ULTRAFILTRATION AND HIGH SODIUM CONCENTRATION DIALYSIS: PATHOPHYSIOLOGICAL CORRELATION

F Locatelli, R Costanzo, S Di Filippo, L Pedrini, P Marai, C Pozzi, R Ponti, S Sforzini*, B Redaelli*

Ospedale di Lecco and *Ospedale di Monza, Italy

Summary

Five stabilised uraemic patients underwent two different procedures using the Gambro Ultradiffuser: ultrafiltration alone for one hour (mean body weight loss 2.97 ± 0.24 kg) and ultrafiltration with simultaneous dialysis for one hour (mean body weight loss 2.92 ± 0.22 kg) using a given dialysate sodium concentration which reproduced the changes in osmolality which occur during ultrafiltration alone. This mean sodium concentration was 154.75 ± 2.02 mEq/L.

The results did not show significant differences for the two procedures as regards tolerance to dehydration. These results underline the key role of osmolar stability in making dehydration tolerable.

Introduction

In 1976 Bergström et al [1] reported that ultrafiltration without dialysis permitted marked body weight loss without side effects such as nausea, vomiting, cramps and hypotension. From their experience they concluded that a rapid fall in plasma osmolality interferes with blood pressure regulation and that ultrafiltration is far better tolerated provided that osmotic shifts are avoided or minimised. Further studies were performed in acute situations to investigate the possible mechanism for the maintenance of blood pressure during ultrafiltration. It has been suggested that the most likely explanation for this maintenance of blood pressure is an increase in peripheral resistance which is not renin-mediated, but more likely catecholamine-mediated [2,3].

The aim of this study is to verify if this well tolerated weight loss during ultrafiltration without dialysis can be accounted for by loss of or failure to acquire substances which interfere with blood pressure, or by the pathophysiological mechanisms induced by ultrafiltration, in which the fall in plasma osmolality during standard dialysis with a mean dialysate sodium concentration between 135 and 140 mEq/L is avoided.
Patients and Methods

Five patients stabilised on regular haemodialysis (3 x 4 hr/week) were studied. Two different procedures were performed three times for each patient:

(i) ultrafiltration without dialysis for 60 min, during which transmembrane pressure was progressively increased from 100 to 350 mmHg;

(ii) haemodialysis for 60 min using a dialysate sodium concentration which simulated the changes in osmolality which occur during ultrafiltration.

The sodium concentration in the dialysate was calculated by adding the amount of sodium required to counterbalance the fall in osmolality due to urea removal to that isonatratic dialysate which prevents a fall in osmolality due to sodium loss by diffusion down the concentration gradient. The required concentration was 154.75 ± 2.02 mEq/L. The other components of the dialysate were K+ 1.5 mEq/L, Ca2+ 3.5 mEq/L, Mg2+ 1.5 mEq/L, Acetate 38.0 mEq/L, Glucose 1 g/L. Transmembrane pressure was progressively increased from 100 to 450 mmHg in order to obtain the same mean weight loss as during ultrafiltration.

Both procedures were performed using a Gambro Ultradiffuser (surface 1.8 m², membrane thickness 11.5 micron) with a constant blood flow of 350 ml/min. Blood pressure, pulse rate and weight loss were measured at 15 min intervals throughout the study.

Blood samples for osmolality, sodium, potassium, calcium, chloride, phosphate, urea, creatinine, total proteins, haematocrit and blood gas analysis were taken at the beginning and at the end of the procedures. Osmolality was measured using the Fiske osmometer, sodium and potassium were measured by flame photometer, urea by the hypobromite method, total proteins by the Biuret method, haematocrit by the microhaematocritum, in triplicate. Other measurements were performed by routine laboratory methods. Plasma samples for determination of catecholamines were frozen.

Statistical significance was evaluated by the paired and unpaired Student t test.

Results

Table I summarises the means ± SD of the clinical and metabolic data at the beginning and at the end of the two procedures. The changes in osmolality, pCO₂, HCO₃⁻ showed no significant difference for the two procedures, while there was a significant decrease in urea, creatinine, potassium (P < 0.001) and phosphate (P < 0.05), and a significant increase in chloride, pH (P < 0.05) and calcium (P < 0.001) during dialysis in comparison with ultrafiltration.

During ultrafiltration the urea-dependent osmolality decrease was 0.82 ± 1.52 mOsm/kg H₂O and the sodium-dependent osmolality decrease was 1.95 ± 6.17 mOsm/kg H₂O and these changes did not reach significance.

