

Antagonism of Medetomidine Sedation in Goats by Atipamezole and Yohimbine*

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Abstract: The alpha 2-adrenoceptor antagonists atipamezole and yohimbine were used to antagonize medetomidine-induced sedation in 6-8-month-old native breed female goats. Intramuscular injection of medetomidine at the dose rate of 40 µg/kg body weight induced sedation and recumbency within 10-20 min in the goats. After recumbency, the goats were injected with saline (5 ml) (control group), atipamezole (0.2 mg/kg), or yohimbine (0.2 mg/kg) via the jugular vein. The duration of recumbency in the control group was 90 ± 9 min (mean ± SE). The effects of sedation continued in the control group goats even after regaining the righting reflex and standing. Atipamezole and yohimbine significantly reduced the recumbency period to 2 ± 1 and 45 ± 8 min, respectively, in comparison to the control group. The signs of arousal consisted of head raising, assuming sternal recumbency, and standing within 1 min in the atipamezole group and within 15-20 min in the yohimbine group. In contrast to the control group, the atipamezole- and yohimbine-treated goats appeared alert after standing. Atipamezole significantly, but partially reversed medetomidine-induced reductions in heart rate and ruminal contractions, whereas yohimbine partially reversed the medetomidine-induced decrease in heart rate only. The data suggest that atipamezole is useful for antagonizing the central nervous system depressant effects of medetomidine in goats. Atipamezole was also superior to yohimbine as a medetomidine antagonist.

Key Words: Alpha 2-antagonist, atipamezole, goat, medetomidine, yohimbine

Introduction

The alpha 2-adrenoceptor agonist medetomidine is most commonly used in wild animals, dogs, and cats as an analgesic, sedative, and muscle relaxant (1-3). The drug also has clinical use in domestic small ruminants, such as sheep and goats (4-12). Medetomidine acts on presynaptic alpha 2-adrenoceptors in the central nervous system, decreasing catecholamine release and turnover, and subsequently inducing sedation in animals (1,12). Due to the profound central nervous system depressant effects of medetomidine in animals, several reports indicate the usefulness of atipamezole or yohimbine as specific alpha 2-adrenoceptor antagonists of the drug in goats (6,7) and sheep (11,12). Medetomidine variably causes bradycardia, ruminal atony, and bloating, with or without hypoxemia in goats (4,7,13) and sheep (5,8,11).

In sheep atipamezole and yohimbine are equally effective in reversing medetomidine-induced loss of the righting reflex (11). In goats yohimbine has not been used to reverse the effects of medetomidine. The purpose of the present study was to examine the antagonistic effects of atipamezole and yohimbine on medetomidine-induced loss of the righting reflex in sedated goats, taking into consideration changes in the heart rate and ruminal motility of the animals.

Materials and Methods

The study included 12 apparently healthy 6-8-month-old female native breed goats. The goats were fed a concentrate diet with water and straw ad libitum. The animals were randomly divided into 3 groups of 4 goats

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each. Each goat was treated with a single intramuscular (IM) injection of medetomidine HCl (40 µg/kg) (Domitor, Orion Corporation, Turku, Finland). In a preliminary experiment this dosage was observed to induce sedation and recumbency in goats. After the onset of recumbency, each goat was placed on its right side and injected with 5 ml of physiological saline solution (control group), 0.2 mg/kg of atipamezole HCl (Orion Corp.), or 0.2 mg/kg of yohimbine HCl (BDH Ltd., Poole, UK) via the jugular vein. Yohimbine was freshly prepared as a 0.2% aqueous solution. The doses of atipamezole and yohimbine were selected from a previous sheep study (11).

The duration of recumbency was determined from the time of antagonist injection to the moment the righting reflex was regained. Heart rate and rumen motility baseline values were determined before injection of medetomidine, and before antagonist administration and immediately after regaining the righting reflex. Heart rate and rumen motility were monitored with a stethoscope. The data were subjected to analysis of variance, followed by the least significant difference test (14). The level of significance was $P < 0.05$.

