INFLUENCE OF DIALYSATE COMPOSITION ON CARDIOVASCULAR FUNCTION IN ISOVOLAEMIC HAEMODIALYSIS

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Summary

Haemodynamic studies were made in eight patients before and during isovolaemic dialysis with five different dialysis solutions which varied with regard to concentration of sodium, acetate, bicarbonate and urea. Low sodium (133mmol/L) in the dialysate induced a fall in blood pressure both with and without urea removal, but no significant fall in peripheral vascular resistance. Acetate in the dialysate at higher sodium concentration (140mmol/L) resulted in peripheral vasodilation but no fall in blood pressure due to a compensatory increase in heart rate and cardiac output. We conclude that a fall in plasma tonicity (sodium) is the most important pathogenetic factor in dialysis associated hypotension; fall in total osmolality (mainly urea) is of no importance and acetate vasodilation can be compensated for haemodynamically provided that tonicity is kept stable.

Introduction

A major problem during haemodialysis is symptomatic hypotension which may hamper efficient ultrafiltration. We showed some years ago that rapid ultrafiltration was far better tolerated without reduction in blood pressure when performed alone than during simultaneous dialysis, indicating that diffusive transport through the dialysis membrane somehow affects blood pressure control [1]. We could also show that dialysis without ultrafiltration (isovolaemic dialysis) may be associated with hypotension [2]. The peripheral vascular resistance was found to decrease during isovolaemic dialysis with acetate-containing dialysis fluid together with a rise in cardiac output and pulse rate [3].

Among factors in dialysis held responsible for cardiovascular instability are reduction in osmolality, reduction in sodium concentration and shift of acetate from the dialysate into the patients [4], but their relative importance has not been systematically investigated. In the present study we attempted to vary these factors independently of each other by modifying the composition of the dialysis fluid.
Material and methods

Eight patients, 5 males and 3 females (age 20–68 years, mean 57 years) were studied after informed consent had been obtained. They all had end stage renal failure with creatinine clearance less than 1.5ml/min and had been treated with regular haemodialysis thrice weekly for more than six months. Two patients had hypertension and two patients had low predialysis blood pressure, one of whom was bilaterally nephrectomised. Each patient was studied six times. In five of the studies the patients underwent isovolaemic dialysis, each time with a different dialysis solution, and in one study isovolaemic sham dialysis, i.e. circulation of blood through the dialyser but without any flow of dialysate. The studies were generally performed with one week's interval and the order of the studies was randomised in each patient. All dialysis fluids were prepared in a 100 L tank containing fixed concentrations of K 4.5mmol/L, Ca 1.75mmol/L, Mg 0.5mmol/L and glucose 5mmol/L. The composition of the different dialysis solutions varied as to sodium chloride concentration, presence or not of urea and presence of bicarbonate or acetate (Table I). Disposable capillary dialysers, area 2.5m²

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<tr>
<th>TABLE I. Concentration of sodium, acetate, bicarbonate and urea (mmol/L) in dialysis solutions I–V</th>
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<tr>
<td>Sodium</td>
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<td>Acetate</td>
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<td>Urea</td>
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(Cordis-Dow) were used together with a Gambro ultradiffusion monitor (UDM) by which net ultrafiltration can be kept at zero by applying positive pressure in the dialysate compartment. Body weight was continuously recorded with a Datex metabolic balance. Blood pressure was automatically recorded every 5 to 15 minutes with an ultrasonic blood pressure manometer (Arteriosonde, Roche) and heart rate with a single electrode pulse meter (Kontron). Cardiac output was measured by dye dilution (indocyanine green) using the A-V fistula for injection of dye and blood sampling as earlier described [3,5]. Cardiac output was determined in duplicate after 25–30 minutes of recirculation without dialysis, and after 60 and 90 minutes, respectively of isovolaemic dialysis (or at corresponding times in the sham dialysis experiments). Mean arterial pressure (MAP) was calculated as diastolic blood pressure plus one-third of the pulse pressure. Cardiac index (CI) was calculated by dividing cardiac output with body surface area. Total peripheral vascular resistance index (TPVRI) was calculated by dividing MAP with CI and was expressed in arbitrary units. Blood samples were obtained during the initial recirculation and after 60 and 90 minutes for determination of urea, sodium and osmolality. The haemodynamic changes recorded in the dialysis experiments were evaluated in relation to the changes during sham dialysis in the same patient using Student's paired 't' test.
Figure 1. Changes in mean arterial pressure (MAP), cardiac index (CI) and total peripheral vascular resistance index (TPVRI) after 60 min and 90 min of isovolaemic dialysis with solution I–V (mean ± SE, n = 8)
Results

The body weight did not change significantly with any of the procedures. Sham dialysis did not induce any significant changes in blood pressure, cardiac index, stroke volume index, heart rate, peripheral vascular resistance or blood chemistries.

*Haemodynamic changes during dialysis (Figure 1)*

There was a significant fall in MAP with solution IV and solution V, i.e. the solutions with low sodium concentration with and without urea. Dialysis with a higher sodium concentration (solution I, II and III), did not result in a significant fall of MAP irrespective of acetate or bicarbonate being present or whether urea had been added or not.

A significant increase was observed with solution I after 60 min (+5.3, p<0.05) and 90 min (+6.6, p<0.02), with solution III after 60 min (+6.6, p<0.02) and 90 min (+13.1, p<0.02) and with solution V after 90 min (+6.9, p<0.05).

A marked increase in CI was observed after dialysis for 90 min with acetate-containing fluid (solution III).

A slight, significant decrease in TPVRI was observed after 90 min with solution I (sodium 140mmol/L, bicarbonate, urea added) and a more marked decrease after 90 min dialysis with solution III (containing acetate).

