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Role of α-Adrenoreceptors In The Regulation of Fore-Stomach Motility in the Goat

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Abstract: The investigation of the effects of intravenous (i.v.) infusion of α2-adrenoreceptor agonists and antagonists on reticuloruminal motility was carried out in conscious goats. The i.v. administration of the α1-agonist phenylephrine (4 μg kg^{-1} min^{-1} for 15 min) or the α2-agonist naphazoline (2.5 μg kg^{-1} min^{-1} for 15 min) reduced both frequency and amplitude of reticulum and rumen dorsal sac contractions. Pretreatment of animals with the α1-antagonist prazosin (20 μg kg^{-1} min^{-1} for 30 min) prevented the inhibitory effects of phenylephrine on reticuloruminal motility. The effects of naphazoline were prevented by yohimbine, an α2-antagonist at 20 μg kg^{-1} min^{-1} for 30 min. Yohimbine, given alone or followed by naphazoline, abolished secondary ruminal dorsal sac contractions. It is concluded that both α12 and α2-adrenoreceptors are involved in the regulation of reticuloruminal motility in the goat. At the dosage of drugs used al and α2-adrenoreceptors appear to play an inhibitory effect on reticuloruminal motility in the goat.

Key words: Adrenoreceptors, regulation, fore-stomach motility, goat

Introduction

The cyclical contractions of the reticulum arid rumen are dependent on vago-vagal reflexes coordinated in the medulla oblongata. Published reports have shown that the adrenergic receptors, located both centrally and it the reticuloruminal wall are involved in the regulation of forestomach motility in ruminants (Ruckebusch, 1983). Many reports indicated that the injection of α-adrenoreceptor antagonists had no significant effects on reticuloruminal motility (Toutain *et al*., 1982; Nicholson *et al*., 1988; Nicholson and Osman, 1992). However, at higher doses Toutain *et al*. (1982) noted that phentolamine (0.2 mg kg^{-1}) and prazosin (0.4 mg kg^{-1}) inhibited reticular motility in sheep and Ruckebusch and Toutain (1984) found that reticular motility of cattle was inhibited by tolazoline at 2 mg kg^{-1}. Brikas (1989) observed that i.v. infusion of yohimbine (20 μg kg^{-1} min^{-1} for 30 min), either alone or followed by naphazoline, abolished secondary ruminal phasic myoelectrical grouped discharges, in sheep.

The injection of α-adrenoreceptor agonists produced a variety of reticuloruminal responses, possibly because of differences in agonists used, their dosage and site of injection. Titchen and Newhook (1968) found that phentolamine and tolazoline blocked the inhibitory effects of adrenaline and noradrenaline on ruminal motility in sheep and goats. Van Miert (1969) found that α-and-β-adrenoreceptor agonistis phenylephrine and isoprenaline, respectively, produced a reduction in the amplitude and rate of ruminal contractions in the goat. Nicholson and Osman (1992) reported that idazoxan, an α2-antagonist, abolished the inhibitory effects of clonidine on forestomach motility and food intake in sheep. Brikas (1989) found that the administration of the α2-agonist naphazoline stopped the reticular phasic myoelectrical grouped discharges (MPGD) and greatly decreased the frequency of ruminal PMGD in sheep. This effect was blocked when the animals were pretreated with the α2-blocker yohirnbine. The administration of the α1-agonist phenylephrine significantly increased the frequency of reticuloruminal PMGD and provoked rumination, an effect blocked by pretreatment of animals with the α-antagonist prazosin (Brikas, 1989). In contrast, Campion and Leek (1995) found that the infection of the α1-agonist phenylephrine was ineffectual in evoking rumination and resulted in a reduced reticular motility. The present study was undertaken to investigate the role of α-adrenoreceptors on reticuloruminal motility in the goat by i.v. infusion of α1-and-α2-adrenorceptor agonists and antagonists.

Materials and Methods

Animals: Four male Nubian goats, 1.5-2.0 years old and weighing 10.0-15.0 kg, were used in the present experiments. Each goat had a long-established rumen cannula by the two-stage method of Jarrett (1948). To facilitate intravenous infusions they were fitted with jugular vein catheters well in advance of all experimental days. These catheters were flushed regularly with sterile saline and filled with heparinized saline.

Training and Feeding Schedule: The goats were housed in individual pens and moved to floor level stands, in which they could not turn round, in the same room as for the experiments. They were rigorously trained to walk into the stands and remain standing there with minimal restraint. A string was passed and tied under the abdomen to prevent the goad from lying dow, but not tight enough to suspend it. The goats were fed on dried alfa alfa and water was available ad libitum.

