Aldosterone: a hormone with adverse autonomic effects?

Homoeostatic control of the cardiovascular system represents the net result of complex interactions between reflex mechanisms (arterial baroreceptors, cardiopulmonary receptors and arterial chemoreceptors) and different neurohumoral systems (renin–angiotensin–aldosterone, vasopressin, nitric oxide, catecholamines and atrial natriuretic peptides) also involved in blood pressure and blood volume circulatory control. Over the years a large amount of experimental and clinical data have been acquired on these interactions, and particular interest has been devoted to the effects of angiotensin II, and the renin–angiotensin–aldosterone axis in general, on vagal control of sinus node activity and on adrenergic modulation of peripheral vascular resistance exerted by the above mentioned reflexogenic areas [1,2].

The paper by Yee and Struthers published in this issue of Clinical Science [3] provides new and interesting information on the interactions between the renin–angiotensin–aldosterone system and the arterial baroreflex modulation of heart rate. The main result of the study is represented by the finding that acute aldosterone administration elicits, in healthy normotensive subjects, a clear-cut impairment in baroreceptor heart rate control, by markedly reducing the bradycardic responses to arterial baroreceptor stimulation elicited by intravenous phenylephrine infusion. Two other results of the study deserve to be mentioned. The first refers to the evidence that the impairment was limited to the effects of arterial baroreceptor stimulation, no alteration in the tachycardic response to nitroprusside infusion being detectable in the subjects examined. The second is that arterial baroreceptor dysfunction was observed at plasma concentrations of the hormone (400–500 pg/ml) that can be found in various pathological states, such as congestive heart failure, primary hyperaldosteronism or secondary hypertension due to renal artery stenosis. This observation certainly strengthens the pathophysiological relevance of the study’s findings.

The intriguing results of the study by Yee and Struthers [3] raise several questions worthy of further investigation. First, does the aldosterone-induced impairment of baroreceptor heart control also apply to the modulation of sympathetic vasconstrictor tone exerted by the same reflexogenic area? I am not aware of any published study addressing this issue in man. It should be borne in mind, however, that a pathological condition or a given intervention may not necessarily elicit similar effects on baroreflex modulation of vagal and sympathetic cardiovascular drive. This is exemplified by the evidence [4,5] that in essential hypertension, arterial baroreceptor control of the heart rate is markedly deranged, but there is no impairment of baroreflex control of efferent postganglionic muscle sympathetic nerve traffic (directly quantified via the microneurographic technique in the peroneal nerve). Additionally data show that acute cigarette smoking can affect the autonomic nervous system by causing a tachycardic response, a profound inhibition of muscle sympathetic nerve traffic and a concomitant stimulation of the adrenal medulla enhancing catecholamine secretion [6]. Second, what are the explanations for the finding that only the heart rate response to arterial baroreceptor stimulation and not deactivation was found to be adversely affected by aldosterone? This question remains unanswered at present. It should be noted, however, that a similar finding has been reported by Guo and Abboud [7] in experimental animals after angiotensin II administration. In this case the authors hypothesized that this was due to a complex influence of angiotensin II on the central integration of the arterial baroreceptor signal, having opposite effects on the heart rate responses to arterial baroreceptor loading and unloading [7]. This may be the case for aldosterone as well.

Third, do the effects of acute aldosterone administration also apply to conditions characterized by chronic elevation of this hormone? Two direct and one indirect piece of evidence suggest that this might not be the case. (1) A 7-day administration of the mineral corticoid fluorocortisone has been shown to produce in man a suppression of muscle sympathetic nerve traffic without altering baroreceptor control of both heart rate and adrenergic cardiovascular drive [8]. (2) Hypertensive patients with primary aldosteronism have been reported to display a sympathetic inhibition compared with patients with essential hypertension with similar blood pressure values [9]. (3) Drugs interfering with the renin–angiotensin–aldosterone system, such as the angiotensin-converting enzyme inhibitors, have been shown to produce different effects on baroreflex control of the cardiovascular system, when acutely or chronically administered to patients with hypertension or heart failure [2–10].

In summary, the study by Yee and Struthers [3] provides one of the first demonstrations that in man aldosterone may exert adverse effects on baroreflex function. Further work in this area should clarify several interesting issues that remain largely unaddressed.

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REFERENCES