During dialysis the urea-dependent osmolality decrease was 7.68 ± 3.16 mOsm/kg H₂O and the sodium-dependent osmolality increase was 7.77 ± 3.31 mOsm/kg H₂O; both changes were significant (P < 0.001). The change in urea-sodium dependent osmolality during ultrafiltration was -3.03 ± 6.54 mOsm/kg.
TABLE I. Clinical and Blood Chemical Data and Changes. Comparison of the Two Procedures (means ± SD)

<table>
<thead>
<tr>
<th></th>
<th>BEFORE</th>
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<th>CHANGES AFTER 1 HOUR</th>
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<tbody>
<tr>
<td></td>
<td>UF</td>
<td>Dialysis</td>
<td>P</td>
<td>UF</td>
<td>Dialysis</td>
<td>P</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>71.1±10.5</td>
<td>71.5±10.7</td>
<td>NS</td>
<td>-2.97±0.24</td>
<td>-2.92±0.23</td>
<td>NS</td>
</tr>
<tr>
<td>Blood volume (Å%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-16.62±11.32</td>
<td>-16.00±5.94</td>
<td>NS</td>
</tr>
<tr>
<td>Osmolarity (mOsm/kg)</td>
<td>323.7±5</td>
<td>327.0±9</td>
<td>NS</td>
<td>+1.0±4.04</td>
<td>+2.62±4.88</td>
<td>NS</td>
</tr>
<tr>
<td>Ht (%)</td>
<td>28.37±7.33</td>
<td>27.97±8.68</td>
<td>NS</td>
<td>+6.23±3.37</td>
<td>+4.63±1.76</td>
<td>NS</td>
</tr>
<tr>
<td>Total proteins (g/100 ml)</td>
<td>6.74±0.70</td>
<td>6.68±0.75</td>
<td>NS</td>
<td>+1.48±1.12</td>
<td>+1.29±0.53</td>
<td>NS</td>
</tr>
<tr>
<td>Sodium (mEq/kg H₂O)</td>
<td>143.0±2.7</td>
<td>144.3±2.1</td>
<td>NS</td>
<td>-1.06±3.34</td>
<td>+4.20±1.79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urea (mg/100ml H₂O)</td>
<td>220.6±60</td>
<td>189.4±28.2</td>
<td>NS</td>
<td>-5.14±9.53</td>
<td>-48.01±19.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine (mg/100ml H₂O)</td>
<td>10.65±1.93</td>
<td>9.94±2.4</td>
<td>NS</td>
<td>-0.52±0.42</td>
<td>-2.63±1.52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Potassium (mEq/kg H₂O)</td>
<td>5.18±0.75</td>
<td>5.02±0.84</td>
<td>NS</td>
<td>+0.74±0.65</td>
<td>-0.67±0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Calcium (mg/100ml H₂O)</td>
<td>8.87±0.24</td>
<td>9.11±0.36</td>
<td>NS</td>
<td>+1.07±0.81</td>
<td>+1.77±0.43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chloride (mEq/kg H₂O)</td>
<td>103.9±3.2</td>
<td>104.0±4.5</td>
<td>NS</td>
<td>-0.29±3.22</td>
<td>+2.53±4.62</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Phosphate (mg/100ml H₂O)</td>
<td>4.0±1.24</td>
<td>3.66±0.80</td>
<td>NS</td>
<td>-0.24±0.22</td>
<td>-0.89±0.67</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>pH</td>
<td>7.37±0.66</td>
<td>7.37±0.06</td>
<td>NS</td>
<td>+0.03±0.04</td>
<td>+0.05±0.04</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>pCO₂ (mmHg)</td>
<td>35.59±3.46</td>
<td>32.79±5.97</td>
<td>NS</td>
<td>-3.27±3.92</td>
<td>-3.86±4.48</td>
<td>NS</td>
</tr>
<tr>
<td>HCO₃⁻ (mMol/kg H₂O)</td>
<td>21.80±4.03</td>
<td>20.23±5.43</td>
<td>NS</td>
<td>-0.60±1.26</td>
<td>-0.38±3.09</td>
<td>NS</td>
</tr>
</tbody>
</table>

H₂O and during dialysis was + 0.02±4.35 mOsm/kg H₂O. These changes were not significantly different during the two procedures (Figure 1). The mean weight loss and the blood volume decrease (calculated from the change in Ht) were not significantly different during the two procedures.

Haematocrit and total proteins increased significantly during both methods (P < 0.001 for both) and the changes were similar for both methods.

