Blood pressure and body water distribution in chronic renal failure patients

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Abstract
Evidence exists of the important role of sodium balance and extracellular fluid volume in the genesis of hypertension in chronic renal failure (CRF). Several studies have shown that patients with advanced CRF have an increased, interstitial and intravascular, extracellular water volume (ECW). The relationship between the increase in ECW and high blood pressure has also been reported. Using electric bioimpedance, body water distribution was studied in 32 patients from our dialysis unit. Twelve of these patients were hypertensive and 20 had normal blood pressure. Hypertensive patients had a significantly greater total body water volume and ECW than the normotensive patients. Given the importance of ECW in controlling blood pressure, one of the main aims of haemodialysis is a suitable extraction of sodium and water during the treatment. Despite technological advances in dialysis therapy, cardiovascular instability during treatment is still a clinical problem. In recent years, new strategies to control ECW, with good haemodynamic tolerance, have been developed. These strategies include haemofiltration, haemodiafiltration and sodium and ultrafiltration profiles.

Keywords: blood pressure; chronic renal failure; extracellular water; intracellular water; plasma volume; sodium concentration

Introduction
Hypertension is a frequent complication of chronic renal failure (CRF), and its prevalence depends on the underlying disease. It may be the result of multiple factors that, subsequently, bring about changes in cardiac output and peripheral vascular resistance.

Evidence now exists of the important role of sodium balance and extracellular fluid volume in CRF hypertension. Early in the course of CRF, plasma and extracellular fluid volumes tend to be normal [1]. At this stage, there is a progressive increase in the fractional excretion of sodium, proportional to the decline in CRF. There is evidence of the determinant role of atrial natriuretic peptide (ANP) in this adaptive decrease in the renal transport of sodium, in response to the diminished filtered sodium load [2]. Finally, in moderate and advanced renal failure, various studies have shown that hypertensive CRF patients have higher exchangeable sodium and blood volumes than CRF patients with normal blood pressure and normal subjects [3].

Body water distribution in CRF
Using isotopic techniques, several studies have shown that patients with advanced CRF have an increased, interstitial and intravascular, extracellular water volume (ECW). When dialysis treatment begins, the ECW tends to normalize. In both situations, the intracellular volume (ICW) remains within the normal range [4]. More recently, it has been demonstrated, by electric bioimpedance, that CRF patients on haemodialysis have an increased ECW compared with control subjects, whereas the ICW is similar in the two groups [5].

The relationship between the increase in ECW and high blood pressure in CRF patients has also been reported. In a group of patients with different degrees of renal failure, increased salt intake was followed by an increase in both plasma and interstitial volume. Patients with higher levels of plasma creatinine showed a greater increase in blood pressure. There was also evidence of a significant positive correlation between the increase in ECW and the increase in blood pressure levels in these patients [6]. A correlation has also been found in CRF patients on haemodialysis between

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increased ECW and plasma volume, and blood pressure [7]. The Tassin group (France), in whose unit the incidence of hypertension is <5%, has studied the relationship between fluid status and blood pressure control in patients from different European countries treated with short and long haemodialysis. Hypertensive patients on short dialysis had a significantly greater ECW than those with normal blood pressure on short dialysis and Tassin’s patients on long dialysis. In Tassin’s patients, the longer haemodialysis sessions allow for greater tolerance to ultrafiltration and improved ECW control [8].

The evolution of blood pressure and body weight was studied in 38 hypertensive patients who began haemodialysis treatment in our dialysis unit in 1999. We recorded blood pressure levels before beginning dialysis treatment (mean blood pressure at the last three visits), pre-dialysis weight at the first session and the number of antihypertensive drugs they were taking. One month after beginning the treatment, we again recorded blood pressure (mean blood pressure at the last three visits), pre-dialysis weight and the number of antihypertensive drugs. Systolic blood pressure decreased from 159 ± 16 to 138 ± 11, and diastolic blood pressure from 93 ± 8 to 77 ± 9 mmHg (P < 0.01). Body weight was significantly reduced, from 72.4 ± 8.1 to 69.8 ± 7.7 kg (P < 0.05) and the number of antihypertensive drugs taken by the patients also dropped from 2.9 to 1.7 (P < 0.05). However, we found no significant correlation between the drop in blood pressure and the reduction in body weight.

Using electric bioimpedance body water distribution was studied in 32 patients from our dialysis unit. Twelve of these patients were hypertensive, and 20 had normal blood pressure. The hypertensive patients had a significantly greater total body water volume (TBW) than the normotensive patients (62% vs 54% of body weight, P < 0.05). ECW was also significantly higher in the hypertensive patients (28% vs 21%, P < 0.01). However, there were no significant differences in ICW content (34% vs 33%) (Figure 1). These results agree with data obtained by other authors [8].

**Extracellular fluid volume control in haemodialysis patients**

Given the importance of ECW in controlling blood pressure, one of the main aims of haemodialysis is the suitable extraction of sodium and water during the treatment. Despite technological advances in dialysis therapy, cardiovascular instability during treatment is still a clinical problem, particularly with the current tendency to shorten dialysis time. In recent years, the concentration of sodium in the dialysate has been steadily increased. Although this measure is effective in improving cardiovascular stability, the dilemma is that it can induce a chronic overload of sodium and water, leading to arterial hypertension and pulmonary oedema.

