sodium–calcium permeability of the membrane and a decrease in its potassium permeability. On the grounds mentioned above it can be postulated that the automatic activity of the pacemaker cells of the atrioventricular valves of the rabbit heart is due principally to the functioning of the slow sodium–calcium channel.

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EFFECT OF ANGIOTENSIN II ON THE HEMODYNAMICS AFTER SYSTEMIC AND PORTAL ADMINISTRATION

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Changes in the general hemodynamics were studied in healthy unanesthetized dogs after injection of angiotensin II for 60 min into the superior vena cava and portal vein at the rate of 27 ng/kg/min. Portal administration of the peptide was found to induce a weaker pressor effect. After systemic injection of angiotensin II the arterial pressure rose as the result of an increase in peripheral vascular resistance, and the minute volume of the circulation was reduced. After portal injection of angiotensin the increase in arterial pressure was due chiefly to an increase in the minute volume of the circulation. The differences in the hemodynamic responses cannot be explained entirely by metabolism of the peptide in the liver. After portal injection of angiotensin II it is possible that depressor substances from the liver enter the blood stream.

KEY WORDS: angiotensin II; hemodynamics; peptide metabolism in the liver.

Directing blood from the kidneys and adrenals into the liver leads to an increase in the metabolism of humoral factors of the renin–angiotensin–aldosterone system [3, 5], and produces a hypotensive effect in vasorenal hypertension [5, 6].

To analyze this effect changes in the hemodynamics were compared after infusion of angiotensin II into the systemic and portal circulation.

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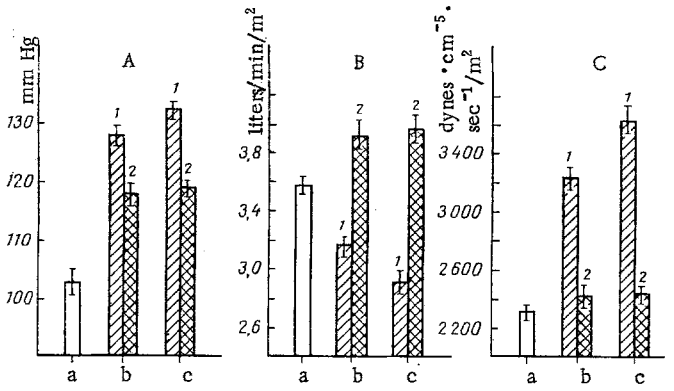

Fig. 1. Changes in hemodynamic indices in healthy dogs following systemic (1) and portal (2) infusion of angiotensin II at the rate of 27 ng/kg/min. Explanation in text. A) Mean arterial pressure; B) cardiac index; C) specific peripheral vascular resistance; a) initial level; b) 30th min; c) 60th min.

EXPERIMENTAL METHOD

Experiments were carried out on 17 unanesthetized noninbred dogs accustomed to the experimental situation, and with catheters previously inserted into the superior vena cava and portal vein. Angiotensin II-amide of Soviet manufacture was infused at the rate of 9 and 27 ng/kg/min in 5% glucose solution for 60 min. Intraportal and systemic infusions of the preparation were given on different days. The arterial pressure was recorded by a tacho-oscillographic method [1]. The stroke volume was calculated on the basis of the ECG, kinetophonocardiogram, and sphygmogram recorded by a physical method synchronously on the Mingograph-34 apparatus [2].

EXPERIMENTAL RESULTS AND DISCUSSION

Infusion of angiotensin II at the rate of 27 ng/kg/min into the systemic blood flow (Fig. 1) caused a moderate but lasting increase in the arterial pressure. Comparison of the results of these experiments with those of infusion of the peptide into the portal vein showed that intraportal injection of the same dose gave a weaker pressor effect. Differences also were found in the mechanism of development of that effect.

After injection of angiotensin into the systemic circulation the arterial pressure rose chiefly on account of an increase in the peripheral vascular resistance to the blood flow while the minute volume of the circulation was reduced.

Conversely, during intraportal infusions of the peptide, the increase in arterial pressure was due chiefly to an increase in the minute volume of the circulation and to a lesser degree to changes in the vascular resistance to the blood flow.

This hemodynamic response to intraportal injection of angiotensin II could be explained by its partial metabolism in the liver, so that small doses of the peptide entered the systemic circulation, where they could not cause any substantial change in vascular tone but had a cardiotonic action. If angiotensin is metabolized in the liver during one passage through the organ to the extent of 60-70% [4], the injection of this substance into the systemic blood flow at the rate of 9 ng/kg/min ought to induce the same response as intraportal injection of the peptide in a dose of 27 ng/kg/min. Experiments were carried out along these lines and it was found that infusion of 9 ng/kg/min into the superior vena cava caused the arterial pressure to rise by 14 mm Hg on account of an increase in the peripheral vascular resistance from 2420 ± 125 to 2916 ± 130 dynes $\cdot$ sec^{-1} $\cdot$ cm^{-5}/m^2, but they did not increase the minute volume of the circulation.

These observations suggest that the weaker pressor effect of portal infusions of angiotensin II cannot be entirely attributed to its metabolism in the liver.

It can tentatively be suggested that after infusion of the peptide into the liver certain intrahepatic changes in the hemodynamics take place, with the result that vasodepressor substances enter the blood stream and the peripheral vascular resistance to the blood flow is altered. In that case the increase in the minute volume of the circulation can be regarded as a compensatory reaction.

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