ADRENOCEPTOR STUDY OF GUINEA-PIG SUPERIOR MESENTERIC – PORTAL VEIN

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INTRODUCTION

Vasoactive agents have been extensively studied in precapillary resistance vessels but little emphasis has been directed to their effect on the venous system even though veins are probably important in governing haemodynamics. Approximately half the blood volume lies within the venous system, therefore a doubling in venous tone could increase the circulating volume by 25% and conversely a reduction in tone could produce cardiovascular collapse (Sutter, 1965). The aim of this study was to determine the types of adrenoceptor involved in the adrenergic responses of guinea-pig superior mesenteric – portal vein.

METHOD

Guinea-pigs of either sex weighing 180 – 300 g were killed by a blow to the head and bled out. The superior mesenteric – portal vein, about 1.5 cm long, was removed and cut along its length to allow Ringer free access to the outside and lumen side of the tissue during the course of the experiment. This preparation was set up in a 10 ml organ bath containing Tyrode Ringer solution, maintained at 36°C and bubbled with compressed air. The composition of the Tyrode was, in mM: NaCl 137, KCl 2.68, $MgCl_2$ 0.87, $CaCl_2$ 1.8, NaH_2PO_4 0.68, $NaHCO_3$ 11.9, glucose 5.56, pH 7.2.

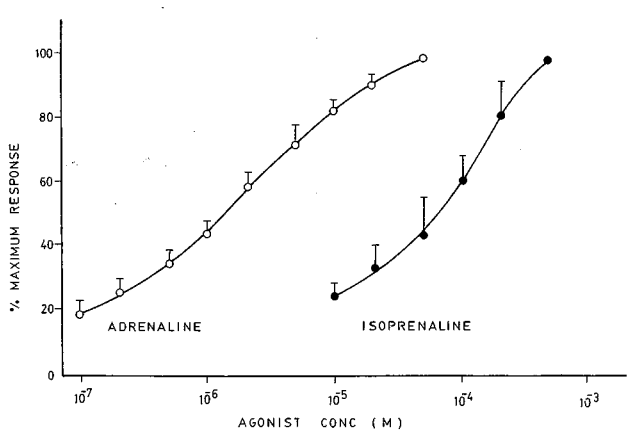
Contractural responses were recorded on a Grass Polygraph (Model 79D) via a Grass force-displacement transducer (Model FTO3C). The tissue was allowed to stabilize for 30 minutes (during which time spontaneous activity developed) before any drugs were added.

Drug additions were made at eight minute intervals using a one minute drug contact time. Using separate tissues, concentration effect curves for adrenaline and for isoprenaline were constructed and the effects of increasing concentrations of phentolamine (2.65×10^{-8}M – 2.65×10^{-6}M) or propranolol (2×10^{-7}M – 5×10^{-5}M) on submaximal responses to adrenaline (10^{-6}M) or to isoprenaline (10^{-4}M) were recorded.

RESULTS

Both adrenaline and isoprenaline (which is generally considered a specific Beta receptor agonist) induced dose-related contractions of superior mesentericportal vein. Adrenaline was greater than ten times more potent than isoprenaline (Fig. 1).

Phentolamine antagonized responses to adrenaline and to isoprenaline. At the highest concentration of phentolamine the responses to adrenaline and to isoprenaline were completely abolished, neither contraction nor relaxation being seen. It is interesting



LEGEND TO FIGURE 1

Concentration-effect curves of adrenaline (●) and isoprenaline (O) on guinea-pig superior mesenteric-portal vein. Vertical bars = s.e., n=4.

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DISCUSSION

Ahlquist (1948) reported that adrenaline and isoprenaline act on vascular Beta receptors at approximately the same concentration. However in this study isoprenaline was significantly less potent than adrenaline in evoking contractions of superior mesenteric-portal vein. This could be explained in one of two ways· firstly, that both Alpha and Beta receptors are present, that Alpha receptors predominate and that stimulation of either Alpha or Beta separately causes contraction, or alternatively that the contraction induced by isoprenaline is not a Beta receptor mediated effect.

The curves showing the relationship between phentolamine concentration and its blocking effect on responses produced by adrenaline and responses produced by isoprenaline (Fig. 2 and 3) are so similar that it is difficult not to suspect that the mechanisms involved in both cases are exactly the same.

The maximum effects produced by phentolamine and propranolol also depend on the type of receptors involved and the response to their individual stimulation. With this in mind the theoretically possible maximum effects of complete Alpha or Beta receptor blockade on this system are summarized in Table I.

The experimental results show that phentolamine could completely block the response to both agonists and that propranolol had no effect on the response to either. These findings best fit case A in Table I where only Alpha receptors are involved. It is therefore likely that the response to isoprenaline is a result of 'non-specific' isoprenaline-induced Alpha receptor stimulation. A receptor interaction of this type by isoprenaline has also been reported in a study using cat eye (Ahlquist, 1966) and it is interesting to note that the potency of isoprenaline in this case was 10 – 100 times less than that of adrenaline.

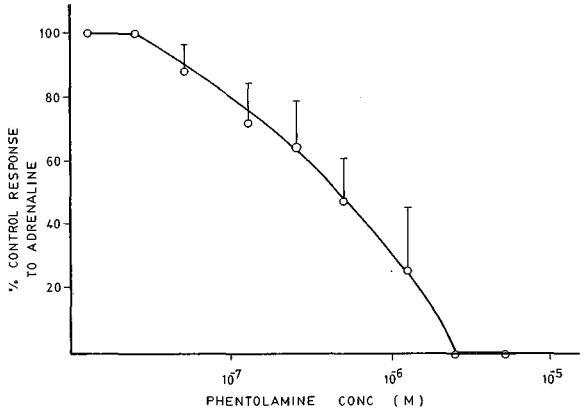
It is therefore suggested that Alpha receptors are the only type of adrenoceptor present in guinea-pig superior mesenteric-portal vein which are involved in the adrenergic control of contraction and that isoprenaline in high concentrations is capable of stimulating these receptors.

