia) at 30 minutes post injection. However, in group C, marked movements of legs, muscle stretching and bellowing were observed due to severe pain during castration (Table 6).

The statistical analysis of the results indicated no significant difference in sedation but significant difference in analgesia ($P < 0.05$) in both the groups at 30 minutes.

DISCUSSION

In this study, hypothermia was observed in animals treated with detomidine or xylazine. The duration of hypothermia was longer in detomidine than xylazine treated group. Almost 90% cases started reversal towards the normal temperature at 120 minutes after

detomidine administration. On the contrary, this picture was seen at 90 minutes in xylazine treated group. These findings are in agreement with the results of Virtanen and MacDonald (1985) in rats.

A marked decrease in pulse rate and pressure was recorded in animals treated with detomidine. The mean maximum decline in pulse rate reached upto 47/minute. The pulse pressure was also very feeble at 30 minutes post injection. The animals treated with xylazine showed decrease upto 60 minutes as 56/minute and then reversal started, but pulse pressure was slightly better. The respiration rate also showed the similar pattern. These finding are in agreement with the results of Aghajanian and Rogawski (1983), who conducted their study in rats.

There was a significant decrease in blood pressure in both the groups. The fall in blood pressure started right after injection. In animals treated with detomidine, decrease in blood pressure continued from 15 minutes to 105 minutes post injection. However, in xylazine treated animals, the decrease continued from 15-45 minutes and reversal started at 60 minutes onwards. Similar findings have also been reported in rats by Dyson *et al.* (1987).

This study revealed rapid reversion in temperature, pulse and respiration in animals treated with xylazine than animals treated with detomidine. Similar observations in rats have also been reported earlier (Livingston *et al.*, 1984).

The animals, in which castration was carried out without the administration of sedative agent at 30 minutes parallel to the test groups, exhibited some changes in clinical parameters. This can be attributed to the severe pain and anxiety due to restraining in lateral recumbency on the ground. Moreover, the animals were also found ataxic after castration.

The present study revealed deep analgesia with detomidine as the animals of this group did not show any sign or indication of pain when castrated at 30 minutes post injection, as reported previously on colic model in horses (Lowe and Hilfiger, 1984). Clarke *et al.* (1983) also reported similar sedative and analgesic effects of detomidine in goats. However, in xylazine treated group, the analgesic effect and muscle relaxation were not upto the mark, which are desired to perform this minor surgical exercise.

The results of this study clearly indicated that detomidine was a drug of choice to perform minor surgical exercises than xylazine in small ruminants.

Acknowledgements

The authors are highly grateful to Orion Corporation, Farnos, Finland for the provision of the medicine (detomidine) used in this research project.

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