The reversal of xylazine hydrochloride by yohimbine and 4-aminopyridine in goats

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ABSTRACT

Yohimbine, 4-aminopyridine, and a combination of the 2 drugs were studied to assess their potential as antagonists to xylazine in goats. Twenty-four small East African goats were divided randomly into 4 groups of 6 goats each in a placebo-controlled study. They were all treated with intramuscular xylazine at 0.44 mg/kg. At the time of maximum sedation, sterile water was administered intravenously to the control group, 0.15% 4-aminopyridine at 0.4mg/kg to Group 2, 0.1% yohimbine at 0.25 mg/kg to Group 3, and the combination of the 2 drugs at the same dose rates to Group 4. The yohimbine/4-aminopyridine combination was also used to antagonise xylazine at 0.88mg/kg in 6 goats. The heart rate, respiratory rate and rate of ruminal movements, the pedal and palpebral reflexes as well as the reaction to noxious stimuli, the standing time and the total recovery time were established and evaluated to assess the effects of the treatments. The drugs reversed the xylazine-induced decrease in the heart rate, respiratory rate and rate of ruminal movements, and also rapidly restored the reflexes as well as the reaction to noxious stimulation. In addition, they significantly ($P < 0.05$) decreased the mean standing time. The mean total recovery time was decreased significantly ($P < 0.05$) by 4-aminopyridine and the yohimbine/4-aminopyridine combination, but non-significantly ($P > 0.05$) by yohimbine. No relapse in sedation occurred. Overall, the combination of yohimbine and 4-aminopyridine produced better responses than the individual drugs, and may therefore be used for rapid reversal of xylazine-induced sedation in goats. Yohimbine or 4-aminopyridine may also be useful for this purpose but recovery may be prolonged.

Key words: small East African goats, xylazine antagonists, xylazine hydrochloride, yohimbine, 4-aminopyridine.

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INTRODUCTION

Xylazine (an α_2-agonist) is the most widely-used agent for chemical restraint in ruminants, including goats. At a dose of 0.02mg/kg administered intramuscularly, xylazine can produce recumbency for 1–2 hours in ruminants, and some residual anorexia and central nervous system (CNS) depression may manifest for up to 24 hours[13]. An antidote for the reversal of xylazine will allow the shortening of the recovery period of goats sedated with xylazine, and therefore reduce the possibility of tympany, regurgitation, pressure damage to nerves or muscles, or other problems associated with the recumbent sedated ruminant[24]. Moreover, because ruminants, and especially goats require small doses of xylazine, an agent to reverse the effects of xylazine will be useful for treating accidental overdoses of xylazine.

Studies have shown that yohimbine and 4-aminopyridine antagonise xylazine in sheep[9], cattle[12], dogs[8,23], cats[10] and some wild animals such as deer[20] and llama[21]. Both drugs reverse xylazine/ketamine anaesthesia in goats[14] and horses[11], xylazine/thiopental anaesthesia in goats[18] and xylazine/pentobarbital anaesthesia in horses[16]. Tolazoline[26] and doxapram[22] are effective in antagonising xylazine in goats. However, there is no information available about yohimbine and 4-aminopyridine as antagonists to xylazine in goats. This experiment was planned to study the effects of 4-aminopyridine, yohimbine and their combination in goats treated with xylazine at 2 and 4 times the routine clinical dose.

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MATERIALS AND METHODS

The study involved 24 small East African goats of both sexes weighing 13–25.5 kg and aged 12–36 months. During the study, the goats were housed in indoor pens and were fed with hay, water and mineral licks (Maclic®, Twiga Chemicals, Nairobi) *ad libitum.* Commercial maize bran and maize germ (Unga Feeds, Nairobi) were supplemented regularly.

A preliminary study to determine the doses of 4-aminopyridine and yohimbine to be used in the experiments was performed. This involved administering varying doses of these drugs to groups of 5 non-sedated goats. The dose rates were considered adequate if they produced signs of mild CNS stimulation such as trembling, muscle twitching and vocalisation, without signs of extreme stimulation such as convulsions.

The study was carried out in 2 phases. During the 1st phase the goats were randomly assigned to 4 groups of 6 goats each. The goats were injected with xylazine (Chanazine®, Chanelle Pharmaceutical) intramuscularly at 0.44mg/kg. At the time of maximum sedation, the goats were injected intravenously with 1mℓ sterile water (controls, Group 1), 0.15% 4-aminopyridine at 0.4mg/kg (Group 2), 0.1% yohimbine at 0.25 mg/kg (Group 3), or a combination of both drugs at the same dose rates (Group 4). During the 2nd phase, the combination of 4-aminopyridine (Kyron Lab.) and yohimbine (Kyron Lab.), which produced the fastest recovery in Phase 1, was used to antagonise intramuscular xylazine at 0.88mg/kg in 6 randomly-selected goats. Control animals were not used because of the risk of xylazine overdose.

