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Angiotensin II Effects on Plasmatic Renin Activity

F. J. Rodríguez, J. Simón and J. Yajeya

Cátedras de Endocrinología Experimental y Fisiología
Facultad de Medicina
Universidad Complutense
Madrid - 3 (Spain)

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Intravenous infusion of angiotensin II into the cat (4.13 μg/45 min) produces a decrease of plasmatic renin activity. This reduction was not modified after the bilateral denervation of the kidneys or section of both carotid and aortic nerves. The reserpinization of the cats does not modify the angiotensin effects on the renin plasmatic concentration. These observations suggest that the sympathetic nervous system and the catecholamines do not alter significantly the effects of angiotensin II on the renin secretion.

The renin-angiotensin system plays an important role in the regulation of electrolyte metabolism and arterial blood pressure. It is well stablished that intravenous infusion of angliotensin II decreases plasma renin activity in different animals and man (4-6, 15, 17, 20, 23).

The mechanism of inhibition of renin secretion by angiotensin remains conflictive, because angiotensin II can excite the peripheral (1, 11, 16) and central autonomic sympathetic system (1), induces catecholamines liberation from the adrenal medulla (4), produces changes in renal sodium excretion (3, 8, 14) and also produces changes in blood pressure (12). In addition to its vasoconstrictor action, angiotensin II could produce inhibition of renin secretion either acting on the macula densa, an intrarenal baroreceptor or by direct inhibition of the juxtaglomerular cells.

In the present experiments the involvement of the sympathetic nervous system, and catecholamines in the mediation of the angiotensin II effects on the inhibition of renin secretion is studied.

Materials and Methods

The experiments were carried out in sodium pentobarbital (30 mg/kg intraperitoneally) anaesthetized cats. The animals were tracheotomized and positive pressure respiration maintained throughout the experiment. Blood pressure was recorded from femoral artery using a Sanborn transducer. Blood samples were collected

from this artery for plasma renin activity (PRA). Angiotensin II (CIBA, 1.000 μg/ml) vehiculed in 5.5 % glucose, was infused at a constant rate of 0.092 ml/min with help of an Harward (Mod. 955) infusion pump, during 45 min through a femoral vein. Rectal temperature was kept between 36.5-38.0° C using radiant heat. Four experimental groups were studied.

Group I: Control experiments. Eleven cats were used for this experiment in which blood arterial samples were collected for PRA before, and after of 45 min of glucose solution 5.5 % infusion and a 45 min of angiotensin II infusion. The total amount infused was 4.13 ml/45 min equivalent to 4.13 μg angiotensin II.

Group II: Reserpinized cats. Six cats were reserpinized by intraperitoneal injection of 3 mg/kg of 20 % reserpine solution 24 hours before the realization of experimental procedure as described for group I.

Group III: Renal denervation experiments. In nine cats the kidneys and abdominal vessels were exposed by a midline incision and then under a stereoscopic microscope all visible nerves leading to the kidneys and those located on the renal artery were sectioned. After all nerves were cut, the renal arteries were carefully stripped of its adventitia. Blood control samples for PRA determination before and 15 min after denervation were collected. The same experimental procedure that in group I was folloved.

Group IV: Barodenervation experiments. Barodenervation were carried out in six cats cutting both carotid and aortic nerves. The carotid nerve was identified as a branch of the glosopharingeal nerve directed to the carotid sinus region. The aortic nerve was identified in it is join with the cranial laringeal nerve. Blood samples before and 15 min after baroreceptor denervation were collected for PRA determination and the same experimental procedure that in the group I was used.

Blood samples (3 ml) were obtained with iced plastic syringes wetted with EDTA-N_{a_2} solution (15 %). The blood was centrifugated at 4.000 rpm during 20 min at 2-4° C. The plasma samples were stored at —20° C until the PRA was measured. The PRA was measured by RIA of angiotensin I following the method repported by HABER *et al.* (7) adjusting the optimal pH of agiotensin I generation for the cat (fig. 1).

All results were statistically analized by variance analysis and the pairwise test for the multiples comparisons (24).

