SUMMARY

1. Papillary osmolality and sodium and potassium concentrations were determined in rats during a control period and during escape from the sodium-retaining effect of deoxycorticosterone acetate and compared with the changes observed after acute frusemide injection.

2. During escape, papillary osmolality ($554 \pm 36$ vs $754 \pm 42$ mmol/kg of papillary water (H$_2$O), $P < 0.005$) and papillary sodium concentration ($131 \pm 7$ vs $182 \pm 8$ mmol/kg H$_2$O, $P < 0.001$) were significantly decreased as compared with the control values, while papillary potassium concentration remained unchanged.

3. Frusemide decreased papillary osmolality to $538 \pm 41$ mmol/kg H$_2$O ($P < 0.005$), papillary sodium concentration to $125 \pm 9$ mmol/kg H$_2$O ($P < 0.001$) and papillary potassium concentration from $80 \pm 2$ to $69 \pm 3$ mmol/kg H$_2$O ($P < 0.05$).

4. The present results suggest that medullary portions of the distal tubule (probably the ascending loop of Henle) may represent one site of tubular sodium chloride rejection during escape from the sodium-retaining effect of deoxycorticosterone acetate.

Key words: ascending loop of Henle, deoxycorticosterone acetate escape, frusemide, papillary osmolality, papillary sodium concentration.

INTRODUCTION

Although it is well established that administration of sodium-retaining steroids, such as deoxycorticosterone acetate (DOCA), produce only transient sodium retention, the precise nature of the renal functional changes which result in escape from the sodium-retaining effect of such steroids is still unclear. Since this escape occurs in the absence of an increased glomerular filtration rate (Davis, Holman, Carpenter, Urquhart & Higgins, 1964), it may result from decreased tubular sodium absorption. Experimental evidence suggests that the nephron site of inhibited sodium absorption during escape may be different from that of deoxycorticosterone acetate (DOCA)-stimulated sodium absorption (O'Neil & Helman, 1977; Schwartz & Burg, 1978), but its exact tubular localization still remains speculative. To date, the proximal tubule, at least from superficial nephrons, can be excluded from participating in the renal adaptation to chronic DOCA administration (Sonnenberg, 1973). By using the microcatheterization technique in the rat it has been suggested that the renal response to prolonged DOCA administration may be explained by enhanced delivery of sodium from juxtamedullary nephrons into the medullary collecting duct (Sonnenberg, 1976). Similar conclusions were drawn from Ringer infusion experiments in the rat (Stein, Osgood & Kunau, 1976). In contrast, other studies have demonstrated an increase in fractional delivery of sodium to the late superficial distal tubule during DOCA administration (Haas, Berndt & Knox, 1979). These studies would therefore suggest that...
sodium and/or chloride absorption is inhibited in the loop of Henle during escape. However, other investigators were unable to detect changes in sodium chloride absorption in the loop of Henle during chronic DOCA administration (Sonnenberg, 1973; Schnermann, Hermle, Schmidmeier & Dahlheim, 1975).

Since changes in ascending loop function induce marked changes in solute concentrations within the inner medulla, in the present study the effects of chronic DOCA administration on papillary osmolality and electrolyte concentrations were investigated in the rat. Furthermore the changes observed during DOCA escape were compared with those after acute injection of frusemide, a potent inhibitor of chloride absorption in the ascending loop of Henle.

**Material and methods**

Twenty-one female Sprague–Dawley rats weighing 230–270 g were equilibrated on a diet containing 0·8 mmol of sodium and 1·8 mmol of potassium/day. Group 1 consisted of six rats which served as controls. Group 2 also consisted of six animals which received DOCA at a daily dose of 3 mg/kg body weight intramuscularly for 7 days. A third group of nine rats was given a single dose of frusemide, 2 mg/kg body weight intraperitoneally. In the control animals and during the DOCA protocol, 24 h urines were collected daily for determination of urinary volume, sodium, potassium and creatinine excretion. Blood for measurements of serum sodium, potassium and creatinine concentrations was taken from control animals and on day 7 of DOCA injection. Papillary osmolality and sodium and potassium concentrations were determined by methods previously described (Ganguli, Tobian, Azar & O'Donnell, 1977). In brief, kidneys of control rats, of animals injected with DOCA for 7 days and of group 3 animals 120 min after frusemide injection were removed and the papillae quickly excised. After wet-weight determination, papillary tissue was dried at 60°C for 48 h to determine the water content. The papillary tissue was then extracted with water to determine osmolality and sodium and potassium concentrations. Papillary and urinary osmolalities were determined by using a Knauer osmometer and serum and urine concentrations of sodium and potassium were measured by flame photometry. Serum and urine creatinine concentrations were determined enzymatically (Wahlefeld, Holz & Bergmeyer, 1974). Glomerular filtration rate was estimated as clearance of endogenous creatinine. Papillary osmolalities and electrolyte concentrations were expressed as mmol/kg of papillary water (H₂O).