After an overnight fasting period, the goats were weighed before being taken to the study area and given a brief period to adjust to their new surroundings and also recover from any excitement. The heart rate, respiratory rate and rate of ruminal movements were then determined and recorded. The heart rate and rate of ruminal movements were determined by auscultation for 1 and 2 minutes respectively, and recorded as beats/minute and contractions/2 minutes respectively. The

Table 1: **Effect of sterile water** (Group 1)**, 4-aminopyridine** (Group 2)**, yohimbine** (Group 3) **and the yohimbine/4-aminopyrine combination** (Group 4) **on the heart rates of goats sedated with intramuscular xylazine at 0.44mg/kg** (mean ± SE)**.**

			Time after administration of antagonists (minutes)						
G	**BX**	**BA**	**5**	**10**	**15**	**20**	**30**	**40**	**50**
1	78.3 ± 6.1	54.7 ± 2.9*	53.3 ± 2.5[a]	52.0 ± 2.7[a]	52.8 ± 3.3[a]	53.3 ± 2.6[a]	51.0 ± 2.7[a]	50.3 ± 2.6[a]	51.7 ± 2.3[a]
2	67.3 ± 1.4	55.7 ± 1.7*	65.7 ± 2.8[b,¶]	67.3 ± 2.6[b,¶]	67.3 ± 2.1[b,¶]	66.2 ± 2.0[b,¶]	64.8 ± 1.9[b,¶]	65.7 ± 1.5[b,¶]	66.0 ± 1.6[b,¶]
3	58.3 ± 3.5	43.5 ± 2.7*	51.8 ± 3.3[a,¶]	50.7 ± 3.8[a,¶]	52.8 ± 3.7[a,¶]	51.8 ± 3.7[a,¶]	52.3 ± 3.8[a,¶]	53.2 ± 3.7[a,¶]	54.2 ± 3.1[a,¶]
4	78.8 ± 6.3	48.8 ± 2.8*	74.5 ± 4.8[b,¶]	76.7 ± 2.7[b,¶]	70.5 ± 5.9[b,¶]	67.8 ± 4.3[b,¶]	64.5 ± 2.6[b,¶]	64.2 ± 2.5[b,¶]	64.0 ± 2.5[b,¶]

G = group.
BX = baseline heart rate.
BA = heart rate after xylazine treatment.
*Significantly different ($P < 0.05$) compared with the pre-xylazine heart rate.
[a,b]Means with different superscripts are significantly different ($P < 0.05$).
[¶]Significantly different ($P < 0.05$) from the pre-antagonist heart rate.

respiratory rate was determined by observation of thoracic and abdominal movement for 1 minute, and recorded as breaths/minute. The presence of pedal and palpebral reflexes as well as noxious stimulation was also determined. The noxious stimuli consisted of pinching with mosquito forceps at the flanks, horn base, scrotal sacs, ventral abdomen and limb extremities. A positive reaction to the noxious stimuli was taken as the withdrawal of the limb for the extremities and twitching of muscles for the other body regions. The reflexes and the reaction to noxious stimuli were recorded as either present or absent. Thereafter, xylazine was injected. The variables were determined again at the time of maximum sedation, and just before the administration of the reversal agents. Sedation was regarded as maximal when the goats became recumbent and could not be aroused easily.

Subsequently, the heart rate, respiratory rate as well as the rate of ruminal movements were monitored at 5, 10, 15, 20, 30, 40 and 50 minutes after the administration of sterile water or the antagonists. The reappearance of reaction to noxious stimulation as well as the reflexes were also assessed at the same time intervals. The standing time was also recorded. This was taken as the time from the injection of the antagonists until the animal could stand unaided when stimulated by hand-clapping, whistling and patting them. The average of the standing times was defined as the mean standing time (MST).

After the animals stood, they were placed in an observation area with hay, maize bran and water available and observed in order to determine the total recovery time. This was taken as the time from injection of xylazine until the time when overt sedation disappeared and the animal could be considered normal in movement and behaviour, including eating and drinking normally. The average of the total recovery times was defined as the mean total recovery time (MTRT).

