

CARTA AL EDITOR

Papaverine Influence in Postischemic Acute Renal Failure

When an almost complete renal ischemia is induced by temporary occlusion of renal artery for a prolonged period of time, upon allowing the renal blood flow to be restored, it is observed that the whole kidney glomerular filtration rate (GFR) and single nephron glomerular filtration rate (SN GFR) are decreased approximately 40 %. The proximal reabsorption of water and sodium is also reduced (1, 3, 4). This reduction of GFR and SN GFR is not due to a transtubular loss of inulin since the SN GFR obtained from micropunctures made in more proximal zones of the proximal tubule (PT) do not differ significantly from the SN GFR obtained from micropunctures in its most distal accessible zones. This indicates that the inulin has not left the tubules during its transit (4). Furthermore when C^{14} -Inulin was injected into the PT of a kidney which had been subjected to a temporary ischemia, all the radioactivity appeared in the urine of this kidney. This seems to confirm that there had not been transtubular leak of this substance (4).

A decrease of the renal blood flow due to changes in the tone of glomerular arterioles has been claimed to be the cause of the reduction of glomerular filtration (5). In order to try to verify this hypothesis, an attempt to study the effect

of an infusion of papaverine after a temporary renal ischemia was made.

Female rat weighing approximately 250 g, nephrectomized at least 20 days before the experiment, were prepared according to the techniques already described (3, 4). After 60 min recuperation and a 60 min control period for taking samples, in a group of 8 rats, a ligation of the renal artery was made. This ligation was released immediately and a $12 \mu\text{g/kg/h}$ papaverine infusion was started. After 30 minutes of infusion, new samples were taken during 60 min, maintaining the infusion of papaverine (Group A). In a second group of 9 rats (Group B) a renal ischemia by ligation of renal artery was induced after a control period (3, 4). After 90 min, the arterial obstruction was removed, and after 30 min of recuperation, a 1 hour study period was carried. A third group of 6 animals (Group C) handled in the same way that group B, received after releasing arterial ligation, an infusion of papaverine, $12 \mu\text{g/kg/h}$. After 30 min, samples was taken for 1 hour, maintaining the papaverine infusion.

0.1 ml of blood was taken before and after each period and urine was collected during the entire period, to determine in both inuline (2). Arterial pressure and diuresis were monitored.

Table I. Influence of a Papaverine Infusion on Normal Kidney and After a Temporary Ischemia.

In parenthesis number of rats. Results are shown as mean \pm S.E.M. Abbreviations: C_{In} = Inuline clearance; U/P_{In} = Urine inulin/plasma inulin ratio; AP = Arterial pressure.

Group	Period	Diuresis μ l/min/kg	C_{In} ml/min/kg	U/P_{In}	AP mm Hg
A (8)	Control	31.2 ± 3.3	6.37 ± 0.53	175 ± 27	82 ± 9
	Papaverine	37.8 ± 3.8	6.17 ± 0.81	159 ± 13	77 ± 9
	p	> 0.1	> 0.4	> 0.3	> 0.1
B (9)	Control	30.9 ± 2.0	6.49 ± 0.24	210 ± 11	98 ± 2
	Ischemia	34.7 ± 4.7	3.34 ± 0.51	96 ± 3	97 ± 2
	p	> 0.15	< 0.0005	< 0.0005	> 0.35
C (6)	Control	31.9 ± 3.0	6.33 ± 0.40	209 ± 10	96 ± 5
	Ischemia + papaverine	31.4 ± 3.9	3.02 ± 0.42	96 ± 7	84 ± 4
	p	> 0.2	< 0.0005	< 0.0005	< 0.05

From this data GFR (inulin clearance) and urinary inulin/plasmatic inulin ratio (U/P_{In}) as an index of renal reabsorption of water, were calculated. The results were analyzed through the Student «t» test for paired and unpaired information, using an Olivetti 101 Programma electronic calculator.

The results obtained in the three groups of animals are shown in table I. Papaverine, administered at the maximum rate that had no influence on the arterial pressure (López Novoa, J. M., unpublished observations), induced in the normal kidney a significant increase of the diuresis without influencing the GFR. When papaverine was infused after renal ischemia, no significant variations were observed.

The results of this experience do not support the hypothesis of arteriolar vasoconstriction as the cause of the decrease of GFR and point to the fact that other mechanisms might be involved. However the effect of higher doses of papaverine or its administration prior to ligation should be explored.

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