Differential effects of prazosin on the pre- and postsynaptic α-adrenoceptors in the rat and dog

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The heart rate decreases and blood pressure increases seen with i.v. clonidine administration to pithed rats, in which their basal heart rates have been elevated by continuous selective electrical stimulation of the thoracic spinal cord, are attributed to a respective activation of pre- and postsynaptic α-adrenoceptors (Drew, 1976). We have performed a biokinetic analysis for both responses and found that the rates of onset and dissipation of the clonidine induced hypertension were much quicker than those for the heart rate reductions.

The effects of phentolamine (1.0 mg/kg, i.v.) and prazosin (1.0, 5.0 mg/kg, i.v.) on the pre- and postsynaptic actions of clonidine were compared. Phentolamine effectively antagonized both the hypertensive and heart rate lowering responses of clonidine. However, prazosin selectively blocked the clonidine induced pressor responses without affecting the heart rate.

Using pentobarbital anaesthetized dogs untreated or treated with desipramine, Lokhandwala & Buckley (1976) reported that phentolamine (2.0 mg/kg) potentiated the chronotropic responses to cardioaccelerator nerve stimulation by inhibiting presynaptic α-adrenoceptors at the level of the cardiac pacemaker.

We have observed that in spinal dogs desipramine (1.0 mg/kg, i.v.) effectively inhibited the tachycardia to tyramine (50 μg/kg, i.v.) and increased the positive chronotropic effects to both i.v. noradrenaline (0.2 μg/kg) and stimulation of the cardioaccelerator nerve (supramaximal voltage for 15 s at frequencies 0.25–2.0 Hz and pulse duration of 0.5 msec). After phentolamine (0.3, 1.0 mg/kg, i.v.) the tachycardias seen with cardioaccelerator stimulation were further increased whereas pressor effects of i.v. noradrenaline were reduced. However, contrary to the finding of Lokhandwala & Buckley (1976), we could not show a potentiation of the tachycardias to stimulation of the cardioaccelerator with phentolamine in the absence of desipramine. Both desipramine and phentolamine caused increases in the basal heart rate levels.

In the spinal dog prazosin (0.3, 1.0 mg/kg, i.v.) increased, as did phentolamine the basal heart rate and potentiated the positive chronotropic responses to cardioaccelerator stimulation only when given after desipramine. At the same time it antagonized the pressor responses to i.v. noradrenaline.

In conclusion, phentolamine inhibited both pre- and postsynaptic α-adrenoceptors in the rat and dog. Prazosin showed a definite selective antagonism for postsynaptic α-adrenoceptors only in the rat. These results suggest that there may be a species difference for the cardiac presynaptic α-adrenoceptors.

References

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Investigation of the bronchoconstriction induced by β-adrenoceptor blocking drugs in guinea-pigs and rats

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β-Adrenoceptor blocking drugs are known to cause bronchospasm in man, especially in asthmatic subjects but this effect has rarely been reported in animals.

In the present experiments, the effects on airways resistance of β-adrenoceptor blocking drugs have been investigated in guinea-pigs and rats using the sensitive method of Green & Widdicombe (1966). Animals were anaesthetized with urethane (1.25 g/kg, i.p.) or pentobarbitone sodium (40 mg/kg, i.p.) and total lung resistance (TLR) and dynamic lung compliance (C_{dyn}) were measured for each inspiration during spontaneous breathing. The resting values in rats and guinea-pigs ranged from 10.5 to 72.5 cm H_2O l^{-1} s^{-1} for TLR and from 0.22 to 1.68 ml/cm H_2O for C_{dyn}.

In guinea-pigs histamine acid phosphate (0.5 to 5 μg/kg, i.v.) produced a short-lasting increase in inspiratory resistance and a corresponding decrease in compliance. This effect was greatly reduced by pretreatment with atropine sulphate (1 mg/kg, i.v.) indicating that the response was reflexly mediated. The