LONG-TERM HAEMODIALYSIS TREATMENT WITH SODIUM REMOVAL BY CONVECTION

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Summary

Forty-three uraemic patients were studied for 60.95 ± 14.46 months of haemodialytic treatment (4 hours, 3 times/week).

After a first dialysis period of 28.95 ± 14.46 months with a dialysate sodium concentration (NaD) of 142 mEq/L blood pressure (BP) and body weight (BW) showed values significantly lower (p < 0.001).

During a following period of 32 months with NaD 148mEq/L BP did not show significant changes.

A more ‘physiological’ removal of water and sodium by convection does not bring about the feared long term cardiovascular side effects if an appropriate dry BW is achieved, probably because of better correction of the cellular overhydration.

Introduction

The ‘unphysiology’ of dialysis, as reported by Kjellstrand [1], is one of the most important causes of the long-term side effects of dialytic treatment.

Severe fluctuations in plasma osmolality, cellular overhydration and extremely rapid ultrafiltration could cause subclinical damage to the cells, leading to progressive damage. Patient cooperation, residual renal function, frequency and duration of dialysis have been taken into account to explain this pathology. On the contrary, the role of dialysate composition, particularly its osmolality, has been undervalued. A change in sodium concentration as little as 1mEq/L can offset the osmotic effects of a change in blood urea as great as 12 mg/100ml. We believe that it is important to minimise osmotic shifts due to ‘unphysiological’ dialysate sodium thus avoiding cellular overhydration and excessive extracellular fluid volume reduction.

During dialysis water and salt can be removed from the patient by diffusion or by convection. Diffusion is more important during hyponatric dialysis, but as the
dialysate sodium concentration approaches that of plasma water, diffusion becomes less important and eventually ceases, at which stage effective water and salt removal can be achieved utilising the convective process of ultrafiltration.

The aim of this study is to verify if long-term sodium removal by convection is effective and safe, despite a zero sodium concentration gradient between plasma water and dialysate. Theoretically this lack of sodium removal by diffusion is easily compensated for by convection. It is, however, necessary to verify if this methodology produces any hazard in its clinical application.

Many benefits have been reported using higher dialysate sodium concentrations [2–6], but also potential hazards may occur in the short (pulmonary oedema) [7] and long-term (hypertension) [8,9] when such concentrations are used without taking the necessary precautions suggested from a knowledge of sodium pathophysiology during dialysis.

Patients and methods

Sixty-two patients were entered into this study. Nineteen did not complete the study because of renal transplantation (11) or death (8). The causes of death were: myocardial infarction, 1, stroke in a diabetic normotensive patient, 1, sepsicaemia, 2, atherosclerotic cachexia, 3 and malignant disease, 1.

Forty-three patients (34 male, 9 female), 19 to 69 years old (mean 47.93 ± 13.16), dialysed for 40 to 83 months (mean 60.95 ± 14.46) completed the study.

Primary renal diseases were: glomerulonephritis, 21, pyelonephritis, 8, cystic kidney disease, 5, renal vascular disease, 5, multi-system disease, 4 (diabetes, 3, Henoch-Schönlein, 1). Creatinine clearance in all cases was below 5ml/min. Before starting haemodialysis 13 patients were normotensive and 30 hypertensive. All of them underwent regular haemodialysis for 4 hours thrice weekly using 1m² surface dialysers. Dialysate flow was 500ml/min and blood flow about 300ml/min.

The study was divided into three periods; the first, lasting 28.95 ± 14.46 months using a dialysate sodium (NaD) of 142mEq/L; the second and third lasting 18 and 14 months respectively, dialysate sodium was 148mEq/L. Such NaD value was chosen to match the theoretical plasma water sodium concentration of a normal healthy man (i.e. calculated from plasma sodium concentration of 140mEq/L and total plasma proteins of 7g %). The theoretical value (148.95mEq/L) was close to the patients’ measured mean value (147.95 ± 3.12mEq/L).

The concentrations of the other dialysate components were the same during the three periods: K⁺ 1.5mEq/L, Ca ++ 3.5mEq/L, Mg ++ 1.5mEq/L, CH₃COO⁻ 38mEq/L and glucose 1g/L.