Results

Medetomidine injected intramuscularly at the dose rate of 40 µg/kg induced sedation in goats, as evidenced by drooping of the head, ataxia, and reluctance to move. The goats became recumbent and lost the righting reflex

within 10-20 min. The duration of recumbency in the control group was 90 ± 9 min (mean \pm SE). The control goats remained sedated even after regaining the righting reflex and standing. Atipamezole and yohimbine significantly ($P < 0.05$) reduced the recumbency period to 2 ± 1 and 45 ± 8 min, respectively, in comparison with the control group. The signs of arousal in the antagonist groups consisted of head raising, moving into sternal recumbency, and standing within 1 min (atipamezole group) or 15-20 min (yohimbine group). In contrast to the control group, the atipamezole- and yohimbine-treated goats appeared alert after standing.

Medetomidine injection significantly decreased heart rate and ruminal motility (Table). Atipamezole significantly, but only partially, reversed medetomidine-induced reductions in heart rate and ruminal contractions, whereas yohimbine partially reversed the decrease in heart rate only (Table).

Discussion

Atipamezole effectively antagonized the depressant effect (recumbency) of medetomidine in goats. Yohimbine was less effective as an antagonist of medetomidine, as it shortened the duration of recumbency by only 50% in comparison to the control group. The antagonistic effects of atipamezole and yohimbine on medetomidine-induced sedation have been reported in sheep (11,12). A similar antagonistic effect of atipamezole has also been reported

Table. Effects of atipamezole and yohimbine (0.2 mg/kg, intravenously) on medetomidine (40 µg/kg, intramuscularly)-induced changes in the heart rate (HR, beats/min) and ruminal motility (RM, contractions/5 min) in goats.

Antagonist	Before medetomidine		Before antagonist		After regaining the righting reflex	
	HR	RM	HR	RM	HR	RM
Saline (5 ml)	76 \pm 29	4.0 \pm 1.1	41 \pm 10 ^a	0 \pm 0 ^a	50 \pm 12	1.3 \pm 0.9 ^{ab}
Atipamezole	68 \pm 6	3.3 \pm 0.3	36 \pm 5 ^a	0 \pm 0 ^a	48 \pm 4 ^{ab}	1.6 \pm 0.3 ^{ab}
Yohimbine	61 \pm 1	2.6 \pm 0.3*	29 \pm 1** ^a	0 \pm 0 ^a	39 \pm 1 ^a	0 \pm 0* ^{†a}

Values are presented as the mean \pm SE of the 4 goat groups. Antagonists were injected after the animals became recumbent (within 10-20 min of medetomidine administration).

*Significantly different than the control group, $P < 0.05$.

†Significantly different than the atipamezole value, $P < 0.05$.

^aSignificantly different than the pre-medetomidine value, $P < 0.05$.

^bSignificantly different than the pre-antagonist value, $P < 0.05$.

in goats (7). The present study confirms the antagonistic action of atipamezole on medetomidine-induced sedation, whereas yohimbine only partially antagonized the effects of medetomidine. A higher yohimbine dose was not tried in the goats because the antagonistic dose of yohimbine (0.2 mg/kg, intravenously) was reported to be highly effective in reversing recumbency in sheep treated with medetomidine (11) or xylazine, another alpha 2-adrenoceptor agonist (15). Atipamezole is a more selective alpha 2-adrenoceptor antagonist than yohimbine (16,17). Both antagonists increase the central release and turnover of norepinephrine (12,16,17), which in turn causes arousal and alertness.

Bradycardia and ruminal atony, as side effects of medetomidine, have been reported in goats (6,7,13) and sheep (5,8,11,12); however, these side effects are transient in nature (7,13) in sheep (5,8,11,12) and goats (13). Therefore, after medetomidine antagonism and arousal, side effects are expected to regress even faster (7,13). In the present study atipamezole partially reversed bradycardia and ruminal atony, whereas yohimbine partially reversed bradycardia only. It is not known whether the timing (10-20 min after

medetomidine administration) of antagonist injection could have influenced the ability of each one to reverse the side effects of medetomidine; however, the reversal of medetomidine sedation was consistent in the atipamezole (2 ± 1 min) and yohimbine (45 ± 8 min) groups. In accordance with the findings of the present study, 0.2 and 0.4 mg/kg of yohimbine intravenously administered was also partially effective in preventing xylazine-induced bradycardia in sheep (18).

In conclusion, the data suggest that atipamezole is useful for antagonizing the central nervous system depressant effects of medetomidine in goats. Atipamezole was also superior to yohimbine as a medetomidine antagonist in goats.

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