REVISTA ESPAÑOLA DE FISIOLOGIA, 35, 433-436. 1979

Effect of Sodium and Osmolarity on Renin Secretion *

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(Received on January 17, 1979)

F. ALBA, C. GARCIA DEL RIO, D. ACUÑA, A. SOLER, L. GARCIA-TORRES and T. QUESADA. *Effect of Sodium and Osmolarity on Renin Secretion.* Rev. esp. Fisiol., 35, 433-436. 1979.

The effect of changes in sodium and osmolarity on renin secretion has been studied in the isolated perfused rat kidney. Perfusion with low sodium buffer (110 mM/l) produced a significant increase in renin secretion compared with control experiments (Na^+:135 mM/l). Since the presence of tubules seems necessary for such an effect to take place, it suggests that the high renin secretion stimulated by a low sodium buffer centers in the Macula densa. Perfusion with high sodium buffer (170 mM/l; osmolarity 350 mOs/l) induces a stimulation on renin release. However, a greater rise in renin is achieved in control experiments if choline chloride increases the osmolarity from 300 to 350 mOs/l. All this suggests that high sodium buffer, independently of its osmotic effects, has an inhibitory role on renin release.

It is now well established that the renin release by juxtaglomerular apparatus may be affected by changes on sodium concentration on extracellular fluid (3, 5, 7-10, 12, 13, 16).

Studies *in vivo* have demonstrated an inverse relationship between sodium concentration and renin secretion (3, 7, 8, 12, 17) but the influence of sodium on extracellular volume and aldosterone secretion may be taken into consideration. *In vitro* results are contradictory: MICHELAKIS (10) using the kidney cortical slices showed the stimulant effect of low sodium on renin but these results were not confirmed by others (1, 13).

By retrograde injections of high sodium solution into the distal tubule, THURAU *et al.* (16) produced an increase on renin release, but other authors (4, 6, 18) suggested that sodium chloride had no direct ionic effect on renin outside its osmotic properties.

The isolated perfused rat kidney permitted the study of the cellular mechanism

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of renin release under conditions in which other factors could be controlled or excluded. By this method we have studied the influence on renin secretion of changes on sodium concentration with or without changes on medium osmolarity.

Materials and Methods

Kidney perfusion. The method of isolation and perfusion of kidney has been described (11). The perfusion fluid was a Hepes (SIGMA) buffered electrolyte dextran solution equilibrated with 100% oxygen. The perfusion fluid was delivered at a constant rate of 8 ml/min. Perfusion pressure was recorded. The first sample was collected after 5-7 min from the start. Samples were also collected 10, 20 and 30 min from first sample.

Renin assay. Perfusate samples were dialyzed successively to pH 4.5 (24 h) and pH 7.5 (24 h) at 4° C against phosphate buffers containing EDTA (Na_2) to remove angiotensinases (14). Samples were then incubated at 37° C for 3 h with nephrectomized rat plasma as substrate.

The enzymatic reaction was stopped by heating the samples to 85°-90° C for 10 minutes. The angiotensin I was measured by radioimmunoassay.

Types of infusion. The buffer solution in experimental groups was of the following composition (mM/l): Ca 3.7, K 5.5, Mg 1.2, glucose 10 and dextran 36 g/l (m.w. 70,000). The sodium concentration, choline chloride added and the osmolarity are summarized on table I.

Table I. *Sodium concentration, choline chloride added and osmolarity of different experimental group.*

Experimental group	Na+ (mM/l)	Choline chloride (g/l)	Osmolarity (mOs/l)
Control	135	—	300
High sodium	170	—	350
Low sodium	110	2.841	300
Control high osmolarity	135	3.977	350

Results

There were no changes on perfusion pressure or flow in any of the experimental groups. A very significant increase ($p < 0.001$) on renin secretion compared with control group (n = 17) was observed when perfusion fluid contains low sodium concentration (n = 11) (figure 1). When high sodium concentration (n = 13) was infused, a significant rise ($p < 0.01$) on renin was also obtained (figure 1).