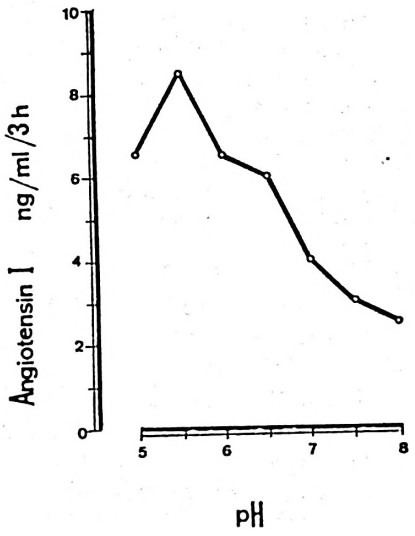

Fig. 1. *Effect of pH on angiotensin I generation from cat plasma, after three hour Incubation at 37° C optimal pH 5.5.*

Results

Normal Cats. The results obtained are showed in figure 2; PRA control value 12.72 ± 1.43 μg AI/ml/3 h ($\bar{x}$ ± se) does not change after 5.5 % glucose intravenous infusion 12.06 ± 1.7 μg AI/ml/3 h (n.s.)

but decreases after angiotensin II infusion 7.26 ± 1.53 μg AI/ml/3 h ($p < 0.05$).

An increase (20-25 mm HG) of the mean arterial blood pressure was observed during angotensin II infusion.

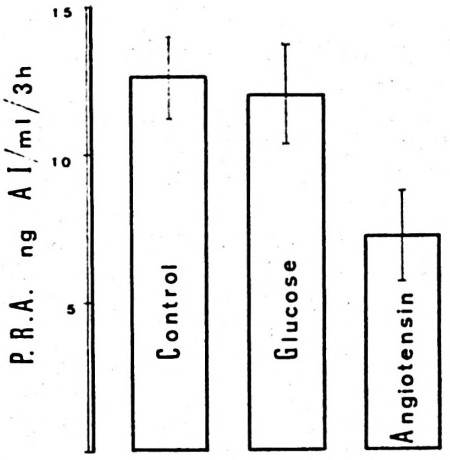

Fig. 2. *Plasma renin activity in normal cats after glucose and angiotensin II infusions.*

Reserpinized Cats. PRA control value 17.17 ± 2.60 μg AI/ml/3 h was not statistically higher than that obtained in normal cats (fig. 3). There was no variation in PRA after 5.5 % glucose intravenous infusion 17.65 ± 2.48 μg AI/ml/3 h (n.s.) but there was a decrease after angiotensin II infusion 8.98 ± 1.54 μg AI/ml/3 h ($p < 0.05$).

Renal Denervated Cats. PRA control value 13.48 ± 1.16 μg AI/ml/3 h increases after renal denervation 17.38 ± 2.72 μg AI/ml/3 h ($p < 0.05$) (fig. 4). This value was not changed after 5.5 % glucose intravenous infusion 16.38 ± 2.73 μg AI/ml/3 h (n.s.) but decreases after angiotensin II infusion 9.39 ± 1.6 μg AI/ml/3 h ($p < 0.05$).

Barodenervated Cats. The PRA control value 13.52 ± 2.26 μg AI/ml/3 h increases after aortic and carotid barodenervation

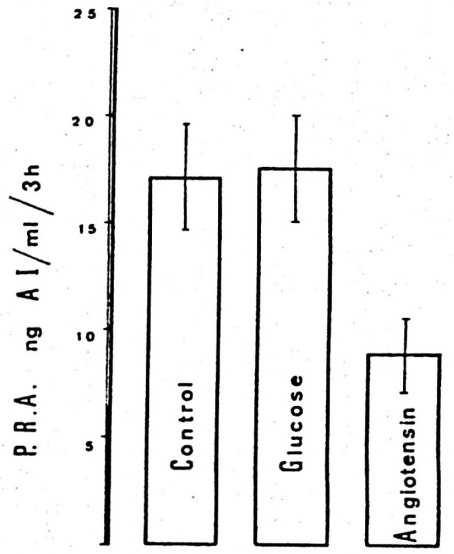

Fig. 3. *Plasma renin activity in reserpinized cats after glucose and angiotensin II infusions.*

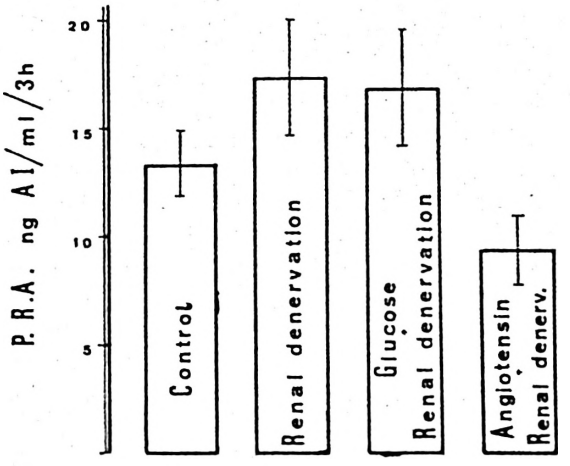

Fig. 4. *Effect of glucose and angiotensin II infusions on plasma renin activity in renal denervated cats.*

21.05 ± 1.70 μg AI/ml/3 h ($p < 0.05$) (fig. 5).