Statistical analysis

The data for the heart rate, respiratory rate and rate of ruminal movements were analysed using the repeated measures analysis of variance (ANOVA), and the Neuman-Keul's multiple comparison test was used to test for significance. Data for the standing time and total recovery time were analysed using 1-way ANOVA and the Tukey's Student range test used to test for significance of difference. In all analyses, $P < 0.05$ was considered significant. SAS statistical software was used for the analysis.

RESULTS

Doses of 0.44 mg/kg and 0.88 mg/kg of xylazine were adequate to produce sustained recumbency and marked sedation. Onset of signs occurred within 10 minutes of administration.

Reversal of xylazine at 0.44 mg/kg

Xylazine produced a significant decrease ($P < 0.05$) in heart rate in all groups (Table 1). The administration of the antagonists produced a significant increase ($P < 0.05$) in heart rate compared with the pre-antagonist value of the same group, but the heart rate was unaltered in the control group. Groups 2 and 4 had significantly ($P < 0.05$) higher rates compared with the control group, but despite the increase in heart rate in Group 3, there was no significant difference ($P > 0.05$) compared with the control group.

Xylazine also produced a significant decrease ($P < 0.05$) in respiratory rate in all groups of goats (Table 2). After the administration of the antagonist drugs, the respiratory rate increased significantly ($P < 0.05$) compared with the pre-antagonist rate of the same group, but the respiratory rate was unaltered in the control group. In comparison with the control group, the antagonists increased the respiratory rate significantly ($P < 0.05$) at some of the times assessed. There was no significant

Table 2: **Effect of sterile water** (Group 1)**, 4-aminopyridine** (Group 2)**, yohimbine** (Group 3) **and the yohimbine/4-aminopyrine combination** (Group 4) **on the respiratory rates of goats sedated with intramuscular xylazine at 0.44mg/kg** (mean ± SE)**.**

			Time after administration of antagonists (minutes)						
G	**BX**	**BA**	**5**	**10**	**15**	**20**	**30**	**40**	**50**
1	21.5 ± 1.9	12.0 ± 1.3*	13.0 ± 1.7	13.0 ± 2.1	10.5 ± 1.1	11.0 ± 1.6	10.0 ± 1.4	12.5 ± 1.9	13.0 ± 1.6
2	19.7 ± 1.1	14.0 ± 0.9*	20.0 ± 1.4[#,¶]	19.3 ± 0.7[#,¶]	20.0 ± 1.1[#,¶]	19.8 ± 2.2[#,¶]	18.7 ± 0.7[#,¶]	17.7 ± 0.6[¶]	18.3 ± 0.4[¶]
3	15.2 ± 1.3	9.2 ± 0.6*	15.5 ± 2.5[¶]	16.0 ± 1.0[¶]	16.0 ± 1.0[#,¶]	14.2 ± 1.1[¶]	13.5 ± 1.1[¶]	13.8 ± 0.8[¶]	14.2 ± 0.7[¶]
4	21.0 ± 1.6	12.0 ± 1.2*	17.2 ± 1.2[¶]	17.4 ± 2.0[¶]	17.8 ± 2.2[#,¶]	18.6 ± 1.9[#,¶]	18.5 ± 2.6[#,¶]	17.0 ± 2.1[¶]	18.0 ± 2.2[¶]

G = group.
BX = baseline respiratory rate.
BA = respiratory rate after xylazine treatment.
*Significantly different ($P < 0.05$) compared with the pre-xylazine respiratory rate.
[#]Significantly different ($P < 0.05$) compared with the control group.
[¶]Significantly different ($P < 0.05$) from the pre-antagonist respiratory rate.

Table 3: **Effect of sterile water** (Group 1)**, 4-aminopyridine** (Group 2)**, yohimbine** (Group 3) **and the yohimbine/4-aminopyrine combination** (Group 4) **on the rate of ruminal movements of goats sedated with intramuscular xylazine at 0.44mg/kg** (mean ± SE)**.**

