PART IV

DIALYSIS: Ultrafiltration

Chairmen:  J Bergström
           H Borgmästars
IMPROVED TOLERANCE TO RAPID ULTRAFILTRATION
WITH THE USE OF BICARBONATE IN DIALYSATE

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Introduction

When large surface area (LS) type dialysers are used, substitution of bicarbonate (LS-B) for acetate (LS-A) in the dialysis fluid eliminates large swings in serum bicarbonate and pCO₂ and is associated with a reduction in dialysis induced morbidity, particularly post-dialysis fatigue¹. During the course of these investigations Bergström et al² reported their results which showed an increased tolerance to rapid ultrafiltration without simultaneous dialysis. They postulated that changes in osmolality during dialysis resulted in vascular instability. Since this manoeuvre would also stop acetate-bicarbonate transfers, we investigated the possibility that acetate-bicarbonate transfer played a part in the dialysis induced vascular instability noted by Bergström.

Methods

The subjects for this study were 5 stable dialysis patients who had been under continuous observation in our dialysis unit for at least 6 months. To demonstrate that LS-B dialysis improves the tolerance to rapid ultrafiltration, it is desirable to perform the LS-A dialyses at the maximum tolerable ultrafiltration rate while still using caution so as not to produce sudden severe episodes of shock. Using our past knowledge of his tolerance to the procedure, we ultrafiltered the individual patient at different increasing hourly rates. If in two consecutive dialyses with the same ultrafiltration rate, or in 3 out of 5 non-consecutive dialyses, complications occurred, this was considered to be the maximum tolerable ultrafiltration rate. This rate varied from 0.3 L/hr to 1 L/hr in different patients. Those patients who tolerated an ultrafiltration rate of more than 1 L/hr on LS-A dialysis were excluded from the study. For the LS-B phase of the study, an ultrafiltration rate 50% to 100% greater than the LS-A rate was used.

Each dialysis in the study began with the ultrafiltration rate set at the proper level as described above. When the patient’s weight dropped to within 0.5 kg of estimated dry weight, the ultrafiltration rate was reduced to near zero. If the
patient became hypotensive before he reached desired weight, ultrafiltration was stopped. Hypotension was defined as a systolic blood pressure less than 100 mmHg except in two chronically hypotensive patients for whom a blood pressure of less than 80 mmHg and less than 70 mmHg was defined as hypotension. Ultrafiltration was also stopped if the patient's blood pressure fell rapidly together with a change of pulse rate, and/or if he developed symptoms which we knew from past experience with that patient indicated that he was nearing the danger point of impending shock (chest pain, nausea, restlessness).

Pulse and blood pressure were measured every 15 minutes from the time ultrafiltration began until the end of the high ultrafiltration portion of the run, and more often if hypotension appeared imminent. Changes in body weight were measured concomitantly by means of electronic bed scales (Potter Model 26B).

All dialyses were performed on a Gambro Major type of dialyser. The dialysate contained either 38 mEq/L acetate or 35 mEq/L bicarbonate. To prevent too rapid a removal of urea and hypokalaemia, 35 mg/dl urea and 3 mEq/L potassium were added to the dialysate which was glucose free and also contained 140 mEq/L Na, 3.5 mEq/L calcium and 1 mg/dl magnesium. Haemodialyses were performed with blood flow of 200 ml/min and a countercurrent dialysate flow of 500 ml/min in a single pass configuration. Care was taken to ensure that, in terms of blood flow and change in osmolality, LS-A and LS-B dialyses were as nearly identical as possible. Changes in osmolality were measured periodically and did not differ significantly between LS-A and LS-B dialyses.

Results

The results are summarised in Table I. A total of 45 LS-A and 37 LS-B dialyses were performed on 5 subjects. With LS-B dialysis we achieved a mean ultrafiltration rate of 1.2 L/hr as compared to only 0.7 L/hr with acetate (p < 0.001).

**TABLE I. Comparison of Maximum Tolerable Ultrafiltration Rates**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean value with LS-A (45 runs)</th>
<th>Mean value with LS-B (37 runs)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of ultrafiltration</strong></td>
<td>2.4 hr</td>
<td>1.9 hr</td>
<td>&lt; 0.003</td>
</tr>
<tr>
<td>Weight loss per run</td>
<td>1.7 kg</td>
<td>2.2 kg</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Ultrafiltration rate</td>
<td>0.7 L/hr</td>
<td>1.2 L/hr</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>% terminated before reaching 'dry weight'</td>
<td>57</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>% 'available' fluid removed</td>
<td>67</td>
<td>79</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>'On' systolic</td>
<td>154 mmHg</td>
<td>155 mmHg</td>
<td>NS</td>
</tr>
<tr>
<td>'On' diastolic</td>
<td>80 mmHg</td>
<td>80 mmHg</td>
<td>NS</td>
</tr>
<tr>
<td>'Off' systolic</td>
<td>109 mmHg</td>
<td>117 mmHg</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>'Off' diastolic</td>
<td>62 mmHg</td>
<td>67 mmHg</td>
<td>NS</td>
</tr>
<tr>
<td>'On' pulse</td>
<td>79</td>
<td>78</td>
<td>NS</td>
</tr>
<tr>
<td>'Off' pulse</td>
<td>97</td>
<td>89</td>
<td>NS</td>
</tr>
</tbody>
</table>
While we needed only 1.9 hr to remove the mean total of 2.0 kg per run when the patient was dialysed against bicarbonate, we needed 2.4 hr to remove 1.7 kg when using acetate in the dialysate. With LS-A dialysis, the run had to be terminated prior to reaching 'dry weight' in 57% of 45 runs. With LS-B dialysis, the run was terminated before reaching 'dry weight' in 23% of 37 runs. With LS-A dialysis 67% of 'available' fluid was removed while 79% could be removed with LS-B dialysis. Average systolic blood pressure was significantly higher at the end of LS-B dialysis.

