PERIPHERAL ACTION OF ANGIOTENSIN II

P. K. JAIN, N, SHUKLA AND S. D. NISHITH

Department of Physiology,
K.G's Medical College, Lucknow - 226 003

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Summary : The effects of angiotensin II were studied on isolated atrial preparations of non-reserpinised and reserpinised rabbits, before and after treating the preparations by propranolol. Peripheral action of angiotensin was cardioaccelerator via direct stimulation of β-receptors of the atria in isolated atrial preparations.

Key words : angiotensin heart rate

INTRODUCTION

Angiotensin shows marked vasopessor effect. It has been demonstrated by several workers that it also shows cardioaccelerator effects (1,8). This cardioaccelerator effect is masked by baroreceptor reflexes which are stimulated by the rise of blood pressure due to vasopressor action of angiotensin. Various sites of action of angiotensin have been shown. These are cardiac accelerator centers in medulla and higher parts of C.N.S., secretion of catecholamines from adrenal modulla, release of catecholamines from sympathetic supply to the heart and direct action of angiotensin on pacemaker. The aim of the present study is to find out the mechanism of peripheral cardio-accelerator action of angiotensin. In this study isolated atrial preparations have been used to exclude all other sites of action of angiotensin.

MATERIAL AND METHODS

Experiments were performed on atrial preparations from 20 healthy male rabbits, in each group weighing between 1 to 1.5 *kg*. The experiments were performed in an organ bath maintained at 37°C. The central bath was filled with Ringer locke's solution. Preparations were placed in central bath and held in position. Continuous O_2 supply was maintained.

The requisite concentrations of angiotensin were obtained by dilution principle. A stock solution of angiotensin was prepared by dissolving 5 *mg* of angiotensin powder 1/*ml* of distilled water. The required doses of angiotensin were freshly prepared before each experiment, by adding distilled water to required dilutions. Dose was 3.3×10^{-10M} (as mentioned by Dempsey *et al.* (5).

Ciplar (Propranolol 1 *mg/ml*) was used in these experiments for blocking the β-receptors in the heart directly. The solution was similarly diluted in distilled water to requisite dilution. Doses used were between 5×10^{-6M} to 5×10^{-5M} as mentioned by Freer *et al*, (7). Propranolol solution was poured in the bath containing the atrial preparation.

In the second group of experiments where reserpinised rabbits were used, reserpine was given intravenously, 1 *mg/kg* body weight, 24 to 48 hrs before the experiments as mentioned by Bonnar-deaux *et al.* (4).

RESULTS

The number of observations in each group are 20. The strength of angiotensin used was 3.3×10^{-10M} as maximum increase in heart rate was observed with this dose. The acceleration in the heart rate was not observed when angiotensin was poured in the bath after treating the atrial preparations with propranolol.

TABLE I : Number of observations N = 20.

Group	*Control HR Mean±SD*	*Effect on HR Mean±SD*	*Significance of difference t*	*p*
Effect of ANG II on atrial preparation.	142.8±25.85	163.2±24.42	2.6	P<0.05 Significant
Propranolol treated atrial preparation.	211.2±18.45	211.2±18.45	0.6	N.S.
After ANG in propranolol treated atria.	211.2±18.45	210.6±18.56	0.1	N.S.
After ANG in reserpinised atrial preparation.	168.9±30.26	178.8±31.26	1.0	N.S.
After ANG in propranolol and reserpinised atria.	162.9±24.02	163.5±24.12	0.1	N.S.

Note : The dose of angiotensin II used in all the experiments was 3.3×10^{-10M}

Accelarator action of angiotensin was observed in atrial preparations from reserpinised rabbits. But when reserpinised preparations were treated by propranolol before pouring angiotensin, no cardiac acceleration was observed.

DISCUSSION

The intact animals the cardio-accelerator action of angiotensin has been described by various workers (2, 8, 10).

The various sites of action are :

1. Direct effect of angiotensin on cardio-accelerator areas in C.N.S.
2. Release of catecholamines, by angiotensin from sympathetic nerve terminals of the heart and also from adrenal medulla.
3. Direct stimulation of β-cells of the heart by angiotensin.

In this study the C.N.S. and adrenal gland have been ruled out as the experiments were done on isolated atrial preparations. The action of angiotensin on heart is cardio-acceleration as also observed by (1, 8). The cardioacceleration observed in the present study is statistically significant (Table I), After using the β-blocker, propranolol the cardioaccelerator action of angiotensin was absent.

In order to find the role of angiotensin on sympathetic nerve terminals, the animals were first reserpinised and then atrial preparation were made, when angiotensin, in same concentration, is added to these preparations mild cardio-acceleration is observed. These findings are in contrast to the findings of (3, 9, 11) was observed that angiotensin sensitises sympathetic nerve terminals stimulating them to secrete more catecholamines. The difference observed in our study can be explained on the basis that the nerve terminals left are very few. As euch angiotensin does not seem to be very effective.

In reserpinised and propranolol treated preparations, the cardio-accelerator effect of angiotensin is not observed. This further strenthens the observation that in isolated atrial preparations, angiotensin acts on β-cells of the heart and brings about cardiac acceleration.

Therefore it is concluded that peripheral cardio-acceleration action of angiotensin is through β-receptors.

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