Chapter V

Discussion

Effect of unilateral ureteral obstruction:

After unilateral ureteral obstruction, there were no alteration in mean arterial pressure, heart rate and packed cell volume. These results are similar to the earlier work (Vaughan et al, 1971). In the present experiment, the unilateral ureteral obstruction caused a marked increase in urine flow rate of the contralateral control kidney. Renal blood flow increased while renal vascular resistance decreased after unilateral ureteral obstruction. This evidence clearly indicates vasodilation in the contralateral kidney. These results are supported by the findings of other investigators (Murphy, 1966; Lonigro, 1973; Arendshorst, 1974). Several lines of evidence indicate that an increase in the renal pelvic pressure above an obstructed ureteral stone might stimulate the synthesis of prostaglandin E_2 in the renal medulla (Gilmore, 1964; Abe, 1973; Schramm, 1975). Thus, the accumulation of a prostaglandin productions would affect the contralateral kidney.

A diminishion of renal vascular smooth muscle tone during the elevation of ureteral pressure (Gilmore, 1964; Vaughan, 1971; Yarger, 1974; Allen, 1978) are probably responsible for initiating the observed changes in renal functions. It was indicated in the previous report that when free-flow of urine was inhibited at any point in the urinary tract, the pressure proximal to the obstructive site would increase approaching glomerular effective filtration pressure. The urinary collecting system had some capacity to protect nephron function

from pressure rise. The protection, however, was limited in some degrees (Canton et al, 1977). It has been reported that renal blood flow increased during elevated pelvic pressure in order to maintain an effective filtration pressure and GFR (Kiil et al, 1967; Abe et al, 1970; Suki et al, 1971). In the present study, there was a slightly increase sodium and chloride excretions of the contralateral kidney after unilateral ureteral obstruction. These results are further supported by the previous findings. It showed a decrease in the tubular sodium reabsorption. (Fulop and Brazeau, 1970; Suki et al, 1971).

Effect of indomethacin after hypertonic saline administration:

After hypertonic saline injection in animals in group I, renal fraction increased by approximately 62% while renal blood flow and cardiac output decreased. Therefore, the reduction of renal blood flow might not relate to the fall of cardiac output. The compensatory alterations should occur to restore normal blood pressure, since total peripheral resistance increased 28% from the control level. In the present study, hypertonic saline injection caused an elevation of urinary excretion of Na from 2.9 ± 2.1 to 5.2 ± 3.1 μEq/min/kg.bw.($P<0.05$). This report focuses on the role of the kidney in response to hypertonic saline injection. It has been reported that extracellular volume expansion lead to a decline in sodium and water reabsorption in the proximal tubules (Earley and Daugharty, 1969; Schrier and de Wardener, 1971). However, volume expansion in the present study might not expect

since plasma volume and packed cell volume remained unchanged during all recorded periods.

An increase in C_{Osm} of contralateral kidney indicated hypertonic saline injection generated local osmotic diuresis. Changes in the rate of urine flow, urinary excretion of sodium, chloride and C_{Osm} after the injection of hypertonic saline can be assumed to be a direct response to a change in sodium chloride concentration in the renal artery. These results are consistent with the result of early study (Chaiyabutr and Malila,1977). With a hypertonic saline solution, the increase in filtered load and the retention of solutes within the tubular lumen have been suggested to depress proximal tubular reabsorption (Giebisch et al, 1964). This might cause a decrease in plasma volume in the latter.

In the present study, intravenous injection of indomethacin after given hypertonic saline solution caused a marked reduction of pelvic pressure (42%). An intrarenal mechanism seem to be responsible for this reduction, since indomethacin did not effect any significant change in the course of systemic circulation. The modulatory role of renal prostaglandins on renal hemodynamics was generally recognized (Oliw et al, 1978). prostaglandins usually modulates renal vascular resistance by exerting a vasodilatory effect. In the present study, not only ureteral obstruction but hypertonic saline infusion also enhance prostaglandin production. It has been reported that the renal prostaglandin increase renal production of renin and intrarenal angiotensin formation (Abe et al, 1977). The previous results were able

to show that under the action of indomethacin (prostaglandin synthesis inhibitor), an increase in renal vascular resistance indicates local renal vasoconstriction. Renin-Angiotensin system can modulate the vasoconstricting effects. This effect can contribute to decrease in renal blood flow, urine flow rate and electrolyte excretion of contralateral kidney. The rate of urine flow and urinary excretion of electrolytes of experimental kidney would be reduced during the administration of indomethacin and it shows parallel changes in the contralateral kidney. However, Kirschenbaum and Stein (1976) reported that Na^+-transport in the collecting duct was diminished, when the local prostaglandin release was inhibited by prostaglandin synthesis inhibitor. These results will cause the declinę of pelvic pressure when indomethacin is administrated after hypertonic saline.