A significant fall in urea was observed after dialysis with solution II and V, whereas with solution I, III and IV, the urea concentration remained stable. The sodium concentration decreased significantly after dialysis with solution IV and V (Table II).

**TABLE II. Changes in plasma sodium and urea after 90 minutes of isovolaemic dialysis with solution I–V (mean ± SE)**

<table>
<thead>
<tr>
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<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
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<tbody>
<tr>
<td>( \Delta \text{Na}^+ )</td>
<td>-0.38±0.41</td>
<td>-0.75±0.84</td>
<td>-1.25±0.49</td>
<td>-2.50±0.42</td>
<td>-4.13±1.17</td>
</tr>
<tr>
<td>( \Delta \text{Urea} )</td>
<td>+0.3 ±0.9</td>
<td>-10.7 ±0.9</td>
<td>-0.4 ±1.0</td>
<td>-0.8 ±1.2</td>
<td>-10.6 ±1.9</td>
</tr>
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Discussion

Conventional haemodialysis combines two processes, dialysis and ultrafiltration which have to some extent opposite haemodynamic effects; ultrafiltration induces vasoconstriction and a decrease in CI whereas dialysis (with acetate) induces vasodilation and an increase in CI and HR [3]. We chose to study isovolaemic dialysis to exclude the influence of ultrafiltration, since our aim was to study dialysis-associated haemodynamic changes.

Our results indicate that low sodium in the dialysate with a decrease in plasma sodium may induce a fall in blood pressure under isovolaemic conditions. Minimising the fall in osmolality by adding urea to the dialysis fluid did not prevent this reduction in blood pressure. A significantly larger fall in blood pressure when
<table>
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<tr>
<td>Na⁺ mmol/l</td>
<td>140</td>
<td>133</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Urea</td>
<td>-</td>
<td>30</td>
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\[ \Delta \text{MAP} \]

\[ \text{mm Hg} \]

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<tr>
<th>-16</th>
<th>-12</th>
<th>-8</th>
<th>-4</th>
<th>0</th>
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Figure 2. Changes in mean blood pressure (MAP) after 90 minutes with dialysate II and IV. The difference was significant (p<0.05)

using solution IV than with solution II (Figure 2) further demonstrates that urea cannot substitute for sodium as a blood pressure stabilising factor. Rosa et al [6] have reported that infusion of mannitol during dialysis significantly reduces hypotension. Mannitol similarly to sodium is mainly confined to the extracellular fluid. An increase or decrease in extracellular concentration of solutes which do not readily penetrate the cells induce osmotic transmembrane water transport and affect the cell volume, i.e. they alter the tonicity of the extracellular fluid. However, the tonicity is not to the same extent affected by changes in extracellular urea, which rapidly equilibrates between extra- and intracellular water. Taken together our results indicate that stability of blood pressure in dialysis depends
on a stable tonicity of the extracellular fluid, a shift in total osmolality (mainly
due to dialytic removal of urea) appears not to be important provided that tonicity
is kept stable. In spite of the significant fall in blood pressure induced by low
dialysate sodium there was only a small and non significant fall in peripheral
vascular resistance and the cardiac output remained constant.

The vasodilatory effect of acetate was confirmed in the present study. How-
ever, blood pressure remained stable due to a compensatory increase in cardiac
output and heart rate. It has earlier been suggested that acetate may have a depres-
sive effect on cardiac function in haemodialysis patients. Our observations that
cardiac performance increases and blood pressure is maintained during dialysis
with acetate contradict this hypothesis. However, at low dialysate sodium more
marked hypotension was observed with acetate than with bicarbonate [7].

In conclusion our results indicate that changes in extracellular tonicity (sodium)
are more prone to induce cardiovascular instability than changes in osmolality by
urea removal. Vasodilation induced by acetate does not result in hypotension
providing extracellular tonicity is kept constant. This requires that cardiac per-
formance can increase adequately in response to vasodilation and may not apply
to patients with cardiac failure.

Acknowledgment

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References

4 Shaldon S. Proc 8th Int Congr Nephrol, Athens 1981: 689

Open Discussion

DAUGIRDAS (Illinois, USA) You said that your dialysis was isovolaemic. Do
you follow haematocrit levels, because if you are dialysing with the 133 sodium
dialysate and not removing weight, your plasma value should still contract based
on osmotic shifts and the reason you found more blood pressure decrease may be
based on the simple fact that with a low sodium dialysate your plasma volume
contracted, whereas with the high sodium dialysate your plasma volume was
unchanged.

BERGSTRÖM As a matter of fact we measured haematocrit, we measured total
protein and we measured body weight before and during these procedures and
there was absolutely no change.
WEHLE May I also say that the weight loss was a mean of 98gm. So it was stable the whole time.

HALVORSEN (Oslo) You showed in your investigations that acetate had not much influence on the blood pressure during dialysis. In Norway we have tried to study this in the whole dialysis population and have measured plasma acetate concentrations during the dialysis in most of the Norwegian patients and we also could not find any correlation between acetate concentration and the clinical state of the patients in accordance with your findings.

HAMPL (Berlin) Could you give me some information about your pH, PCO₂ and bicarbonate values in dialysate composition in acetate and bicarbonate dialysate?

WEHLE There were only a few changes between these two and we have measured, as Dr Bergström said, all these values and we have not seen very great changes.

HAMPL I mean the differences in the dialysate, I think the PCO₂ values in the bicarbonate dialysate must be very different from the acetate dialysate.

WEHLE Yes, we have only measured this in one patient and we will of course measure the dialysate.