

LETTER TO THE EDITOR

NEGATIVE INOTROPIC EFFECT OF SYMPATHOMIMETIC AMINES IN RABBIT ATRIA

Sir,

The negative inotropic effect of sympathomimetic amines has scarcely been reported in literature. Wenzel and Su (3), while studying the interactions of sympathomimetic amines with their antagonists on isolated rat ventricular strips, observed that phenylephrine initially produced a negative inotropic effect which was later on followed by usual positive inotropic response. Similarly epinephrine produced an initial depression of contractile amplitude when administered in presence of nethalide, a beta blocker. He attributed this inhibitory response to activation of alpha inhibitory receptors, whose existence till then was unclaimed. The usual positive inotropic response following initial inhibition was supposedly due to stimulation of alpha excitatory receptors.

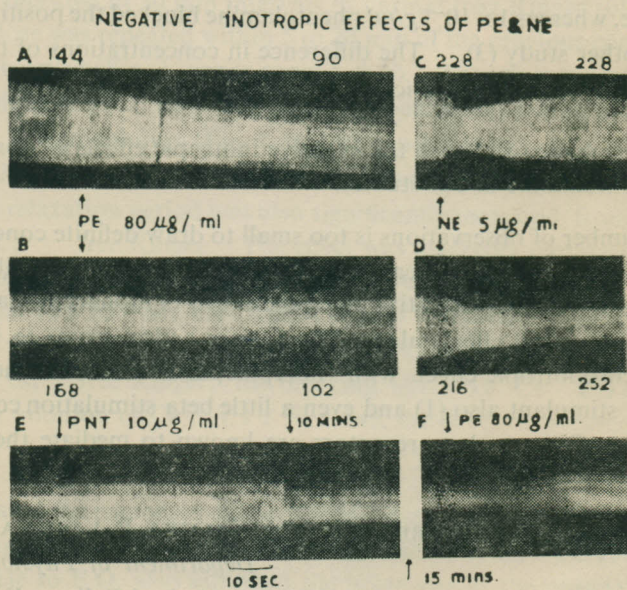


Fig. 1: Negative inotropic effects of phenylephrine (Panel A & B) and norepinephrine (Panel C & D). The numerals above panel A and C and below panel B and D represent atrial rate per minute. Blockade of negative inotropic effect of phenylephrine by phentolamine (Panel E & F). Panel E is continuation of panel B.

During an endeavour to characterise adrenoceptors in the rabbit atrium, by using isolated spontaneously beating preparations from normal and reserpinised animals, we have found that in 5 observations phenylephrine 80 µg/ml produced a negative inotropic effect lasting for less than a min. The mean control contractile amplitude declined by 25%. Wenzel and Su (3) had re-

corded a depression of approximately 3% at a concentration of 1×10^{-5} g/ml of phenylephrine. The initial inhibition was followed by negative chronotropic response (Fig. 1, A&B) as the control mean rate of 160/min decreased to 104/min (35% decline), but the amplitude of these contractions showed a tendency towards normalisation and sometimes exceeded the control levels (Fig. 1 B). The usual inotropic response was not recorded and the negative chronotropic effect was followed by records tending towards the control rate and amplitude. In 4 cases, norepinephrine, 5 μ g/ml resulted in a similar depression of magnitude of contraction, the mean decline in amplitude was 39%. But in no case a negative chronotropic response with concomitant increased amplitude was registered (Fig. 1, C&D), as the mean control rate of 230/min rose to 248/min. The delayed (usual) positive inotropic effect was not observed.

The negative inotropic response of phenylephrine (80 μ g/ml) was blocked, and positive inotropic response unmasked by 10 μ g/ml phentolamine treated for 15 minutes (Fig. 1, E & F). A concentration of 1×10^{-6} g/ml of phentolamine was employed to block the inhibitory response of 1×10^{-5} g/ml of phenylephrine in study of Wenzel and Su (3). The usual positive inotropic effect of phenylephrine (80 μ g/ml) in our other experimental observations was antagonised by 40 μ g/ml of phentolamine, whereas 1×10^{-5} g/ml phentolamine blocked the positive inotropic response of phenylephrine in other study (3). The difference in concentrations of the drugs used in two studies could be due to species variance.

No attempt was made to abolish the negative inotropic effects of norepinephrine by lower concentrations of phentolamine in our studies.

Though the number of observations is too small to draw definite conclusions, nevertheless, in agreement with Wenzel and Su (3), it can be speculated that probably inhibitory alpha receptors do exist in rabbit atria and mediate negative inotropic effects of alpha receptor agonists and occasionally the negative chronotropic effects also. The former action seems to be more likely. The absence of negative chronotropic effect with norepinephrine could be due to the fact that norepinephrine is a beta stimulant also (1) and even a little beta stimulation could have nullified the negative chronotropic effects, as beta receptors are known to mediate the chronotropic effects predominantly (2).

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