The osmolarity of high sodium concentration buffer was 350 mOs/l. In an attempt to dissociate the effects of high sodium from high osmolarity on renin secretion, the osmolarity of control buffer was increased to 350 mOs/l by choline chloride. The release of renin in this group (n = 8) is significantly increased compared

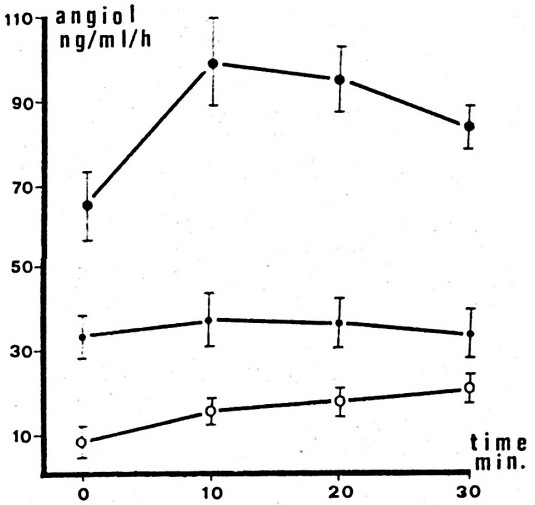

Fig. 1. *Effect of high and low sodium buffer on renin secretion.*
Control (Na^+: 135 mM/l) (O—O), high sodium (Na^+: 170 mM/l) (✻—✻) and low sodium (Na^+: 110 mM/l) (●—●).

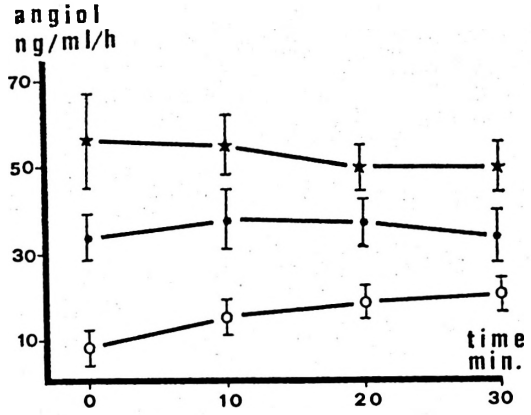

Fig. 2. *Effect of high osmolarity on renin secretion.*
Control (300 mOs/l) (O—O), high sodium (350 mOs/l) (✻—✻) and control plus choline chloride (350 mOs/l) (★—★).

to high sodium ($p < 0.05$) and control experiments ($p < 0.01$) (figure 2).

Discussion

From the present results it can be concluded that perfusion of kidney with an isosmolar low sodium (110 mM/l) buffer causes an increase on renin secretion (figure 1). The effect of low sodium on renin release could be produced by a direct stimulation of juxtaglomerular cells or by an activation of Macula densa on distal tubule.

MICHELAKIS (10) demonstrated on renal cortical slices of rat that very low sodium concentration (50 mM/l) increased renin release. However, there were no significant variations on renin when sodium concentration was changed from 144 to 100 mM/l. More recently AOI *et al.* (1) and SARUTA and MATSUKI (13) on rat kidney slices and BLENDSTRUP *et al.* (4) and FREDERIKSEN *et al.* (6) on isolated glomeruli were unable to stimulate the release of renin by low sodium concentration.

The lack of response of renin in these preparations could be due to the absence of tubular elements. Therefore, it is difficult to attribute the effect of low sodium on renin secretion (figure 1) to a direct stimulation of juxtaglomerular cells. In our preparation, in which extrarenal influences has been excluded and tubules are conserved, low sodium causes a significant rise on renin. This suggests that low sodium could stimulate renin by an activation of Macula densa.

The kidney perfusion with a buffer of high sodium concentration (170 mM/l) induces a stimulation of renin release although this effect was lower than that obtained by 110 mM/l of sodium (figure 1). THURAU (15) was the first to propose that an increase in sodium concentration at Macula densa activates renin release. Others (2, 5, 16) have also supported this idea. However, the osmolarity of high sodium buffer was 350 mOs/l and it has been shown that high osmolarity increases the release of renin (6, 18). In fact, if the osmolarity of the control buffer (300 mOs/l) is raised to 350 mOs/l by choline chloride, the increase in renin is greater than that obtained by high sodium buffer (figure 2). These results could be interpreted assuming that high sodium buffer in spite of its osmotic property has an inhibitory effect on renin release.