**Results**

In the control animals (group 1) papillary osmolality averaged 754 ± 42 mmol/kg H₂O and papillary sodium and potassium concentrations measured 182 ± 8 and 80 ± 2 mmol/kg H₂O respectively. The renal response to chronic DOCA injection in six rats (group 2) is illustrated in Fig. 1. Marked sodium retention was present during day 1 of DOCA only, whereas urinary sodium excretion subsequently equaled control values during the entire study period. Urinary osmolality averaged 993 ± 131 mmol/kg before DOCA injection and was unchanged in animals during ‘escape’ on day 6 of DOCA (902 ± 123 mmol/kg). On day 7 of DOCA injection papillary osmolality had significantly decreased by 27% to 554 ± 36 mmol/kg H₂O (P < 0·005) and papillary sodium concentration by 28% to 131 ± 7 mmol/kg H₂O (P < 0·001), while papillary potassium concentration remained unchanged (81 ± 1 mmol/kg H₂O). These changes occurred in the absence of...
significant changes in glomerular filtration rate which was 0.61 ± 0.04 before and 0.65 ± 0.05 ml/100 g body weight on day 6 of DOCA injection. Similarly, frusemide (group 3) decreased papillary osmolality by 29% to 538 ± 41 mmol/kg H₂O (P < 0.005) and papillary sodium concentration by 31% to 125 ± 9 mmol/kg H₂O (P < 0.001). In addition, papillary potassium concentration fell to 69 ± 3 mmol/kg H₂O (P < 0.05).

**Discussion**

In the present study papillary osmolality and papillary sodium concentration were significantly decreased in rats during escape from the sodium-retaining effect of DOCA. This effect could theoretically be due to decreased delivery of sodium chloride out of the proximal tubule with a consequent decrease in ascending loop chloride absorption, a direct inhibition of ascending loop reabsorptive capacity, inhibition of sodium absorption along the medullary collecting duct or increased medullary blood flow with enhanced washout of papillary toxicity. To date a role of the proximal tubule in DOCA escape, including juxtamedullary nephrons, seems rather unlikely (Knox, 1973; Rastegar, Agus, Connor & Goldberg, 1972). Furthermore, more recent studies have demonstrated additional sodium absorption along the medullary collecting duct during DOCA escape, while during control studies net addition of sodium to the tubular fluid was observed (Haas et al., 1979). Although an increase in medullary blood flow during DOCA injection cannot be excluded, it seems questionable if a small increase in papillary perfusion would result in such a striking decrease in papillary sodium concentration as observed in the present study. Haemodynamically induced decreases in papillary osmolality and sodium concentration would decrease the osmotic gradient of solutes along the ascending loop of Henle and should therefore in part be compensated by increased sodium chloride absorption at this site of the nephron.

Therefore, the results of the present study favour medullary portions of the distal tubule (probably the ascending loop of Henle) as one site of tubular sodium chloride rejection during DOCA escape. This could either be due to decreased chloride absorption or an increased backleak of solutes in this part of the nephron. This hypothesis is also supported by the present results obtained in animals injected with frusemide, a potent inhibitor of ascending loop chloride absorption (Suki, Rector & Seldin, 1965). Frusemide significantly decreased papillary potassium concentration whereas 6 days of DOCA injection under the experimental conditions chosen in the present study had no effect on inner medullary potassium concentration. From the results of the present study, this different effect of the two experimental conditions on papillary potassium concentration remains unexplained. However, the observed decrease in papillary osmolality and sodium concentration after frusemide was almost identical with the changes observed during chronic DOCA injection. These results may therefore suggest similar changes in ascending loop function under both experimental conditions.

**References**