Convective techniques (haemofiltration and haemodiafiltration) improve haemodynamic stability and allow a higher ultrafiltration rate. This is probably due to their effect on peripheral vascular resistances, though it has also been related to a lesser total extraction of sodium than in haemodialysis. Recently it has been reported that it is possible to achieve a zero balance between sodium and water gain during the interdialysis period and the extraction of sodium and water during dialysis, thus improving cardiovascular stability during dialysis and avoiding the risk of volume overload [9].

Our group studied the effect of sodium concentration in the dialysate and of convective transport on cardiovascular stability and body water distribution during dialysis. Nine stable haemodialysis patients were dialysed successively, using a random sequence, with a concentration of sodium in the dialysate of 136 mEq/l (Na = 136), 146 mEq/l (Na = 146) and haemofiltration (HF, sodium concentration 139 mEq/l). Dialysis time was 3.5 h, and the exchange volume in HF was 40% of body weight. The urea reduction ratio was similar in the three types of treatment (less in HF, but not statistically significant). Thirty minutes before beginning and immediately after the haemodialysis or HF session, the compartmental distribution of body water was measured using electric bioimpedance. We also measured the percentage decrease of plasma volume, through the changes in haematocrit. Blood pressure was recorded at 30-min intervals, during the haemodialysis or HF session. We observed that ECW dropped significantly with Na = 136, remained unchanged with Na = 146 and dropped, to a lesser degree but still significantly, in HF (Figure 2A). Intracellular water volume remained unchanged with Na = 136 and dropped significantly with Na = 146 and HF (Figure 2B). Plasma volume decreased by 13% with Na = 136, 6.9% with Na = 146 and 8.8% with HF, despite the fact that the ultrafiltration rate was similar in the three types of treatments. The reduction in

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**Fig. 1.** Differences in body water distribution between normotensive and hypertensive patients. Hypertensive patients have TBW and ECW higher than normotensives. ICW is similar in both groups.
plasma volume with Na = 136 was statistically significant with regard to the decrease with Na = 146 and HF. As a consequence of the changes in plasma volume, we observed that blood pressure during dialysis remained stable with Na = 146 and HF. However, with Na = 136, blood pressure decreased significantly after the third hour of dialysis (Figure 3). This means that when a low concentration of sodium is used in the dialysate in order to achieve a negative balance, a drop in ECW occurs, mainly at the expense of plasma water. This leads to haemodynamic instability, and the patient can suffer intradialytic hypotension. However, when a high concentration of sodium is used, the decline in plasma volume is less marked, ECW remains unchanged and ICW is reduced. In other words, there is a shift of water from inside the cell towards the interstitial and intravascular spaces, leading to a high rate of plasma refilling. For this reason, the use of high concentrations of sodium in the dialysate results in excellent cardiovascular stability. The disadvantage of using high sodium concentrations is that the patients have a positive balance of sodium and their thirst increases, resulting in a chronic overload of sodium and water, which can lead to arterial hypertension and pulmonary oedema.

**Fig. 2.** (A) Extracellular water changes with the three types of treatment. With Na = 136 and HF, ECW significantly decreases. With Na = 146, ECW did not change. (B) Intracellular water decreases with the three type of techniques. With Na = 136, ICW did not change. With Na = 146 and HF, ICW significantly decreased after dialysis.

**Fig. 3.** Blood pressure remained stable with Na = 146 and HF. However, with Na = 136, blood pressure decreased significantly after the third hour of dialysis.

**Strategies to control extracellular water volume in dialysis**

The strict control of ECW in patients on haemodialysis requires a low-sodium diet and optimum ultrafiltration, i.e. the highest rate per session without the appearance of haemodynamic intolerance. In general, in most patients, optimum ultrafiltration can be obtained using a sodium concentration of 138 mEq/l and a session duration of 3.5–5 h. However, with this strategy, it is not always possible to produce an equilibrated balance between the ultrafiltration rate and the plasma refilling rate. Furthermore, the current tendency to shorten dialysis time means that this balance is often not achieved. The results of the Tassin unit show that, with longer dialysis periods, it is possible to maintain patients at their dry body weight, with excellent haemodynamic tolerance, which allows for good blood pressure control without the need for antihypertensive drugs [8,10]. Therefore, in patients prone to hypotension during dialysis, the dialysis time needs to be increased.

According to our preliminary results, another ultrafiltration strategy, based on the compartmental movements of the water depending on the concentration of sodium, is the use of sodium profiles [11]. By combining a high concentration of sodium, which allows for a high ultrafiltration rate, because the plasma refilling is high, and a low concentration of sodium, to achieve an equilibrated balance of sodium, the tolerance of some patients can be improved [12]. A simultaneous ultrafiltration profile can optimize this treatment strategy.
The use of convective techniques also allows the necessary ultrafiltration rate to be reached in order to maintain a suitable dry body weight, with improved haemodynamic tolerance over conventional haemodialysis.

New strategies currently are being developed which permit an equilibrated balance between sodium gain in the interdialysis period and sodium extraction during dialysis [9]. The application of a kinetic model of on-line conductivity in the plasma ultrafiltrate allows for a small negative sodium balance to be programmed in each session, which would help to improve blood pressure control, with good cardiovascular tolerance in hypertensive patients.

References