			Time after administration of antagonists (minutes)						
G	**BX**	**BA**	**5**	**10**	**15**	**20**	**30**	**40**	**50**
1	2.8 ± 0.3	0*	0 [a]	0 [a]	0 [a]	0 [a]	0 [a]	0 [a]	0.3 ± 0.2 [a]
2	1.7 ± 0.2	0*	0 [a]	0 [a]	0.4 ± 0.2 [a]	0.8 ± 0.2 [b,¶]	1.0 ± 0.0 [b,¶]	1.0 ± 0.0 [b,¶]	1.2 ± 0.2 [b,¶]
3	1.8 ± 0.2	0*	0 [a]	0 [a]	0 [a]	0.3 ± 0.2 [a]	0.5 ± 0.2 [b,¶]	1.0 ± 0.0 [b,¶]	1.0 ± 0.0 [b,¶]
4	1.5 ± 0.2	0*	0 [a]	0.2 ± 0.2 [a]	0.7 ± 0.2 [b,¶]	0.8 ± 0.2 [b,¶]	1.0 ± 0.0 [b,¶]	1.2 ± 0.2 [b,¶]	1.3 ± 0.2 [b,¶]

G = group.
BX = baseline rate of ruminal movements.
BA = ruminal movements after xylazine treatment.
*Significantly different ($P < 0.05$) compared with the pre-xylazine rate of ruminal movements.
[a,b]Means with different superscripts are significantly different ($P < 0.05$).
[¶] Significantly different ($P < 0.05$) from the pre-antagonist rate of ruminal movements.

difference ($P > 0.05$) between Groups 1, 2 and 3.

Xylazine abolished the ruminal contractions at the time of maximum sedation, and this effect persisted for variable time periods in the groups (Table 3). The ruminal movements were recorded first in Group 4 and last in Group 3. They were not recorded in the control group for at least 40 minutes. At some of the times assessed, Groups 2, 3 and 4 had significantly higher ($P < 0.05$) rate of ruminal movements compared with the pre-antagonist value of the same group and also when compared with the control group.

The antagonists significantly decreased ($P < 0.05$) the MST, whereas the MTRT was significantly ($P < 0.05$) decreased in Groups 2 and 4 (Table 4). In Group 3, a slight but not significant reduction in the MTRT was noted. The reduction of both variables was greatest in Group 4, and its values were significantly smaller ($P < 0.05$) than for Group 3.

At the time of maximum sedation, the reflexes were markedly depressed or absent, and there was loss of reaction to the noxious stimulation at the flanks, horn base and ventral abdomen but not at the limb extremities and scrotal sacs. Intravenous administration of the antagonists, alone and in combination, rapidly reversed the 2 variables.

Reversal of xylazine at 0.88 mg/kg

The combination of yohimbine and 4-aminopyridine, which produced the greatest reduction in MST and MTRT in the 1st phase of the study, was used to antagonise xylazine at 0.88 mg/kg. Xylazine significantly decreased ($P < 0.05$) the heart rate, respiratory rate and rate of ruminal movements from pre-xylazine values of 64.8 ± 3.8, 17.8 ± 1.2, and 2.8 ± 0.3 to 49.0 ± 1.6, 14.0 ± 1.9 and 0 respectively, at the time of maximum sedation. The antagonist combination reversed the xylazine-induced decrease in the heart rate and rate of ruminal movements, but produced a slight improvement in the respiratory rate. At the time of maximum sedation, there was loss of the noxious stimulation at the flanks, ventral abdomen and around the horns, while the reflexes were absent. Both returned rapidly. The MST and MTRT were 11.6 ± 0.9 and 307.5 ± 2.1 minutes respectively.

Neither relapse to recumbency nor marked sedation were observed in either phase of the study. However, some residual sedation persisted for varying lengths of time. Upon standing, the animals in all groups began to eat hay and maize bran immediately when offered.

DISCUSSION

Xylazine at 0.2 mg/kg is adequate to induce marked sedation in ruminants[13]. Goats are more sensitive to xylazine than sheep and cattle[24]. The doses of xylazine used in this study were 2 and 4 times the recommended dose in clinical procedures. The effects produced by xylazine at these doses were generally as expected, and are well-documented[7,13].

Table 4: **Effects of various antagonists on the mean standing time** (MST) **and mean total recovery time** (MTRT) **in goats sedated with intramuscular xylazine at 0.44mg/kg** (mean ± SE)**.**

Group	MST	MTRT
Sterile water	91.7 ± 1.4	381.9 ± 1.9
4-aminopyridine	16.8 ± 1.4*	207.5 ± 1.9*
Yohimbine	23.3 ± 1.2*	366.2 ± 2.7
Yohimbine/4-aminopyridine	5.7 ± 0.3*	201.2 ± 2.7*

*Significantly different ($P < 0.05$) from the control value.