Recording: Reticulum and rumen dorsal sac contractions were recorded by placing small (40 mm^3) air-filled balloons in these two compartments. These were connected with pressure transducers linked to a 4-channel recorder (Rikadenki, WK 450, Germany). In these animals rumination activity was recognized as triphasic contractions of the reticulum, whereas non-ruminating (resting) motility was that with a biphasic pattern.

Drugs: In these experiments the following drugs were used: i) L-phenylephrine HCL (Sigma Chem. Co., USA) and naphazoline (HCL (Sigma Chem. Co. USA) as α1-and α2-adrenoeceptor agonists, respectively and ii) prazosin HCL (Pfizer Limited, Sandwich, England) and yohimbine HCL (Sigma Chem. Co. USA) as α1-and-α2-adrenoreceptor antagonists. respectively. Shortly before use, the given doses of the drugs were dissolved in no more than 20 ml of sterile normal saline.

Protocol: The recording of reticulorumial contractions of each goat was performed daily. At 07.00 hours, the animal was placed in a loose box, the balloons were introduced into the reticulum and rumen dorsal sac and connected to the recorder with a recording speed of 25 mm min^{-1}. Each of the four goats were subjected to each experiment of the following series.

a. The goat was given through the jugular vein catheter (i.v.) phenylephrine (4 μg kg^{-1} min^{-1} for 15 min) and naphazoline (2.5 μg kg^{-1} min^{-1} for 15 min)
b. The goat received i.v. for 30 min prazosin (20 μg kg^{-1} min^{-1}) and yohimbine (20 μg kg^{-1} min^{-1})
c. During these experiments, the animals received i.e phenylephrine or naphazoline, preceded by the i.v. administration or prazsoin or yohimbine, respectively.

At the beginning of each experiment, one hour of control recording preceded the drug administration, then recording was continued for 1-2 hours after the infusion was stopped.

Statistical analysis: Reticulo-ruminal motility was determined by counting the number of complexes occurring in 15 or 30 min periods before, during and after the administration of drugs. The results were expressed as mean ± SE. Differences were evaluated using the paired Student's Hest and significance was accepted where $p<0.05$.

Results

Effect of α-adrenoreceptor agonists: The i.v. infusion of phenylephrine at a dose rate of 4 μg kg^{-1} min^{-1} for 15 min^{-1} tended to reduce both reticulum and rumen dorsal sac contractions. This reduction was evident during the infusion period and it was statistically significant ($p<0.05$) at 30 min for the reticulum and at 30 and 60 min post-infusion for the rumen dorsal sac (Table 1).

The administration of naphazoline at a dose rat of 2.5 μg kg^{-1} min^{-1}. for 15 min, caused a progressive inhibition of reticuloruminal motility (Fig. 1). The reduction of reticular motility was significantly different ($p<0.05$) from control during the infusion period and for up to 120 min after the infusion was stopped (Table 1). Concerning rumen dorsal sac contractions, they were reduced during the infusion and the reduction was significantly ($p<0.05$) different for up to 60 min after the infusion was stopped.

Effects of α-adrenoreceptor antagonists: The administration of prazosin at a dose rate of 20 μg kg^{-1} min^{-1} for 30 min had no significant effect on reticulum and rumen dorsal sac contractions (Table 2). On the other hand, i.v. infusion of

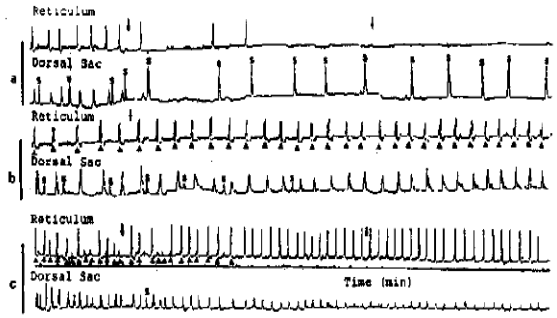

Fig. 1: The blocking effect of yohimbine on naphazoline-induced inhibition of reticulo-ruminal motility in a conscious goat.
a) Naphazoline alone (2.5 μg kg^{-1} min^{-1} for 15 min) abolished reticulum and primary rumen dorsal sac con-tractiions, but had no effect on secondary contractions
b) Yohimbine alone (20 μg kg^{-1} min^{-1} for 30 min) progress-ively abolished rumen secondary contractions and induced ruminatiion (arrow heads)
c) Yohimbine infusion prior to naphazotine blicked the inhibitory effect of naphazoline on frestomach contract ions.