After 30 minutes ultrafiltration and dialysis the systolic pressure dropped significantly (respectively P < 0.001 and P < 0.005). The diastolic pressure drop was not significant during ultrafiltration but was significant during dialysis (P < 0.005). The mean arterial pressure fell significantly during ultrafiltration and dialysis (P < 0.001 for both). After one hour ultrafiltration and dialysis a significant fall in systolic (P < 0.001), diastolic (P < 0.005) and mean (P<0.001) pressure occurred. The behaviour of blood pressure was similar for the two methods.
Figure 1. The effect of ultrafiltration and dialysis on percent changes in weight loss, Ht, total proteins and on urea and sodium dependent osmolality, total osmolality, systolic, diastolic, mean pressure and pulse rate.
Pulse rate showed a non-significant decrease after 30 minutes and a non-significant increase after one hour ultrafiltration; during dialysis the increase in pulse rate was significant after 30 minutes as well as after one hour ($P < 0.001$). The variations in pulse rate were significantly different during the two procedures after 30 minutes as well as after one hour ($P < 0.001$).

Both procedures were well tolerated without adverse clinical effects and hypotension was never symptomatic. No intravenous fluid replacement was required to correct the excess ultrafiltration, a decrease in transmembrane pressure having always been successful.

Discussion

Body weight stability in normal individuals, in normal caloric balance, depends on the constancy of body fluid volume. But the osmolality of the extracellular fluid is even more constant than its volume. The most important function of the normal kidney is to regulate the extracellular fluid composition. Uraemic patients progressively lose this function with expansion of the extracellular fluid volume. During haemodialysis acute side effects may occur either due to changes in body fluid volumes, and particularly plasma volume, or to changes in osmolality.

Until now comparative studies between ultrafiltration and dialysis have been carried out using hyponatric dialysate. For this reason many authors have found that the only significant element which could explain the results obtained with ultrafiltration was the stability of osmolality during this procedure.

To evaluate the role of the two variables in the maintenance of a stable blood pressure during ultrafiltration it is necessary to keep one of them constant. In our experience it has been possible to reduce the incidence of headache, vomiting, cramps and hypotension by the use of isonatric dialysate despite high mean hourly dehydration during dialysis. These observations led us to choose sodium chloride as the osmotic agent to compensate for the fall in osmolality which occurs during dialysis.

The results obtained in our study of the two procedures show parallel body weight loss and fall in plasma volume without a significantly different drop in blood pressure. The only significant clinical difference was the increase in pulse rate during dialysis.

Summarising the metabolic differences between the two procedures, we found significant falls in plasma urea, creatinine, potassium and phosphate during dialysis and significant increases in plasma sodium, calcium, chloride and pH. No significant changes in the remaining parameters, and particularly in osmolality, occurred.

The clinical parameters which remain the same are body weight loss and changes in blood pressure during the two treatments. This can be explained only by the common metabolic conditions, the most important being, in our opinion, the constant plasma osmolality. The differences in pulse rate changes must be explained by the metabolic differences occurring during the two treatments.
Henrich et al [4] studied the role of potassium during ultrafiltration. Despite similar decrease in body weight and blood pressure, pulse rate increased significantly only during isokalaemic dialysis, but not during hypokalaemic dialysis.

In our investigation the action of sodium on the changes in pulse rate could relate to different increases in peripheral resistance due to sodium loading during hypernatric dialysis. This difference may reflect a difference in behaviour of baroreceptors [5]. In our opinion other factors must be considered, particularly acetate and catecholamines.

During dialysis acetate is transferred, particularly when using, as here, large surface area dialysers and high flows [6]. It is well known that acetate reduces peripheral resistance and can thus induce compensatory increases in pulse rate. In fact ultrafiltration during dialysis with dialysate containing bicarbonate instead of acetate reduced the blood pressure drop and the increase in pulse rate [7,8].

Lastly, catecholamines, which we did not examine in detail in this study, must be considered. It has been shown that during dialysis catecholamines do not increase significantly but during ultrafiltration the increase is significant [2,3,9]. The dialysance of catecholamines could induce hypotension during dialysis. It has been assumed that uraemic patients undergoing regular haemodialysis show high levels of catecholamines independent of their blood pressure [10].

In our opinion the most likely explanation of the pulse rate increase during dialysis is a decrease in peripheral resistance due to assimilation of acetate with the consequent adrenergic response.

Conclusions

By maintaining plasma osmolality constant it was possible to obtain similar body weight loss and plasma volume decrease and similar behaviour of the blood pressure with both methods.

This is very significant, especially if we consider that the volume decrease obtained caused a highly significant blood pressure decrease even with ultrafiltration, confirming that the two procedures had been carried to the furthest lengths possible with our patients.

These results may have importance because of their possible clinical application.

Acknowledgments

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References

5 McGrath, BP, Tiller, DJ, Bune, A, Chalmers, JP, Korner, PI and Uther, JB (1977) *Kidney Internat.*, 12, 294