Arterial smooth muscle effects of aldosterone: action on ionic fluxes

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Summary
1. Aldosterone given acutely to male Wistar rats stimulated ouabain-sensitive and ouabain-insensitive 22Na efflux from tail arteries.
2. These effects of aldosterone seem to depend on the activation of specific mineralocorticoid receptors, as they are blocked by antimineralocorticoid drugs.
3. The results suggest that aldosterone may have a physiological role in the control of vascular tone.

Key words: aldosterone, artery, mineralocorticoid, vascular tone.

Introduction
There is an increase of Na+ and K+ fluxes from arteries in DOCA and salt hypertension [1, 2]. During the early, mineralocorticoid-dependent, phase of DOCA and salt hypertension in rats there is an increase in ‘passive’ (ouabain-insensitive) 22Na efflux and 86Rb efflux from the rat tail artery smooth muscle [3]. In order to examine whether these changes are due to a primary action of mineralocorticoids, or secondary to salt overload, we have studied the acute effects of aldosterone and aldosterone antagonists on 22Na efflux from rat tail artery.

Methods
The experiments were performed on 200 g male Wistar rats which had been adrenalectomized by the supplier and were maintained on 0.9% NaCl in water until they were studied, which was not more than 7 days after adrenalectomy. Rats were purchased from Iffa Credo, France.

The methods used for the study of 22Na effluxes from the rat tail artery have been published [4]. The evaluation of 86Rb efflux was performed with an experimental protocol adapted from Mauger et al. [5]. The rat tail arteries were excised from rats which had been injected with aldosterone, alone or 2 h after injection of antimineralocorticoid drugs.

Results
Effects of adrenalectomy on ionic fluxes
Corticoids have a tonic physiological effect on transmembrane sodium fluxes as the total 22Na efflux from the rat tail artery is greatly reduced in adrenalectomized rats (control: 0.137 ± 0.002 min⁻¹, n = 8; adrenalectomized: 0.103 ± 0.005 min⁻¹, n = 9, P < 0.001). All the experiments were performed on adrenalectomized rats.

The ouabain-sensitive and -insensitive fractions of Na flux were evaluated by comparing 22Na effluxes in the presence and in the absence of ouabain (3 mmol/l). At this concentration the sodium pump is completely inhibited [4]. The reduction of Na efflux in adrenalectomized rats is due entirely to a lower activity of the sodium pump (ouabain-sensitive 22Na efflux in controls: 0.053 ± 0.004 min⁻¹, n = 8; adrenalectomized: 0.031 ± 0.003 min⁻¹, n = 9, P < 0.01); the ouabain-insensitive fraction was the same in control and adrenalectomized rats. Similarly, 86Rb efflux was not different in control (0.0112 ± 0.001 min⁻¹, n = 12) and adrenalectomized rats (0.0107 ± 0.0003 min⁻¹, n = 10).

Acute effects of aldosterone on 22Na efflux
Rats were killed at different times after the subcutaneous injection of 10 µg of aldosterone/kg. As shown in Fig. 1 the mineralocorticoid induces a bimodal increase in total 22Na efflux. There was an increase in ouabain-insensitive 22Na efflux, which was bimodal, with an early plateau between 15 and 60 min and a second plateau at 4 h. The ouabain-sensitive 22Na efflux was increased by 1 to 2 h after the aldosterone injection with a plateau by 3 h, when the efflux had doubled. Dose–response curves to aldosterone were constructed by studying the effect
of a range of doses of the mineralocorticoid. The animals were killed 2 h after the injection. Aldosterone induces a dose-dependent increase in total $^{22}\text{Na}$ efflux, the $ED_{50}$ being 2 $\mu$g/kg. The ouabain-sensitive and -insensitive fractions were equally increased.

**Acute effects of antimineralocorticoids on $^{22}\text{Na}$ efflux**

To study the action of antimineralocorticoid drugs, they were injected subcutaneously 1 h before the subcutaneous injection of aldosterone. The animals were killed 2 h later. Under these conditions, RU 28318 [17$\beta$-hydroxy-3-oxo-7$\alpha$-propyl(17$\alpha$)pregn-4-ene 21 potassium carboxylate] and spironolactone show a dose-dependent inhibition of the effect of aldosterone on both ouabain-sensitive and -insensitive fractions of $^{22}\text{Na}$ efflux from the rat tail artery.

**Action of aldosterone on $^{86}\text{Rb}$ efflux**

The subcutaneous injection of the mineralocorticoid induces an increase in $^{86}\text{Rb}$ after a delay of at least 3 h, a plateau being attained between 4 and 5 h after administration. This effect of aldosterone (studied at 4 h) was dose-dependent, with an $ED_{50}$ at 3 $\mu$g/kg.

**Discussion**

The present results indicate that the acute administration of aldosterone to adrenalectomized rats increases passive (ouabain-insensitive) and sodium pump-dependent (ouabain-sensitive) $^{22}\text{Na}$ efflux from the rat tail artery. These actions occur at doses and time lapses which are similar to those needed to obtain an effect on urinary sodium and potassium excretion in rats [6]. The actions of aldosterone on $^{22}\text{Na}$ efflux are complex. After a clear-cut increase in passive sodium efflux, occurring as early as 15 min after the injection, there appears to be a second, delayed stimulation of the sodium pump, accompanied by a further increase in ouabain-insensitive $^{22}\text{Na}$ efflux. These late effects of aldosterone are similar to those which have already described in other invertebrate and vertebrate systems [7], and may be due to the appearance of an intracellular aldosterone-induced protein [8], after activation of cytosolic and nuclear receptors. The early acute action of aldosterone on ouabain-insensitive $^{22}\text{Na}$ efflux is too fast to be mediated by a protein-synthesis step. Both acute and late effects of aldosterone on Na efflux appear to be mediated by specific mineralocorticoid receptors as they are inhibited by antimineralocorticoid drugs.

It is concluded that aldosterone may have a physiological role in the control of vascular tone.

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**References**