Systolic and diastolic blood pressure and pulse rate were taken pre-dialysis after ten minutes lying and post-dialysis ten minutes after reinfusion. Body weight before and after dialysis, mean intradialytic weight loss and mean interdialytic weight gain were also recorded.

Sodium concentration in plasma water (Naₚ) was calculated using the following formula:

\[ Naₚ = \frac{\text{measured plasma concentration} \times 100}{99.1 - 0.73 \text{ Pr}}, \]

where Pr is the plasma total proteins concentration.
To evaluate the intradialytic tolerance we recorded the amount of osmotically active substances that it was necessary to give during dialysis. It is difficult to give quantitative evaluations of symptoms such as hypotension and cramps, varying in intensity and duration.

Cardiothoracic ratio, fundus oculi and electrocardiographic signs of hypertension were also evaluated.

The results concern the data collected during the last two months of each period. Antihypertensive therapy and its variation during the periods were taken into account. Plasma and dialysate sodium concentrations were measured by flame photometer. Statistical significances were evaluated by the paired Student ‘t’ test.

Results

Table I shows the basal values (B) of Na\textsubscript{P}, systolic and diastolic blood pressure as well as the predialytic and postdialytic values found during the last two months of the Na\textsubscript{D} 142 period (period I) and of the Na\textsubscript{D} 148 periods (periods II and III). Pre and postdialytic body weight, mean intradialytic weight loss, body weight gain during the short and long interdialytic periods, and the mean amount of osmotically active substances infused to correct intradialytic hypertensive episodes, as well as statistical evaluations, are reported.

Blood pressure and body weight showed a significant fall during period I compared with basal values. Then blood pressure did not show significant changes during II and III in comparison with I, and during III in comparison with II.

No significant changes were found between I and II as regards pre and postdialytic body weight, while a significant fall occurred during III in comparison with I and with II.

Mean weight gain during both short and long interdialytic periods, and the mean intradialytic weight loss were significantly higher during II and III than I, and significantly lower during III than II.

The amount of osmotically active substances infused to treat cramps or hypotension during dialysis was significantly lower during II and III than during I, and not significantly higher during III than during II. Cardiothoracic ratio, fundus oculi and electrocardiographic signs of hypertension did not show significant changes during the three periods of observation, although they tended to deteriorate.

Discussion

Hypotension, particularly during short dialysis, is common. Thus we considered it important to employ a dialytic strategy which is more ‘physiological’ from an osmotic point of view in an effort to reduce the incidence of hypotensive episodes.

The amount of osmotically active substances we infused during dialysis is at first sight remarkable in absolute values, but it is little when compared to the
TABLE I. Behaviour of pre and postdialytic systolic blood pressure, diastolic blood pressure, body weight and intradialytic weight loss (IWL), interdialytic weight gain (IWG) during short and long period, intradialytic infusions in 43 patients before starting haemodialysis (HD) and during dialysis with dialysate sodium concentration (Na\textsubscript{D}) of 142 and 148mEq/L (two periods) and relative plasma water sodium concentration (Na\textsubscript{H\textsubscript{2}O \ per})