▲ = rumination; S = rumen secondary contractions

yohimbine at a dose of rate of 20 μg kg^{-1} min^{-1} for 30 min significantly ($p<0.05$) increased reticulum contractions during the infusion period and at 30, 90 and 120 min after the infusion was stopped (Table 2). Yohimbine administration had no significant effect on dorsal rumen contractions. However, during the infusion of yohimbine there was a progressive inhibition of secondary rumen contractions, which were completely abolished 10-15 min after the beginning of yohimbine infusion (Fig. 1). The administration of yohimbine was always associated with rumination activity that lasted for 2 hours following the termination of infusion (Fig. 1).

Blocking effects of α-adrenoreceptor antagonists: The reduction of the frequency of reticuloruminal contractions observed during and after the i.v. administration of phenylephrine (4 μg kg^{-1} min^{-1} for 15 min) was completely blocked when the goats were pretreated i.v. with prazosin at a dose rat of 20 μg kg^{-1} min^{-1} for 30 min (Table 3).

The reduction of reticuloruminal motility caused by the i,v, infusion of naphazoline (2.5 μg kg^{-1} min^{-1} for 15 min) did not occur when the goats were pretreated with yohimbine at a dose rate of 20 μg kg^{-1} min^{-1} for 30 min (Fig. 1 and

Table 1: Mean ± S.E. reticulo-ruminal contractions after adrenoreceptor antagonists infusion in 30 min successive interval in goats (N = 4)

Time (min)	Phenylephrine 4 μg kg^{-1} min^{-1} for 15 min		Naphazoline 2.5 μg kg^{-1} min^{-1} for 15 min	
	Reticulum	Rumen	Reticulum	Rumen
-30	13.0 ± 0.7R	20.8 ± 1.4	15.5 ± 0.9	23.5 ± 1.2
-15	16.0 ± 1.3R	24.8 ± 2.3	15.5 ± 0.5R	23.0 ± 1.0
+15	13.3 ± 1.5	18.5 ± 2.1	7.8 ± 1.0*	11.3 ± 1.1
30	12.5 ± 0.7	18.3 ± 0.7	2.5 ± 0.5*	7.0 ± 0.9*
45	9.8 ± 0.7*	14.5 ± 0.9*	4.0 ± 1.4*	7.5 ± 1.7*
60	11.3 ± 0.8	16.5 ± 0.9	2.3 ± 0.9*	5.8 ± 0.8*
75	12.5 ± 1.0	18.0 ± 1.5*	3.3 ± 0.8*	8.3 ± 1.5*
90	11.8 ± 0.5	16.8 ± 0.6	6.3 ± 1.5*	13.0 ± 2.6
105	14.5 ± 0.3	22.5 ± 1.5	4.8 ± 1.4*	10.8 ± 2.4
120	12.0 ± 0.5	18.5 ± 1.1	6.5 ± 1.1*	13.3 ± 2.1
135	13.3 ± 1.3	19.8 ± 1.8	6.3 ± 0.7*	14.0 ± 1.1

* Significantly different from control ($p < 0.05$); R = rumination

Table 2: Mean ± S.E. reticulo-ruminal contractions after adrenoreceptor antagonists infusionin 30 min successive interval in goats (N = 4)

Time (min)	Prazosin 20 μg kg^{-1} min^{-1} for 15 min		Yohimbine 20 μg kg^{-1} min^{-1} for 15 min	
	Reticulum	Rumen	Reticulum	Rumen
-30	31.5 ± 1.5	48.5 ± 1.7	37.5 ± 0.8	53.5 ± 0.8
+30	31.3 ± 1.9	50.5 ± 1.4	50.5 ± 3.3R	55.3 ± 3.0
60	30.5 ± 1.3	54.0 ± 1.4	54.0 ± 3.0R	58.0 ± 3.3
90	30.3 ± 1.6	52.8 ± 1.6	47.0 ± 2.6R	54.5 ± 2.8
120	30.8 ± 0.5	48.3 ± 2.5	48.0 ± 1.6R	59.3 ± 2.5
150	31.7 ± 1.2	49.8 ± 1.9	47.0 ± 1.1R	56.0 ± 1.2

*Significantly different from control ($p < 0.05$); R = rumination

Table 3: Mean ± S.E. reticulo-ruminal contractions after adrenoreceptor antagonists infusion followed by adrenergic receptor agonists in 15 min interval in goats (N = 4)

