THE EFFECT OF ALDOSTERONE AND DEXAMETHASONE ON THE DILUTING CAPACITY OF THICK ASCENDING LIMBS IN EXPERIMENTAL ADRENAL INSUFFICIENCY

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Micropuncture experiments have been performed on functionally isolated loops of Henle of adrenalectomised rats in order to analyse the action of corticosteroids on the function of the thick ascending limb ion transport system. Since the direct evaluation of transport parameters of the diluting segment in vivo is difficult due to the subsurface localisation, the following pulse-stopped microperfusion technique has been used to determine the time course and the endpoint of electrolyte dilution: mid-proximal surface tubules were blocked with solid paraffin and the loop of Henle was perfused with a test solution consisting of 110 mM NaCl and 80 mM mannitol.

After passing the loop the fluid was drained out of the corresponding early distal tubule into a continuously recording conductivity micro probe, which allowed the determination of total electrolyte content of tubular fluid.

The test solution was run into the loop segments at a perfusion rate of 90 nl/min. Then the perfusion was stopped to allow equilibration within the loop according to the local ion transport capacity. After defined time intervals between 5 and 60 seconds, the fluid was forced out of the loop again into the conductivity probe by re-establishing the initial high perfusion rate. Conductivity transients were measured as the consequence of different ion contents of tubular fluid along the loop. The first fraction of fluid which reached the probe derived from the ascending limb — the diluting segment — and was characterised by a significantly lowered ion activity, i.e., NaCl concentration compared with the test solution.

The dilution process, as a function of time was terminated after 60 seconds, thereafter no further dilution was measured.

With the method described the time course and the endpoint of dilution was used to assess the diluting capacity of the thick ascending limb in vivo.

Experiments were performed between the first and the second week after bilateral adrenalectomy. Adrenalectomised rats were kept on Altromin rat pellets and on isotonic saline solution as drinking fluid to compensate for extracellular fluid loss. The diluting capacity was studied in untouched control rats (ctrl) and in the four following groups of adrenalectomised rats:
1) unsubstituted; 2) acutely aldosterone substituted (Aldocorten 10 µg/100 g body weight, iv, 3 hours before the micropuncture experiments); 3) acute dexamethasone substitution (Dexa Scheroson 50 µg/100 g bw, iv, 3 hours before the micropuncture experiments); 4) chronic dexamethasone substitution (Fortecortin 50 µg/100 g bw, im, 3 days before micropuncture experiments).

The results are shown in Figure 1. On the ordinate the conductivity values are given as corresponding NaCl concentrations. The abscissa indicates the time interval of perfusion stop in seconds. The diluting capacity was lowest in group 1, the 60 sec equilibration concentration was 54.5 ± 6.5 mM NaCl (mean ± SEM, n=12), the latter value was significantly higher than in controls, 28.5 ± 3.5 mM NaCl (n=13), p < 0.001. Acute aldosterone substitution, group 2, had no significant effect on the decreased diluting capacity of adrenalectomised rats. Dexamethasone substituted before the experiments led to a significant amelioration of the impaired diluting capacity. Complete normalisation was achieved.
when adrenalectomised rats were treated chronically with dexamethasone (group 4): equilibrium concentration decreased to $26.6 \pm 3.5$ mM NaCl ($n=14$), a value significantly different from unsubstituted adx rats ($p < 0.001$). No significant difference existed between results of group 4 and controls.

Since acute and chronic dexamethasone substitution led to an amelioration or a normalisation, respectively, of the diluting capacity, we conclude that the electrolyte reabsorption of the thick ascending limb of Henle's loop depends on the action of glucocorticoid hormones. It has been demonstrated recently that electrolyte dilution occurs from the operation of an active chloride transport mechanism within the thick ascending limb\textsuperscript{1,2}, thus our results further indicate a steroid dependence of the chloride pump.

References

1 Burg, M and Green, N (1973) *Amer. J. Physiol.*, 224, 659