Discussion

Tolerance to ultrafiltration is significantly increased when bicarbonate is substituted for acetate in dialysis fluid. Whether this effect partially or completely explains the observations of Bergström et al (1976) remains to be determined by comparing tolerance to rapid ultrafiltration on LS-B dialysis with that obtained using ultrafiltration without dialysis.

Since the LS-A and LS-B dialyses were identical in every controllable aspect, such variables as osmolality change could not account for the difference in ultrafiltration tolerance.

It is not clear at this point whether the accumulation of acetate ion or the secondary changes in acid-base status (or both) are the cause of the vascular instability we have noted with LS-A dialysis. Recently, however, Kirkendol et al noted that the IV infusion of acetate into dogs will result in a dose-dependent impairment of cardiac contractile force and a concomitant drop in blood pressure. Hence, elevation of plasma acetate could account for part of the increase in vascular instability with LS-A dialysis.

The work of Arieff et al has relevance to the discussion of LS-A versus LS-B dialysis. He noted that with 'fast' dialysis in dogs (which would correspond to LS-A dialysis in humans) there was a consistent fall in CSF bicarbonate that did not occur with 'slow' dialysis. The fall in CSF bicarbonate was accompanied by an unexplained increase in brain osmolality which resulted in brain swelling. It is possible that this same sequence could take place during LS-A dialysis in humans, since the abrupt fall in plasma bicarbonate noted previously might contribute to a fall in CSF bicarbonate. Obviously, it will be of interest to repeat Arieff's experiments using bicarbonate instead of acetate in the dialysis fluid.

Novello et al have suggested that some patients may be especially intolerant to dialysis with acetate containing dialysate. We recently dialysed a critically ill hospitalised patient who had developed acute renal failure following mitral valve replacement surgery. Between 19 October 1976 and 1 November 1976 she gained weight steadily despite daily dialysis with a standard Gambro dialyser (1 M²). Each time even modest ultrafiltration was tried she developed severe hypotension. On 1 November 1976 her weight reached a high of 80 kg (dry weight estimated 64kg). On 2 November bicarbonate was substituted for acetate in the dialysis fluid, and during the next five dialyses the patient lost 14 kg by ultrafiltration with considerable improvement in pulmonary congestion and clearing of peripheral oedema. That these results are significant is suggested by the fact that during the period of 1 November onward her cardiovascular func-
tion continued to deteriorate, and the continuous dose of pressors she had been on since surgery gradually had to be increased. She died on 12 November 1976 of cardiovascular collapse. This case further documents the experience of Novello et al. and indicates that switching from acetate to bicarbonate may reduce the morbidity associated with dialysis of the critically ill patient.

Critically ill patients such as described above seem to represent one end of a wide spectrum of patients with respect to intolerance to dialysis with acetate. The other end of the spectrum is represented by those patients who are neither symptomatic nor develop vascular instability on LS-A dialysis and who were excluded from this study. In the middle are patients such as those included in the present study. If it can be shown that the degree of intolerance to dialysis with acetate is correlated with an inability to metabolise the acetate ion, then the adverse effects of LS-A dialysis probably could be ascribed more to the direct toxic effects of acetate ion than to the adverse effects of sudden changes in acid-base balance.

Acknowledgments

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References


Open Discussion

CHAIRMAN (J BERGSTROM, Stockholm) I would like to open the discussion by showing one slide and making a comment. The slide (Figure 1) summarises results in 6 patients with problems of overhydration and who were investigated by the Stockholm group (Bergström, Asaba, Fürst, Shaldon & Wehle). Each patient underwent rapid ultrafiltration for one hour (mean weight reduction 2.0 kg), using the RP-6 dialyser, at the beginning of five dialysis treatments at weekly intervals. Ultrafiltration was undertaken without dialysis (controls), with simultaneous dialysis using acetate (40 mmol/L) or bicarbonate (25 mmol/L) in the dialysis fluid at a dialysis sodium concentration of 133 or 145 mmol/L, respectively.