Time (min)	Yohimbine 20 20 μg kg^{-1} min^{-1} for 30 min + Naphazoline 25 20 μg kg^{-1} min^{-1} for 15 min		Prazosin 20 20 μg kg^{-1} min^{-1} for 30 min + phenylephrine 4 20 μg kg^{-1} min^{-1} for 15 min	
	Reticulum	Rumen	Reticulum	Rumen
-30-15	18.0 ± 1.2R	24.7 ± 1.6	15.3 ± 1.1	22.7 ± 1.2
-15-0	16.0 ± 1.2R	23.0 ± 1.7	15.7 ± 1.8R	22.3 ± 1.1
*0-15	18.0 t 0.9R	20.3 ± 0.5	16.3 ± 0.9R	21.3 ± 0.9
15-30	27.7 ± 3.9R	27.7 ± 3.9	16.0 ± 0.9	23.0 ± 0.9
0-15	23.0 ± 1.7R	23.3 ± 1.6	17.3 ± 1.3	24.3 ± 2.2
15-30	20.7 ± 1.8	21.7 ± 1.3	15.7 ± 0.8	23.0 ± 2.1
30-45	16.0 ± 1.2	17.0 ± 0.6	16.7 ± 0.5R	23.3 ± 1.9
45-60	16.0 ± 0.9	17.3 ± 0.2	15.7 ± 0.7	19.3 ± 1.1
60-75	15.0 ± 0.6	16.0 ± 0.3	14.3 ± 0.5	18.7 ± 0.9
75-90	16.7 ± 0.7	18.7 ± 0.9	16:3 ± 0.2	20.7 ± 1.3
90-105	15.7 ± 0,9	17.3 ± 0.4	14.7 ± 0.7	19.7 ± 0.9
105-120	14.7 ± 0.5	16.7 ± 0.7	15.0 ± 1.5	20.0 ± 0.9
120-135	15.3 ± 0.4	17.3 ± 0.4	12.0 ± 0.9	17.7 ± 1.1

*Significantly different from control ($p < 0.05$); R = rumination

Table 3). In these cases, the inhibition of rumial secondary contractions induced by yohimbine infusion continued after the administration of naphazoline (Fig. 1). Also rumination activity was present during control period and during the infusion of yohimbine. However, the administration of naphazoline suppressed rumination activity (Table 3).

Discussion

The present work supports previous data in indicating that the adrenergic receptors are involved in the regulation of reticulo-ruminal motility (Ruckebusch, 1983). Phenylephrine, an α1-adrenergic agonist, decreased the frequency and amplitude of reticuloruminal contractions and failed to evoke rumination. This agrees with observations by Van Miert (1969) when phenylephrine was given intrajugularly and Campion and Leek (1995) with phenylephrine given into the coeliac artery. This contrasts with the findings of Brikas (1989) that the i.v. fusion of phenylephrine (2.5 μg kg^{-1} min^{-1} for 30 min or 4 μg kg^{-1} min^{-1} for 15 min) increased the frequency of reticuloruminal cyclical contractions and provoked rumination sheep. When the goats were intravenously pretreated with prazosin, a highly selective antagonist for the α1 -receptors (Hoffman, 1984) which did not in itself exert any excitatory or inhibitory influence on reticuloruminal activity, the effects of phenylephrine on reticuloruminal motility were completely blocked.

The involvement of the α2-adrenoreceptors in the regulation of goat reticuloruminal motility was studied in the present work using the fairly selective α2-agonist naphazoline (Lees, 1981). Infusion of this drug caused a progressive inhibition of reticulo-ruminal motility which was significantly different from the control period. This confirms previous reports that intravenous injection of α2-agonists depressed the amplitude and/or frequency or reticulo rumination contractions (Toutain *et al.*, 1982; Guard and Schwark, 1984; Ruckebusch and Toutain, 1984; Brikas *et al.*, 1986; Brikas, 1989; Nicholson and Osman, 1992; Campion and Leek, 1995). The inhibitory effects of naphazoline did not occur when the goats were intravenously pretreated with yohimbine, a quite selective antagonist for the α2- adrenoreceptors.

In the present study, yohimbine infused i.v. at a dose rate of 20 μg kg^{-1} min^{-1} or 15 min, either alone or followed by naphazoline, caused a progressive inhibition of secondary rumen contractions. These contractions were completely abolished 10-15 minutes after the beginning of yohimbine infusion. This agrees with observations by Brikas (1989) when yohimbine was infused into the jugular vein of sheep. In contrast, Guard and Schwark (1984) reported no change in the rate of rumen contractions when yohimbine was given as a bolus into the jugular vein of calves. The incidence of rumination observed during the present study associated with the i.v. infusion of yohimbine remains obscure. However, Nicholson and Belkhiri (1990) reported that rumination may be stimulated by a recording balloon in the reticulum of sheep. But since the same method was adopted for recording forestomach motility in the goats used in the present work, the stimulation of rumination activity by yohimbine needs further investigations.

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