

## The effect of large oral doses of vitamin C on the chronotropic action of isoprenaline in man

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(introduced by P. TURNER)

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It was found in dogs (Houston, Wilkens & Levy, 1976) that intraduodenal administration of isoprenaline together with vitamin C caused a much greater increase in the heart rate (HR) than was observed after administration of isoprenaline alone. No potentiating effect was detected when isoprenaline and the vitamin were injected intravenously. The purpose of this study was to investigate the influence of large oral doses of vitamin C on the positive chronotropic action of isoprenaline in man. Twenty patients (11 men and 9 women; mean age 47 years) participated in the study. Patients with signs or symptoms of renal or liver malfunction, heart disease, arterial hypertension or gastrointestinal disease were excluded from the group. Fasted overnight, the subjects took vitamin C and/or isoprenaline on three consecutive days, according to a Latin-square design. On one morning, after recording HR and blood pressure (BP) 30 mg of isoprenaline was given in a sustained action tablet (PROTERNOL®, Key Pharmaceuticals, Inc.), and HR as well as BP were recorded every ten minutes till the isoprenaline-induced tachycardia had worn off. On another day the patients took one gram vitamin

C per os at 7.00, 8.00, 9.00, 10.00 and 11.00 h. At 9.00 they also received 30 mg of isoprenaline, and the parameters were recorded every tenth minute. On a third day at 7.00 h a bolus injection of 5 µg of isoprenaline was administered intravenously in 1 min, and HR and BP were measured every minute till the isoprenaline-induced circulatory changes had disappeared. The doses of 1 g of vitamin C were administered in each hour till 11.00 h, when the isoprenaline challenge had been repeated as before.

Resting HR was identical ( $72 \pm 5$ ;  $71 \pm 5$  beat/min respectively) on both days with the oral administration of isoprenaline. Maximum HR increase was  $16 \pm 3$  beat/min following isoprenaline alone while isoprenaline plus vitamin C produced a HR increase of  $12 \pm 4$  beat/min. The difference is statistically not significant (NS). However, the area under the HR curve was significantly less in case of the concomitant administration of isoprenaline and vitamin C than in case of isoprenaline alone ( $P < 0.01$ ). There was a positive chronotropic response of  $26 \pm 4$  beat/min following the bolus injection of isoprenaline. The response was almost identical ( $25 \pm 5$  beat/min) after vitamin C pretreatment. There was no significant change in BP.

These data suggest that vitamin C in large oral doses is decreasing the chronotropic effect of the concomitantly administered isoprenaline in man.

### Reference

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## Antagonism by (+)-amphetamine of the inhibition of [<sup>3</sup>H]-noradrenaline overflow obtained by alpha-adrenoceptor agonists or bretylium in the perfused cat spleen

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In the rabbit perfused heart (+)-amphetamine counteracts the block of adrenergic transmission induced by guanethidine and clonidine but not by tetracaine (Starke, Wagner & Schumann, 1972). The concentrations of amphetamine employed in these experiments increased by themselves the release of norad-

renaline induced by nerve stimulation (Starke, *et al.*, 1972). Consequently, an algebraic sum of effects resulting from interactions at different receptor sites cannot be excluded. The aim of the present experiments was to reexamine and clarify the antagonism by amphetamine of the effects of alpha-adrenoceptor agonists on transmitter release induced by nerve stimulation.

The present experiments were carried out in the perfused cat spleen prelabelled with [<sup>3</sup>H]-noradrenaline. The nerves were stimulated at 1 Hz during 5 min. In the controls the fraction of the total tissue radioactivity released per shock was  $12.10 \pm 1.24 \times 10^{-5}$  during the first period of stimulation ( $S_1$ ) and  $12.17 \pm 1.04 \times 10^{-5}$  ( $n = 4$ ) in  $S_2$ . When the results were expressed as the ratio obtained between two consecutive periods of nerve stimulation the value