<table>
<thead>
<tr>
<th>Months of HD</th>
<th>Na\textsubscript{H\textsubscript{2}O \ per} mEq/L</th>
<th>Na\textsubscript{D} mEq/L</th>
<th>Systolic BP mmHg</th>
<th>Diastolic BP mmHg</th>
<th>Body weight kg</th>
<th>IWL kg</th>
<th>Infusions ml/session</th>
<th>IWG kg</th>
<th>Short period</th>
<th>Long period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before HD</td>
<td>–</td>
<td>–</td>
<td>161.31 ± 23.44</td>
<td>96.52 ± 12.85</td>
<td>65.42 ± 12.85</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<td>–</td>
</tr>
<tr>
<td>28.95</td>
<td>147.95 ± 14.46</td>
<td>142</td>
<td>151.85 ± 23.99</td>
<td>89.70 ± 10.91</td>
<td>62.33 ± 12.56</td>
<td>3.09</td>
<td>233.23 ± 195.59</td>
<td>2.85</td>
<td>3.75</td>
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<tr>
<td>(I)</td>
<td>± 3.12</td>
<td>±23.79</td>
<td>±11.77</td>
<td>±0.73</td>
<td>±195.59</td>
<td>±0.69</td>
<td>±0.89</td>
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<tr>
<td>46.95</td>
<td>147.42 ± 14.46</td>
<td>148</td>
<td>149.82 ± 25.61</td>
<td>88.25 ± 13.84</td>
<td>62.43 ± 12.33</td>
<td>3.68</td>
<td>104.14 ± 88.60</td>
<td>3.38</td>
<td>4.33</td>
<td></td>
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<tr>
<td>(II)</td>
<td>± 2.88</td>
<td>±29.97</td>
<td>±15.34</td>
<td>±11.98</td>
<td>±1.05</td>
<td></td>
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</tr>
<tr>
<td>60.95</td>
<td>147.37 ± 14.46</td>
<td>148</td>
<td>151.97 ± 29.76</td>
<td>89.02 ± 12.74</td>
<td>61.37 ± 12.10</td>
<td>3.49</td>
<td>123.03 ± 121.36</td>
<td>3.19</td>
<td>4.05</td>
<td></td>
</tr>
<tr>
<td>(II)</td>
<td>± 3.40</td>
<td>±31.50</td>
<td>±13.64</td>
<td>±11.69</td>
<td>±0.84</td>
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Significance: vs values before HD 142 vs 148 I 142 vs 148 II 148 I vs 148 II

a : p < 0.05  d : p < 0.001  e : p < 0.05  h : p < 0.02
b : p < 0.01  f : p < 0.01  k : p < 0.01

Note: Values are shown as mean ± standard deviation.
notable intradialytic weight loss. The required amount of infusion decreased significantly during NaD 148, although the intradialytic weight loss was significantly higher, indicating an improved intradialytic vascular stability. This stability persists, while the other measures lose their effectiveness quickly. However, interdialytic weight gain is, in our opinion, a very great problem arising from such a strategy.

Increased appetite, due to a more stable plasma osmolality, seems to be the major factor inducing significantly increased interdialytic weight gain; the problem of thirst was not different from that usually seen. Another important factor is probably a lax attitude of mind about dietetic habit, due to progressively lower self-control and the relatively easy intradialytic correction of the weight gain.

The positive effects and the possibility to correct, by ultrafiltration, even remarkable weight gains, must not mask the risk of salt and water overload with this kind of dialytic strategy. This risk is mainly due to poor patient compliance and the lack of careful evaluation of the importance of reducing the dry body weight.

In our opinion it is important to stress that when we increase the NaD, to avoid acute (pulmonary oedema) and long-term (hypertension) side effects the same salt and water removal as that carried out during hyponatric dialysis is not enough. In fact by utilising a NaD closer to that of plasma water it is possible to correct the chronic cellular overhydration, so that it is possible to achieve a lower dry body weight. The non-observance of such a precaution explains the side effects reported [7–9], while observing this precaution will explain favourable results [2–6,10].

If we analyse the blood pressure values we find that there are no other changes than the expected significant decrease in predialytic systolic and diastolic values which occur after the start of dialysis. Nevertheless the blood pressure values tend to rise, not significantly, during the last period, although the dry body weight shows a further significant decrease.

Cardiothoracic ratio, fundus oculi and electrocardiographic signs of hypertension did not show significant changes during the three periods of observation, although they tend to deteriorate. This fact has to be considered carefully because the antihypertensive therapy was not reduced. However, considering the long period of follow-up and the age of the patients, we wonder if this trend is only a natural evolution of the disease.

Dialysate sodium concentrations lower than that of patients plasma water are ‘unphysiological’. In fact marked sodium removal by diffusion induces cellular overhydration. This can result in acute side effects such as the disequilibrium syndrome and long-term potential negative effects on the metabolic processes. On the contrary, salt and water removal by convection is harmonic and does not induce cellular overhydration. In our opinion the ‘physiological’ NaD seems to be that of the patient’s plasma water corrected for the sieving coefficient and for the programmed ultrafiltration. In fact the convective removal of water and sodium results in hyponatric ultrafiltrate due to the sodium sieving coefficient [5]. This induces a retention of sodium with respect to water directly proportional to the ultrafiltration rate. Moreover using the ‘physiological’ NaD the required ultrafiltration is higher than during standard haemodialysis because ultrafiltration must compensate for the lack of sodium removal by diffusion.