Effect of indomethacin after hypotonic solution administration :

Injection of 2.5% dextrose in water as hypotonic solution did not affect mean arterial pressure, heart rate and packed cell volume. Cardiac output, plasma volume and blood volume increased slightly while renal blood flow did not change. Therefore, these results led to an unalteration of renal fraction. After the injection of dextrose solution, the rate of urine flow increased approximately 50% associated with an increase in C_{Osm}. This osmotic diuresis after administration of dextrose solution is similar to the results reported by Canton et al (1977).

Indomethacin intravenous injection caused pelvic pressure decreased by approximately 22%. This reduction might infer only to the

process by which prostaglandin action was inhibited by indomethacin. It has been shown that increased delivery of sodium chloride to distal tubule induced the macula densa feedback mechanism in induce renin release and intrarenal angiotensin formation(Stein and Reineck, 1974). In the present study in comparison to hypertonic saline group, an increase in renin-angiotensin system activity during given indomethacin would not occur since plasma sodium concentration did not significantly change. The filtered load of sodium at macula densa may not expect to enhance renin-angiotensin system activity. Inhibition of prostaglandin synthesis abolishes the action of vasodilatation. Renal blood vessel may constrict and cause renal blood flow and urine flow of the contralateral kidney fall . then the slight decline of pelvic pressure is appeared.

Effect of indomethacin after furosemide administration :

The present experiment showed that acute dehydration developed after furosemide administration. An increase in packed cell volume was observed. The decrease in blood volume and cardiac output were accompanied by a marked increment of urine flow rate of the contralateral kidney. Thus, the reduction of cardiac output inferred to a decrease in stroke volume and venous return, since heart rate was not altered after furosemide administration. However, renal hemodynamics (GFR, RBF) were not affected by this decrease in cardiac output. It has been reported by many investigators that natriuresis and diuresis following administration of furosemide,were at least in

part mediated by prostaglandins (Attallah, 1979; Burg, 1976; Dunn and Hood, 1977; Hook and Bailie, 1977). This was supported by the observation that furosemide administration leads to an increase in renal venous prostaglandin E (Williamson et al, 1975).

Administration of indomethacin in the present study suspected to suppress the action of intrarenal prostaglandin completely. However, indomethacin had no effect on furosemide induced renal functional changes. In the present study, glomerular filtration rate and renal blood flow do not change after indomethacin administration. Therefore, the intravenous injection of indomethacin causes a slight decline of pelvic pressure (17%).

Effect of indomethacin after ADH administration:

In the present study, one unit of ADH was intramuscular injected and produced the state of hydration in the animals as the results in Table 4. It showed a marked increase in cardiac output from the increment of venous return and stroke volume are shown after ADH. There was no significant change in renal hemodynamics after ADH. Indomethacin intravenous injected after ADH decreased pelvic pressure by approximately 8%. It was reported in the earlier that the state of hydration may influence the action of indomethacin. In the experiments on pigs and rats (Sjodin and Holmlund, 1982), indomethacin given after the obstruction showed similarly reduction in the pelvic pressure, but only if the fluid intake was moderate or low. High fluid intake abolished the effect of indomethacin. Kendler et al (1978) indicated that pain

was associated with elevated ADH levels.

It has been shown that indomethacin enhanced the effects of ADH in vivo (Anderson et al, 1975; Fejes-Toth et al, 1977). However, the possibility remains since prostaglandins might release ADH by a central mechanism (Vilhardt and Hedqvist, 1970). It may be mentioned that after indomethacin, 1) hydration status is greater and it cannot suppress glomerular filtration and sodium concentration at macula densa. 2) There is no stimulation of renin-angiotensin activity since renin secretion might be inhibited by ADH. (Anderson et al, 1975). This mechanism may serve as a feedback loop to adjust GFR. The decrease in renin release and without angiotensin II presented in urine would not lead to change in GFR. The few reduction of pelvic pressure was also found in this experiment.

Conclusion:

These results interpret to conclude that unilateral ureteral obstruction may enhance prostaglandin activity, it causes the elevation of pelvic pressure and changes in the contralateral renal functions. During treatment with different solutions after ureteral obstruction, the balance of intrarenal vasodilator hormones (e.g.prostaglandin) and vasoconstrictor hormone may be involved. Plasma hyperosmolality status may enhance prostaglandin activity. When the inhibition of prostaglandin by indomethacin was used, a marked decrease in pelvic pressure was found. The other conditions, as plasma hypoosmolality, acute dehydration from furosemide and hydration status from ADH might

not stimulate prostaglandin and renin-angiotensin activities, the great decrease in pelvic pressure was not found.

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