That value was not modified by 5.5 % glucose infusion 20.47 ± 2.13 μg AI/ml/3 h; but decreases after angiotensin II infusion 9.45 ± 1.98 μg AI/ml/3 h ($p < 0.05$).

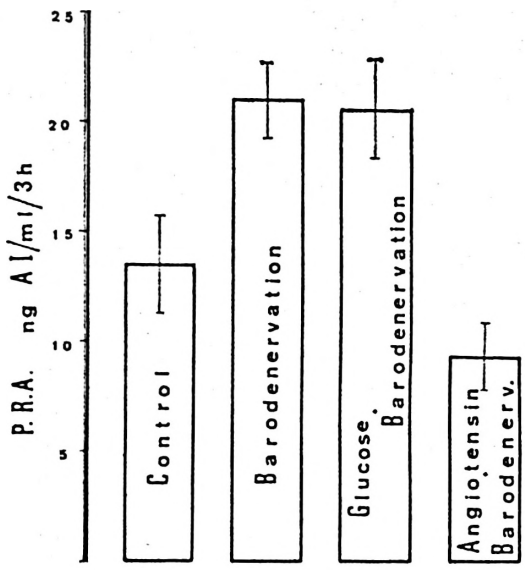

Fig. 5. *Plasma renin activity after glucose and angiotensin II infusion in barodenervated cats.*

Discussion

The results on the inhibition of renin secretion by angiotensin II confirmed on the cat earlier findings in other animal species (4, 5, 15, 17, 20, 23) and man (6).

Three different control mechanisms appear to be involved in the regulation of the renin secretion: *a*) changes of intrarenal perfusion presure (9), *b*) variations of sodium concentration in the macula densa (18, 21), *c*) activity of the sympathetic nervous system through the catecholamines (9, 10, 22). However the diversity of these factors do not exclude the possibility of a final common pathway.

The mechanism by which angiotensin II exerts the inhibitor effects on the plasma renin activity can not be explained alone by the raised systemic arterial pressure nor directly by the effect on the postulated renal baroreceptor (19). In fact that inhibition is independent of arterial pressure values (6, 20). However it is not obtained with a sinthetic analog of the angiotensin (23), the 1-sar-8-ala-Angiotensin II deprived of pressor effects but in this experiment are equally obtained in the normal cat, in the barodenervated cats with higher values of systemic arterial pressure as well as inthe reserpinized cat with arterial pressure lower than 90 mm HG.

The macula densa mechanism can not explain the inhibitory effect of angiotensin on PRA since in dogs with an experimental non filtering kidney the inhibitory effect of angiotensin on PRA was also repported (17).

Previous repports showed that the catecholamines and the sympathetic nervous system were also involved in the control of renin secretion (9, 10). The probably existence of intrarenal betareceptors was assumed (10, 22) since propanolol was shown to inhibite renin secretion (22). At the other hand angiotensin does stimulated the effects of norepinephrine and causes the release of catecholamines from the adrenal gland (1, 11, 13, 16). The results repported in this paper discard the catecholamines and sympathetic nervous system play a role on the inhibitory effect of angiotensin on renin release.

It suggest a direct action of angiotensin on myoepitheloid cells of the yuxtaglomerular apparatus probably through an inhibition of renin release since other results from our laboratory have shown that the inhibition of the release is associed with an increase of renal renin concentration, and an increase of the granularity yuxtaglomerular index (2, 15).

Resumen

La infusión intravenosa de angiotensina II en el gato (4,13 μg/45 min) produce una disminución de la concentración de renina plasmática, no siendo modificada, tras la denervación de ambos riñones, sección de los nervios carotídeos y aórticos ni tras la reserpinización previa del gato. Estas observaciones sugieren que ni el sistema simpático, ni las catecolaminas,

modifican de una manera significativa la actuación de la angiotensina II sobre la secreción de renina.

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