While dialysing against NaD 142mEq/L, nearly all our patients show NaP values
similar to the NaD, and only two patients show a NaP lower. Thus a NaD of 142mEq/L can be defined as ‘physiological’ for nearly all our patients.

Dialysing with NaD of 148mEq/L the NaD is often ‘pharmacologically’ high; in fact 19 out of 43 patients show NaP lower than NaD. Therefore there could be the hypothetical risk of accumulation of sodium from the dialysate due to the inverse sodium concentration gradient if inadequate ultrafiltration is achieved.

On the other hand, dialytic treatment using a NaD ‘pharmacologically’ low with respect to the NaP of the patients could involve some problems in performing haemodialysis with respect to intradialytic dehydration and hence the achievement of the dry body weight.

Conclusions

A ‘physiological’ removal of water and sodium by convection is effective and does not bring about the feared long-term cardiovascular side effects if an appropriate dry body weight is achieved. It achieves a better correction of cellular overhydration. Utilising NaD ‘pharmacologically’ higher than NaP it is necessary to follow the patients carefully with respect to blood pressure behaviour.

References


Open Discussion

PONTICELLI (Milan) Your strategy is based on a strong ultrafiltration during dialysis, which allows harmonic dehydration. However, important complications have been reported during isolated ultrafiltration, including cardiac arrhythmias and arrest. Did you observe any important side effects in your own patients during dialysis?

PEDRINI No, we did not observe any important side effects. The side effects are reported by some authors during isolated ultrafiltration when performing dehydration in a short time, hence reaching very high rates of ultrafiltration. In this study we realise the harmonic dehydration allowed by convection by distributing it during the whole time of the dialysis. So we did not reach the elevated ultrafiltration rates that are linked to the side effects observed by these authors.
DI GIULIO (Paris) I agree with your result and the approach. In which sense do you think that the ultrafiltration rate will influence the sodium concentration in the equivalent of plasma water? You have said that ultrafiltration rate, because of the Gibbs-Donnan factor, represents a sparing mechanism for sodium loss through convection. Moreover, sodium concentration in the ultrafiltrate is generally lower but convection because of the high ultrafiltration rate brings out a larger amount of sodium. In which sense do you think that the equivalent concentration in the dialysate equilibrates the ultrafiltrate concentration of sodium so that the amount of sodium removed by ultrafiltration is limited?

PEDRINI According to the sieving coefficient for each litre of ultrafiltrate about 6mEq of sodium are not ultrafiltered. This can increase the pool of body sodium. But it is not in our opinion a very important factor because this retention of a few mEq of sodium can easily be removed by increasing ultrafiltration just a little. You can eliminate these relatively few mEq of sodium by increasing for instance ultrafiltration by 100ml. So you do not achieve an increase in body sodium pool. To be aware of this fact is very important because this awareness allows us to reach the right dehydration using ultrafiltration, in the right way. I would add that the side effects observed are linked to this fact because if this precaution is not observed hyper-hydration occurs and long-term (hypertension) and short-term (pulmonary oedema) side effects occur.

MAN (Paris) May I ask Dr Gotch to comment about these experimental clinical results related to your sodium volume model?

GOTCH I do not know exactly how to comment; I think it certainly is very interesting data. I was concerned that there was not a lot of clinical information given, and apparently you looked mainly at the change in steady state blood pressures, or you were concerned mostly about whether you induced hypertension, but it did not really address the question of intradialytic morbidity in those symptoms. I did have one question though, were those patient-months or months between the studies?

PEDRINI They were months of dialysis patients.

GOTCH Over how many months did the 142 sodium versus 148 sodium go on?

PEDRINI There were 28 months of dialysis with dialysate sodium concentration of 142.

GOTCH It is patient-months then.