Blockers of the central α_2-adrenoceptors such as yohimbine, tolazoline, piperoxan, idazoxan and atipamezole have been used to antagonise xylazine in various species[3,4,17]. These antagonists act by occupying and interacting with α_2-adrenergic receptors, thus denying the α_2-agonists access to these receptors. In the process, they enhance the release of norepinephrine and other excitatory neurotransmitters[3,17]. They may also be capable of influencing serotonergic, dopaminergic, cholinergic and γ-aminobutyric receptors[7]. Yohimbine is a mixed α-adrenoceptor antagonist, but is more specific for the α_2-adrenoceptors[3,7].

Effects of xylazine are also reversed by the analeptics 4-aminopyridine, doxapram and caffeine, which are physiological antagonists to CNS depressants[3,4,17]. The drug 4-aminopyridine acts by facilitating uptake of neuronal calcium ions and enhancing acetylcholine release. It also produces a selective block of potassium ion channels in excitable membranes[2].

The results obtained in this investigation showed that the administration of 4-aminopyridine, yohimbine or their combination was appropriate to reverse the xylazine-induced bradycardia, bradypnoea and ruminal atony. Similar results were also obtained in cattle[12] and in sheep[9]. At 0.88 mg/kg of xylazine, however, the combination of 4-aminopyridine and yohimbine produced only a slight improvement in the respiratory rates.

Administration of the antagonists, alone and in combination, also reversed xylazine-induced CNS depression, as evidenced by the rapid return of the reflexes. The 2 selected reflexes are among those used to monitor the level of anaesthesia, and their reappearance is usually interpreted as a sign of acquisition of variable degrees of consciousness[25]. This finding is in agreement with the results of other studies. For instance, in xylazine-treated sheep, yohimbine reduced the time to reappearance of the head-drooping reflex[9]. Yohimbine, 4-amino-

pyridine and their combination were also reported to cause rapid return of front and hind limb withdrawal reflexes in xylazine-treated cattle[12].

There are conflicting reports on the analgesic effects of xylazine. Some authors have reported persistence of pain even at the maximum depth of sedation[1,19]. Others have reported adequate analgesia[6,15]. The presence of analgesia that varied in intensity and duration in various body regions has been reported[5,13]. It was minimal in the extremities, at the horn base and the flanks. In the present study, the reaction to noxious stimuli was consistently present at the limb extremities and scrotal sacs even in the deeply-sedated animals. Analgesia in other body regions was rapidly reversed by the intravenous injection of the antagonists, alone and in combination.

It is very important in goats, as in any other ruminants, to recover to a standing position as soon as possible after sedation or anaesthesia[24,25]. The hazards of regurgitation, excessive salivation, aspiration and ruminal tympany are present during the recovery period, while the animal is weak and has not regained appropriate control of reflexes and cannot stand up[24]. The antagonists, alone and in combination, significantly reduced the MST, which expresses the time required to gain full control of motor activities. Similar effects have been observed in sheep[9], cattle[12] and llamas[21]. The reduction was greatest when yohimbine and 4-aminopyridine were combined, followed by 4-aminopyridine. The animals were stimulated to stand by hand-clapping, whistling and patting them. This was necessary because sedated animals tend to remain recumbent if not stimulated to rise.

The antagonists, alone and in combination, also reduced the MTRT, which is the time from the injection of xylazine until overt sedation disappears. The reduction was greatest with the yohimbine/4-aminopyridine combination, followed by 4-aminopyridine. Most authors have, however, reported non-significant reductions of the MTRT in xylazine-treated cattle[12] and dogs[8], and in xylazine/ketamine-anaesthetised horses[11] and goats[14].

Overall, the combination of yohimbine and 4-aminopyridine produced better responses. The results of this study demonstrated the superiority of the combination of yohimbine and 4-aminopyridine over the individual drugs in antagonising xylazine in goats. The individual drugs may be used for the same purpose but the recovery may be prolonged.

