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The effects of α- and β-sympathicomimetics on rumen motility and heart rate frequency in conscious goats

In the ruminal smooth muscle preparation *in vitro* there exist α-stimulatory and β-inhibitory adrenergic receptors. The effect of adrenaline, either contraction or relaxation, is the result of interactions with both types of receptors (van Miert & Huisman, 1968). It is of interest to note that Titchen & Newhook (1968), who made their experiments with anaesthetized vagotomized sheep and lambs or with vagotomized decerebrate preparations of lambs, reported similar adrenergic mechanisms near the reticulo-omasal orifice.

Adrenaline is known to cause a single slow contraction of reticulum, rumen and abomasum in unanaesthetized vagotomized sheep (Habel, 1956). This is also the case in the anaesthetized goat with intact vagi. However, normal cyclical movements of the reticulo-rumen cease after the vagus nerves have been cut or after induction of anaesthesia. An intravenous injection of adrenaline in the conscious ruminant always gives an inhibition of the regular contractions of the rumen, although it is not known whether α- or β-adrenergic receptors, or both, are involved in this phenomenon. I now report the effects of sympathicomimetics activating α- or β-adrenergic receptors.

Materials and methods. An open-ended water filled polyethylene tube was passed into the rumen intra-nasally, and the other end connected to a pressure transducer. An electrically driven slow-infusion pump was also connected to prevent occlusion of the tube with food particles. The volume of fluid administered was 1 ml/min. Pressure records made in this way show the well-known regular contractions of the rumen occurring with a frequency of about 1/min. The frequency and the amplitude

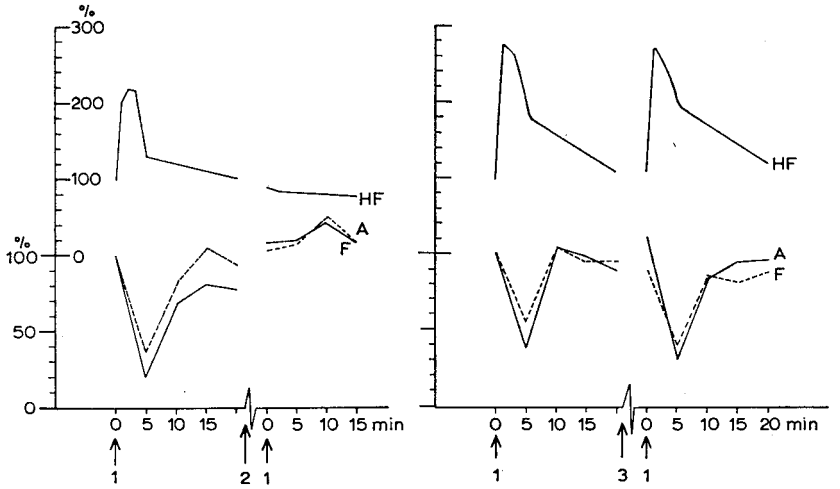

FIG. 1. Mean change in rumen motility for 3 goats to isoprenaline 2·5 μg/kg i.v. (= 1) before and after propranolol 0·5 mg/kg i.v. (= 2) or dibenamine 2·5 mg/kg i.v. (= 3) respectively. A—Summation during 5 min intervals of amplitude, expressed as percentage of the initial value. F—Frequency/5 min expressed as percentage of the initial value. HF—Change in heart rate.

of the contractions were measured every 5 min, and expressed as percent of the initial value. Heart rate was taken from an electrocardiogram using a Elema-Schönander Mingograph. The drugs were dissolved in saline and given as an intravenous injection or by a continuous slow infusion.

For specific α-receptor stimulation phenylephrine 2·5 μg/kg min^{-1} and oxymetazoline 0·2 μg/kg min^{-1} were used; for specific β-stimulation isoprenaline 0·1 μg/kg min^{-1} or 2·5 μg/kg, adrenaline 1 μg/kg min^{-1} or 7·5, 10 or 20 μg/kg, dibenamine 15 μg/kg min^{-1} or 2·5 mg/kg, propranolol 0·5 and 1 mg/kg or 10 μg/kg min^{-1}, Du 21445 [1-isopropyl-amino-3-(2-methylthiophenoxy)-propan-2-ol], also a strong β-blocking agent 10 μg/kg min^{-1} or 1 mg/kg, were also used.

Results and discussion. After an intravenous injection or infusion, during 15 min of isoprenaline, the heart rate is suddenly increased, while rumen motility is depressed. Both effects were completely blocked by propranolol or Du 21445 but not by dibenamine (Fig. 1). Therefore the inhibitory response to isoprenaline must involve activation of β-receptors.