The figure shows that the systolic blood pressure which is stable with ultrafiltration only and falls slightly when using a high dialysate sodium concentration, is much more reduced when the dialysate sodium concentration is kept low. These changes were apparently related to the changes in plasma osmolality.
Acetate had no effect on blood pressure at the higher sodium concentration, but possibly a small (not significant) effect when used in the low-sodium dialysate. From our investigation it appears that the cause of hypotension during dialysis with rapid ultrafiltration is multifactorial. Shifts in osmolality (sodium concentration) seem to be more important than the effect of acetate. However, it is possible that the role of acetate becomes relatively more important when using a large surface dialyser, because the shifts of acetate and bicarbonate will be more rapid than when using a 1 m²-dialyser.

CAMBI (Parma) Considering that the variation in saline infusion during dialysis may largely change the bicarbonate concentration itself — did you measure serum bicarbonate at the end of dialysis and was this difference significant also in relation to any saline infusion that you may have done?
GRAEFE We have published our blood gas data previously and what we could show was that if we used bicarbonate in the dialysate there was a steady rise in the bicarbonate in the plasma, while if we used acetate in the dialysate there was at first a drop in the bicarbonate, down to 14 mEq in a couple of patients from 23–24 in the beginning, and then at the end of dialysis they were up to 23–24. Then, 2 or 3 hours after dialysis they were up to about 32–33 mEq of bicarbonate. So there is a difference in the shift of the plasma bicarbonate whether you use acetate or bicarbonate. The peak of the plasma bicarbonate — if you should dialyse against bicarbonate — is reached at the end of the dialysis and there is a steady rise, while during dialysis against acetate you have at first a drop and the larger, the more intense the small molecular clearance of the dialysate the more significant the drop.

COLOMBI (Switzerland) Can you tell us something about problems with bicarbonate and calcium in the dialysate? Have you not had any problems to keep them in solution?

GRAEFE What you have to do is prepare a diluted bath; you cannot use concentrates with a proportioning pump system. But I think one of the larger companies is preparing or has already prototypes of a proportioning system for bicarbonate.

SHALDON (Stockholm) If I may criticise your experimental design — it would seem more logical to me if you had compared your two systems with the model described, which was pure ultrafiltration, because I am most unimpressed by your bicarbonate results in terms of 25% significant blood pressure drop at a rate of 1.2 kg per hour and I do not really think that you have any right to compare your results with Bergström’s on that basis, not having a control with pure ultrafiltration. The second question that I think is extremely important before we all rush back to bicarbonate is, could you give us the incidence of these symptomatic patients that you chose for this work, in relation to the total population available to you?

GRAEFE In our research centre we have a total of about 50 patients, in-centre and out-centre, and we have just chosen those who had bad problems with ultrafiltration. That means patients who could not tolerate more than 0.7–0.8 litres per hour and these were those seven patients. I think the point you make is not really quite right. At this point we are comparing the Bergström method with a bicarbonate method, and that is a different study. What we want to point out is that the explanation that changes in plasma osmolality are the major factor in creating vascular instability, as proposed by Dr Bergström, is not true in this absolute way but that there are other factors too, like acetate.

BAILLOD (London) May I address a comment to the Chairman? We now have facilities for rapidly changing the blood compartment using the new technique, but has anyone got any information on what we are doing to the extracellular or intracellular compartments for example. Short efficient dialysis, even frequently up to five times per week gives increasing phosphate levels, indicating overall poorer dialysis clearances.

CHAIRMAN (BERGSTROM) We know for sure that the intravascular compart-
ment is contracted by studying haematocrit and plasma protein. It must be inferred that the total extracellular compartment is considerably decreased just counting how much fluid we are taking away. We may take away 4 litres in one hour. What actually happens between extra- and intracellular compartments is far more difficult to evaluate and I think to do this we need a tracer method, but I cannot see any easy explanation or any forces which would readily take water out of the cells in the extracellular compartment except maybe a minor increase in the interstitial oncotic pressure which may be of some significance. I do not think anyone has made these studies yet.

SARGENT (Berkeley) I would like to address a comment to one of the previous discussants concerning the difficulty of preparing bicarbonate dialysis. We have currently a three-compartment machine and the way it is done is that you obviously have to separate the calcium and the magnesium from the concentrate bicarbonate. This is done by having two concentrate streams, one of which contains acid so that when the two streams mix you adjust the pH to the level at which the calcium and magnesium salts do not precipitate.

PAPADIMITRIOU (Thessaloniki) I would like to ask Dr Graefe, if you have any data comparing the cardiac performance when you use acetate and when you use bicarbonate dialysis solutions.

GRAEFE The pulse rate came up the same way in both studies and blood pressure fell lower in the group which was dialysed against acetate. So from the rise in the pulse frequency we concluded that both groups were stressed to a similar degree.