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REFERENCES

1. Allert A J, Adams R H 1987 Pharmacological considerations in selection of tranquillisers, sedatives and muscle relaxant drugs used in inducing animal restraint. *Journal of the American Veterinary Medical Association* 191: 1241–1244
2. Boothe D M 1995 Anticonvulsant drugs and analeptics agents. In Booth N H, McDonald L E (eds) *Veterinary pharmacology and therapeutics* (7th edn). Iowa State University Press, Ames: 372–394
3. Brander G C, Pugh D M, Bywater R J, Jenkins W L 1991 *Veterinary applied pharmacology and therapeutics* (5th edn). Baillière Tindall, London
4. Brondke D, Kowollik N 1988 Xylazine antagonists in animals: a review of the clinical aspects. *Veterinary Medical Review* 59: 108–119
5. Byagagaire S D 1982 Xylazine hydrochloride and ketamine hydrochloride combinations for general anaesthesia in Sheep. MSc thesis, University of Nairobi
6. Dehghani S, Sharifnia N, Yahyaei M R, Souri, A 1991 Clinical, haematological and biochemical effects of xylazine, ketamine and their combination in caprine and feline. *Journal of Veterinary Anaesthesia* (Special suppl.). *Proceedings of the 4th International Congress of Veterinary Anaesthesia, Utrecht, Netherlands,* 25–31 August 1991: 129–133
7. Gross M E, Booth N H 1995 Tranquillisers, alpha$_2$-adrenergic agonists and related agents. In Booth N H, McDonald L E (eds) *Veterinary pharmacology and therapeutics* (7th edn). Iowa state University Press, Ames: 311–357
8. Hatch R C, Booth N H, Clark J D, Crawford L M, Kitzman J V, Wallner B 1982 Antagonism of xylazine sedation in dogs by 4-aminopyridine and yohimbine. *American Journal of Veterinary Research* 42: 1009–1014
9. Hsu W H, Schaffer D D, Hanson C E 1987 Effect of tolazoline and yohimbine on xylazine-induced CNS depression, bradycardia and tachypnea in sheep. *Journal of the American Veterinary Medical Association* 190: 423–426
10. Jensen W A 1985 Yohimbine for the treatment of xylazine overdosing in a cat. *Journal of the American Veterinary Medical Association* 187: 627–628
11. Kitzman, J V, Wilson R C, Hatch R C, Booth N H 1984 Antagonism of xylazine and ketamine anaesthesia by 4-aminopyridine and yohimbine in geldings. *American Journal of Veterinary Research* 45: 875– 870
12. Kitzman J V, Booth N H, Hatch R C, Wallner B 1982 Antagonism of xylazine sedation by 4-aminopyridine and yohimbine in cattle. *American Journal of Veterinary Research* 43: 2165–2169
13. Knight A P 1980 Xylazine. *Journal of the American Veterinary Medical Association* 176: 454–455
14. Kruse-Elliot K T, Riebold T W, Swanson C R 1987 Reversal of xylazine-ketamine anaesthesia in goats. *Veterinary Surgery* 16: 321
15. Mbiuki S M 1981 Xylazine analgesia in cattle. *Veterinary Medicine and Small Animal Clinician* 76:1463–1464
16. McGruder J P, Hsu W H 1985 Antagonism of xylazine/pentobarbital anaesthesia by yohimbine in ponies. *American Journal of Veterinary Research* 46: 1276–1281
17. Mohammad F K 1987 Xylazine antagonists in animals: a review of pharmacological aspects. *Veterinary Medical Review* 1: 3–8
18. Mora G, Messen J, Cox J F 1993 Effects of yohimbine on xylazine-thiopental anaesthetised Creole goats. *Small Ruminant Research* 11: 163–169
19. Prajapathi A K, Jani B M, Mehta U M 1994 Clinical and physiological effects of different intramuscular dosages of xylazine in goats. *Indian Veterinary Journal* 71: 607–609
20. Renecker L A, Olsen C D 1985 Use of yohimbine and 4-aminopyridine to antagonise xylazine-induced immobilisation of North American cervidae. *Journal of the American Veterinary Medical Association* 187: 1199–1201
21. Riebold T W, Canes A J, Schundlzer W B 1986 Reversal of xylazine-induced sedation in Llamas, using doxapram or 4-aminopyridine and yohimbine. *Journal of the American Veterinary Medical Association* 189: 1059–1061
22. Saleh A S 1993 Antagonistic effect of doxapram treatment with special reference to the acid-base balance in goats. *Assiut Veterinary Medicine Journal* 29: 208–214
23. Schaffer D D, Hsu W H, Hopper D L 1986 Antagonism of xylazine-induced depression of shuttle-avoidance responses in dogs by administration of 4-aminopyridine, doxapram or yohimbine. *American Journal of Veterinary Research* 47: 2116–2121
24. Taylor P M 1991 Anaesthesia in sheep and goats. *In Practice* 13: 31–36
25. Thurmon J G, Benson G 1984 *Current veterinary therapy. food animal practice* (5th edn). W B Saunders, Philadelphia
26. Youssef H A, Nelson D R, Kassem M M 1991 The electromyographic effects of tolazoline after xylazine treatment on the gastrointestinal tract of goats. *Assiut Veterinary Medicine Journal* 25: 160–168