Infusions of oxymetazoline or phenylephrine were accompanied by bradycardia and a reduction of the amplitude and frequency of rumen contractions. After pretreatment with dibenamine—an injection or infusion during 90 min—the bradycardia caused by these α-sympathicomimetics is less and the inhibition of rumen

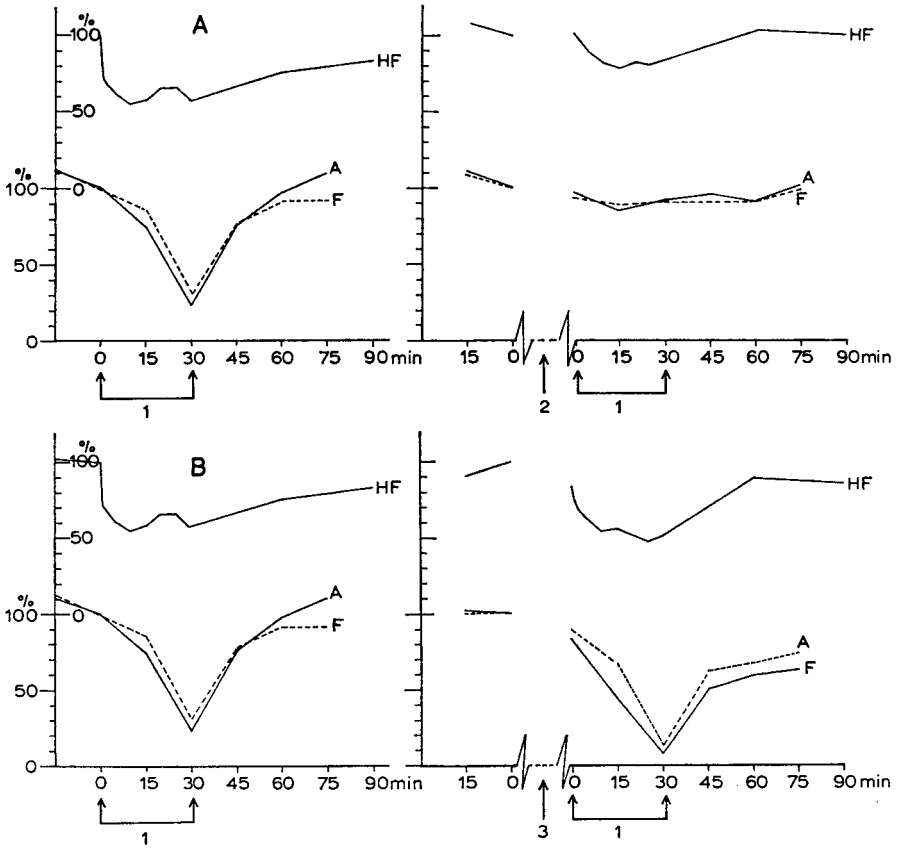

FIG. 2. Mean changes in rumen motility and heart frequency for 3 goats to phenylephrine 2·5 μg/kg min^{-1} (= 1). A. Before and after an infusion of dibenamine 15 μg/kg min^{-1} during 90 min (= 2). B. Before and after an infusion of propranolol 10 μg/kg/min during 90 min (= 3).

contractions is blocked. On the other hand, propranolol has no influence on the inhibitory response to phenylephrine (Fig. 2). Therefore this inhibitory response to phenylephrine must involve activation of α-receptors. The bradycardia caused by phenylephrine could also be prevented by a prior intravenous injection of atropine 0·15 mg/kg. Therefore it seems to be probable that the bradycardia induced by phenylephrine or oxymetazoline is reflex in origin, due to the pressor response of these α-sympathicomimetics, which causes stimulation of the baroreceptors in the carotid sinus and aortic arch with consequent vagal slowing of the heart.

Before propranolol or Du 21445, an injection of adrenaline, 20 μg/kg, caused tachycardia, but after β-blockade the heart rate was depressed, probably attributable to a greater vasoconstrictor response (α-receptor stimulation). There was however no change of the inhibitory response of rumen motility to adrenaline. A low dose of adrenaline as injection, 7·5 μg/kg, or infusion caused bradycardia; β-blocking agents had no influence on this effect. After α-receptor blockade by dibenamine, as an injection or infusion during 120 min, the inhibition of the rumen contractions by adrenaline, 10 or 20 μg/kg, is less, while tachycardia is antagonized. The antagonistic effect of a combination of dibenamine and propranolol in relation to the effect of adrenaline on rumen motility is no greater than with dibenamine alone. An analysis of the cardiac responses and the effects on rumen motility to phenylephrine and isoprenaline after pretreatment with dibenamine or propranolol, indicates that the dosage of both blocking agents was sufficient to produce significant blockade of α- and β-receptors in the cardiovascular system and reticulo-ruminal wall. Adrenaline activates both α- and β-receptors in the ruminal smooth muscle strip. However, *in situ* only dibenamine was able to antagonize the adrenaline effect; this was not so with β-blockers, although the doses of both blocking agents were adequate. On the basis of *in vitro* observations it has been concluded that in the ruminal wall both α-stimulatory and β-inhibitory adrenergic receptors are present (van Miert & Huisman, 1968). *In situ*, α- and β-sympathicomimetics both interfere with the normal rhythmic reticulo-ruminal contractions. The effect of adrenaline seems to be primarily affected by interaction with α-adrenergic receptors. What exactly happens *in situ*, when α- or β-adrenergic receptors in the ruminal wall are stimulated, is not known. Increased tonic activity of the reticulo rumen after stimulation of α-adrenergic receptors, followed by reflex inhibition of the normal cyclical movements, is only one possibility. However, with the method I have used it is not possible to check this hypothesis.

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