Haemodynamics of renoprival hypertension in man: studies during graded fluid withdrawal

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Summary

1. Frequent measurements of arterial pressure, cardiac output, heart rate and body weight were carried out in three hypertensive anephric subjects during the reversal of hypertension by carefully controlled stepwise fluid withdrawal over a period of 24 days.

2. The initial 5% decrease of body weight was associated with decrements of arterial pressure and total peripheral resistance of 15 and 35% respectively, whereas cardiac output had risen by 25%. After a further decrease in body weight by 5%, arterial pressure was lowered another 15% without a change in total peripheral resistance, and cardiac output had returned to base line.

3. These data do not support the concept that whole-body autoregulation is an important factor in the pathogenesis of renoprival hypertension.

Key words: autoregulation, cardiac output, fluid withdrawal, over-hydration, peripheral resistance, renoprival hypertension.

Introduction

In the anephric state fluid balance is not controlled by the excretory function of the kidneys but is determined only by fluid intake and ultrafiltration rate during haemodialysis. The inadequacy of body fluid-volume control often leads to sodium- and water-overload with arterial hypertension as a result. The mechanism by which fluid overload initiates the development of hypertension is not fully understood. Long-term salt- and water-loading in anephric man (Coleman, Bower, Langford & Guyton, 1970) and in partially nephrectomized dogs (Coleman & Guyton, 1969) has been reported to initiate a phase of high-cardiac output hypertension. In a later phase cardiac output fell to control values, and hypertension was maintained by an elevated total peripheral resistance. This biphasic pattern is thought to be a consequence of so-called whole-body autoregulation (Coleman, Granger & Guyton, 1971). The hyperperfusion of the tissues in the initial phase elicits an autoregulatory response, which results in vasoconstriction. Autoregulation in this context means that the individual tissues have the intrinsic property to regulate their own blood flow via changes in vascular resistance with parallel changes in perfusion pressure as a result. Various factors have been invoked as stimuli for this autoregulatory response. Experimental evidence has pointed to the role of metabolic factors, such as oxygen demand and local accumulation of vasodilating metabolites, in the intrinsic regulation of tissue blood flow. Changes in vascular wall tension and in tissue pressure are alternative suggestions (Johnson, 1964).

If indeed a process of whole-body autoregulation by metabolic factors is responsible for the elevated peripheral resistance in salt- and water-induced hypertension, one would expect the cure of hypertension by fluid withdrawal to be associated with an initial decrease in cardiac output followed by a decrease in resistance (Coleman et al., 1971). We have tested this aspect of the theory by monitoring the changes in systemic haemodynamics during the reversal of hypertension in three anephric subjects. Recent haemodynamic studies on the development of hypertension in fluid-overloaded anephric patients did not show a uniform pattern (Kim, Onesti, Del Guercio, Greco, Fernandez, Eidelson & Swartz, 1980). Discrepancies might have been caused by the abrupt and irregular cardiovascular effects of
intermittent haemodialysis in these patients. For correct interpretation of the data it is mandatory to avoid as much as possible fluctuations in fluid intake and ultrafiltration rate. Careful control of these factors in our patients resulted in a progressive stepwise decrease in body weight over a period of 24 days. For frequent determinations of cardiac output at short intervals we applied a relatively non-invasive isotope-dilution technique with the use of low doses of radioactivity and precordial counting with a single-probe system (Man in 't Veld, Wenting, Verhoeven & Schalekamp, 1978).

Patients and methods

The patients, ages 28, 41 and 45 years, had undergone bilateral nephrectomy 2–7 years before the study. They were selected for this study because they had neglected advice on fluid intake and were hypertensive (systolic pressure >150 mmHg, diastolic pressure >90 mmHg). After explanation of the therapeutic nature of the study the patients gave their consent. None of them had overt peripheral oedema or clinical signs of pulmonary congestion. The patients were dialysed three times a week for 3–4 h. RP6-disposable polyacrylonitril-membrane kidneys were used with Rhodial-75 single-patient monitors. These units have recirculating dialysate, which contains 140 mmol of sodium/l, and the system facilitates careful control of body weight by separate collection of ultrafiltered fluid.

Arterial pressure, heart rate and cardiac output were measured immediately before and after each haemodialysis session, while the patient had been recumbent for at least 1 h. Arterial pressure was measured with the London School of Hygiene sphygmomanometer (model MK 4) (Rose, Holland & Crowley, 1964) to avoid observer bias and digit preference. Heart rate was derived from an electrocardiogram. After rapid injection of 200 μCi of technetium-99m-labelled human serum albumin, cardiac output was measured by precordial counting of radioactivity (Man in 't Veld et al., 1978). Time–activity curves were registered for 1 min, and blood samples for determination of radioactivity were drawn 5 and 10 min after injection. The detection system consisted of a thallium-activated sodium iodide crystal and a photomultiplier tube in conjunction with a conical-lead collimator.

Results

Carefully controlled ultrafiltration during haemodialysis and the adequate patient compliance with respect to fluid-intake restriction led to a gradual 10% decline in body weight in all patients with a concomitant decrease of mean arterial pressure from 120 to 85 mmHg (Fig. 1). Initially, the drop in pressure was associated with a decrease of total peripheral resistance, whereas cardiac output rose. With further fluid withdrawal the pressure declined through the return of cardiac output to the control value, whereas total peripheral resistance did not change. It should be noted that the transitory increments in body weight between the haemodialysis sessions were associated with increments in arterial pressure and resistance, and with a decrement in cardiac output. In general, the haemodynamic changes, when measured before each haemodialysis session, followed the same pattern as those measured after the haemodialysis sessions. We also followed one patient on the days between two consecutive haemodialysis sessions (Fig. 1, left panel). These data again showed an initial decrease in resistance, and a decrease in cardiac output in the second half of the study.

No consistent pattern of changes in heart rate was observed throughout the study, although heart rate after haemodialysis tended to be somewhat higher than before.

Discussion

By careful control of body weight, and by frequent determinations of cardiac output at short intervals, we were able to study the haemodynamic changes leading to reversal of hypertension in fluid-overloaded anephric subjects. Initially, the arterial pressure fell despite an increase of cardiac output. Our data do not clarify the underlying mechanism. Possibly, an altered balance between left ventricle pre- and after-load contributed to the rise in cardiac output. The haemodynamic pattern of the reversal of hypertension in our patients, that is an initial decrease in resistance with a subsequent decrease in cardiac output, is difficult to reconcile with a major role of whole-body autoregulation of flow by metabolic factors in the observed sequence of haemodynamic events. Other mechanisms, such as a reduced vascular wall tension or decreased tissue pressure might have contributed to ‘passive’ vasodilatation (Coleman et al., 1970; Manning, Coleman, Guyton, Norman & McCaa, 1979). In such a concept changes in cardiac output are a consequence rather than a cause of changes in vascular resistance.

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References