Resumen

Se estudia en riñón aislado y perfundido de rata el efecto de la concentración de sodio y de la osmolaridad del medio de perfusión sobre la secreción de renina.

La perfusión con un tampón de bajo contenido en sodio (110 mM/l) produce un aumento significativo en la secreción de renina en comparación con los experimentos controles (Na^+: 135 mM/l). Para obtener este efecto parece ser necesaria la presencia de túbulos, lo que sugiere que el bajo sodio estimula la secreción de renina actuando a nivel de Mácula densa. La perfusión con un tampón de alto contenido en sodio (170 mM/l) (osmolaridad: 350 mOs/l) induce una estimulación en la secreción de re-

nina. Sin embargo, se alcanza una mayor secreción de renina, en comparación al grupo de alto sodio, si en los experimentos controles la osmolaridad (300 mOs/l) se aumenta hasta 350 mOs/l con cloruro de colina. Estos datos sugieren que el medio de alto contenido en sodio tiene un efecto inhibidor en la secreción de renina que no depende de sus propiedades osmóticas.

References

1. AOI, W., WADE, M. B., ROSNER, D. R. and WEINBERGER, M. H.: *Am. J. Physiol.*, **227**, 630-634, 1974.
2. BIRBARI, A.: *Pfluegers Arch.*, **377**, 29-37, 1972.
3. BLAIR-WEST, J. R., BROOK, A. H. and SIMPSON, P.: *J. Physiol.*, **267**, 321-338, 1977.
4. BLENDSTRUP, K., LEYSSAC, P. P., PULSEN, K. and SKINNER, S. L.: *J. Physiol.*, **246**, 653-672, 1975.
5. COOKE, C. R., BROWN, T. C., ZACHERLE, B. J. and WALKER, G. W.: *J. Clin. Invest.*, **49**, 1630-1638, 1970.
6. FREDERIKSEN, O., LEYSSAC, P. P. and SKINNER, S. L.: *J. Physiol.*, **252**, 669-679, 1975.
7. FREEMAN, R. H., DAVIES, J. O., GOTSHALL, R. W., JOHNSON, J. A. and SPIELMAN, W. S.: *Cir. Res.*, **35**, 307-315, 1974.
8. GOTSHALL, R. W., DAVIS, J. O., SHADE, R. E., SPIELMAN, W., JOHNSON, J. A. and BRAVERMAN, B.: *Am. J. Physiol.*, **225**, 344-349, 1973.
9. HUMPHREYS, M. H., REID, I. A., UFFERMAN, R. C., LPEBERMAN, R. A. and EARLEY, L. E.: *Proc. Soc. Exp. Biol. Med.*, **150**, 728-734, 1975.
10. MICHELAKIS, A. M.: *Proc. Soc. Exp. Biol. Med.*, **137**, 833-836, 1971.
11. PEART, W. S., QUESADA, T. and TENYI, I.: *Br. J. Pharmac.*, **59**, 247-252, 1977.
12. PEYTREMANN, A., VEYRAT, A. and MULLER, A. F.: *Acta Endocrinol.*, **67**, 159-183, 1970.
13. SARUTA, K. and MATSUKI, S.: *Endocrinol. Japon.*, **22**, 137-140, 1975.
14. SKINNER, S. L.: *Cir. Res.*, **20**, 391-402, 1967.
15. THURAU, K.: *Am. J. Med.*, **36**, 698-719, 1964.
16. THURAU, K., BAHLEIM, H., GRUNER, A., MASON, J. and GRANGER, P.: *Cir. Res.*, **30** (suppl. 2), 182-186, 1972.
17. TUCK, M. L., DLUHY, R. G. and WILLIAMS, G. H.: *J. Clin. Invest.*, **53**, 988-995, 1974.
18. YOUNG, D. B. and ROSTORFER, H. H.: *Am. J. Physiol.*, **225**, 1009-1014, 1973.