Table I **Theoretical responses to adrenergic receptor stimulation of guinea-pig superior mesenteric-portal vein in the presence of complete Alpha or Beta receptor blockade.**

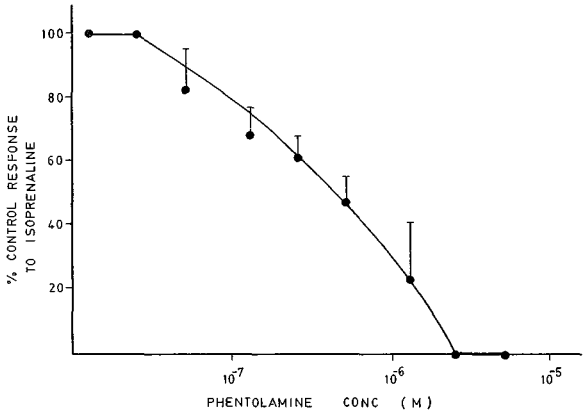
Case	Receptors Stimulated	Possible Responses produced by receptor stimulation	Expected maximum effect of Alpha Receptor Blockade	Expected maximum effect of Beta Receptor Blockade
A	Alpha	Contraction	Complete blockade	No change in response
B	Beta	Contraction	No change in response	Complete blockade
C	Alpha + Beta	Contraction Contraction	Incomplete blockade	Incomplete blockade
D	Alpha + Beta	Contraction Contraction	Relaxation	Increase in contraction
E	Alpha + Beta	Relaxation Contraction	Increase in contraction	Relaxation

to note that, even though the concentration of isoprenaline used was 100 times greater than that of adrenaline, the two curves (Fig. 2 and 3) showing the effect of increasing concentrations of phentolamine are superimposable. Complete blockade of both adrenaline and isoprenaline was obtained at the same concentration of phentolamine (2.65×10^{-6}M).

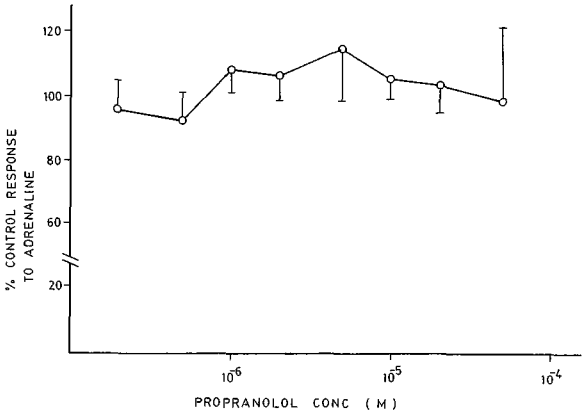
Propranolol at concentrations up to 2×10^{-5}M had no significant effect on the response to either adrenaline or isoprenaline (Fig. 4 and 5). At concentrations of propranolol greater than this, partial blockade was seen on half the tissues tested. In these tissues it was found that contractural responses to histamine (5×10^{-7}M) were reduced by 5×10^{-5}M propranolol to 55% (+7%, n=4) of control values. This indicates that at 5×10^{-5}M, propranolol has a non-specific membrane stabilizing effect, a property for which propranolol is well known (eg. Wu and Narahashi, 1973).



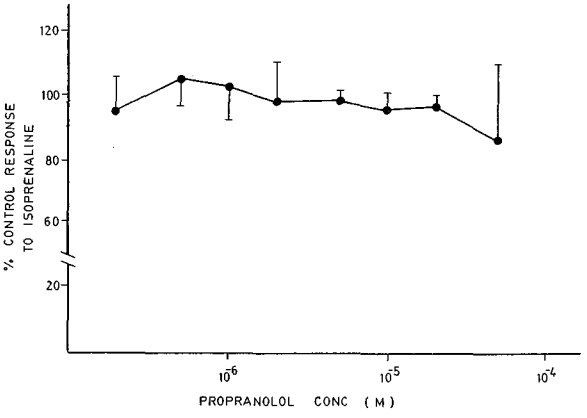
LEGEND TO FIGURE 2
Effect of increasing concentrations of phentolamine on the response to adrenaline (10^{-6}M). Vertical bars = s.e., n = 4.



LEGEND TO FIGURE 4
Effect of increasing concentrations of propranolol on the response to adrenaline (10^{-6}M). Vertical bars = s.e., n = 4.



LEGENT TO FIGURE 3
Effect of increasing concentrations of phentolamine on the response to isoprenaline (10^{-4}M). Vertical bars = s.e., n = 4.



LEGEND TO FIGURE 5
Effect of increasing concentrations of propranolol on the response to isoprenaline (10^{-4}M). Vertical bars = s.e., n = 4.

SUMMARY

The effects of phentolamine and propranolol on contractural responses of guinea-pig superior mesenteric-portal vein to adrenaline and isoprenaline were investigated. Phentolamine was capable of completely abolishing the response to adrenaline and to isoprenaline while propranolol had no effect on responses to either agonist. It is suggested that Alpha receptors are the only type of adrenoceptor involved in adrenergic control of contraction of this vein and that isoprenaline is capable of stimulating these receptors.

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