PART III

TECHNICAL ASPECTS OF HAEMODIALYSERS
Chairman: Dr W Drukker
A Clinical Trial with a Glucose-free Dialysate

N ALWALL, K E HAGSTAM, B LINDEGARD and T LINDHOLM
University Hospital, Lund, Sweden

Most dialysis centres use, as a routine, dialysis fluid containing glucose, most often in concentrations between 100 and 2000 mg/100 ml. Higher concentrations of glucose have also been used (Drukker et al, 1964; Potter, 1966; Mendelssohn et al, 1967). There are several motives for adding glucose to the dialysis fluid:

1. to achieve normal plasma-osmolality in the dialysate in spite of subnormal electrolyte concentrations (Kolff et al, 1944)

2. to dehydrate the patient, by osmosis, during the dialysis treatment (van den Bossche & Kolff, 1948; Holmes & Nakamoto, 1959; Mendelssohn et al, 1967)

3. to avoid hypoglycaemia during treatments (Leonards et al, 1961)

4. to avoid the dialysis disequilibrium syndrome (Drukker et al, 1964; Kennedy et al, 1964), and

5. to add calories during the dialysis (Kennedy et al, 1964).

Several authors have questioned the advantages and pointed out the risks of high content of glucose in the dialysate. Thus, both a pronounced post dialysis hypoglycaemia (Gutman et al, 1967; Rigg & Bercu, 1967) and a hyper-osmolar syndrome (Potter, 1966; Mendelssohn et al, 1967) have been described. Moreover, the risk of accentuation of the disequilibrium syndrome after dialysis has been pointed out (Drukker et al, 1964; Papplus et al, 1967). In regular dialysis treatment no advantages of 1800 mg/100 ml glucose in the dialysate, compared with 900 mg/100 ml could be found (Hagstam et al, 1969).

A problem of great practical importance, especially when using a central tank system, is that addition of glucose to the dialysate forms substrate for bacterial and fungal growth in containers and piping. Also, in dialysis on a larger scale one cannot disregard the cost of glucose.

Use of glucose-free dialysate has, in experiments on dogs, proved able to induce grave hypoglycaemia with convulsions (Leonards et al, 1961). In
certain dialysis centres glucose-free dialysate has been tested clinically (Bergström, 1969; Nösé, 1969). The effects on the patients' blood sugars have been slight, nor does it seem that any other untoward events have been noted. At this clinic we have, over a number of years, been using a dialysate containing about 1 g/100 ml glucose (Alwall, 1963). Since a new large dialysis department, with automatic central tank system was put into use in 1968, the disadvantages of glucose-containing dialysate from a micro-biological point of view have created a problem. Because of this a series of tests have been performed to study possible side effects of the use of glucose-free dialysate.

MATERIAL AND METHODS

The series of tests were carried out on 6 patients, 3 men and 3 women, with irreversible kidney insufficiency, who were treated regularly with haemodialysis twice a week, and were in a stable phase. Average age was 34 (range 17-56). Body weight averaged 58 kg (range 30 - 78 kg).

The dialysis treatments were performed with a disposable kidney of the Alwall type (1968) and the period of treatment was about 7.5 hours. Blood flow was on average 160 ml/min (range 100-200 ml/min). The dialysate flow was 1 litre/min. The study was carried out over a period of 6 weeks in which the dialysate contained 900 mg/100 ml glucose during the first 3 weeks (period A) and was glucose-free during the last 3 weeks (period B). The difference in the composition of the dialysates is shown in Table I.

### Table I. Composition of the two dialysates

<table>
<thead>
<tr>
<th></th>
<th>Dialysate A</th>
<th>Dialysate B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium mEq/l</td>
<td>130</td>
<td>140</td>
</tr>
<tr>
<td>Acetate mEq/l</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td>Glucose</td>
<td>900</td>
<td>0</td>
</tr>
<tr>
<td>Osmolality mosm/kg H2O</td>
<td>306</td>
<td>294</td>
</tr>
</tbody>
</table>

The same concentrations of potassium (2.0 mEq/l), calcium (3.0 mEq/l) and magnesium (0.5 mEq/l) were used in both solutions. At each dialysis treatment the patients received a questionnaire in which they were asked to note possible symptoms during the treatment, during the remainder of the dialysis day, and during each one of the intervening days, respectively. The questionnaire had the following headings: headache, dizziness, difficulty in seeing, muscle cramps, muscle twitchings, difficulty in walking, nausea, vomiting, thirst, oedema, difficulty in breathing, itching, tiredness, difficulty in sleeping, anxiety/unrest, chill, fever, faintness, abnormal hunger.
and other possible symptoms. The patients were asked to grade the symptoms as slight or severe. The former were at processing given 1 point and the latter 2 points. The highest amount of points a patient could reach in a period of 3 weeks, was 1026 points. The patients had been informed of the test series and had agreed to take part. However, they knew nothing about its purpose, nor at which point period A was followed by period B.

Apart from the routine treatment records used, the staff in the dialysis department also made notes on records with a set of headings largely corresponding to the above mentioned. Before and directly after each dialysis, tests were made to determine the blood sugar as well as sodium and osmolality in plasma. For each dialysis tests were also made to determine urea-N, creatinine and potassium in plasma, as well as concentration of haemoglobin.

During the trial period a complete EEG was recorded once before dialysis, on each patient. During each dialysis treatment a one-channel bipolar EEG was recorded once an hour from the right centro-parietal region. The electrodes were placed in positions C4 - P4 according to the 10 - 20 system (Jasper, 1958). The graphs were evaluated according to conventional principles. Manual frequency analysis according to Sulg (1969) was performed on the one-channel curves taken before, in the middle of and immediately after the first and third dialysis treatment in the two periods A and B. The analyses were performed on artefact-free and representative 20 second curve sections. The percent activity time for each of the frequency classes 1 - 20 c/sec were calculated as well as the EEG frequency index. This was defined as the ratio between total number of identified waves, including superimposed activity, and the total accumulated period time for frequency classes 1 - 20 c/sec.

RESULTS

One of the patients did not fill in his questionnaires in the prescribed way, and thus only the data from 5 patients were included in the following account. These patients noted 289 symptom points altogether, of which 184 were reported during period A with glucose-containing dialysate and 105 during period B with glucose-free dialysate (Table II). The difference between these frequencies was significant (p < 0.001). Seventeen of the symptoms included in the questionnaires were reported by the patients. During the period of treatment with glucose-free dialysate (B), the number of points for tiredness, muscle cramps and nausea were significantly lower and the number of points concerning thirst significantly higher than during the period of treatment with the glucose-containing dialysate (A) (Table II). For the rest of the symptoms no difference in frequency was noted.

In the staff records, as in those of the patients, a significantly lower frequency of muscle cramps was found during the period with the glucose-free
Table II. Occurrence of complaints during period A, with glucose, and during period B, without glucose in the dialysate

<table>
<thead>
<tr>
<th>Complaint</th>
<th>Period A</th>
<th>Period B</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle cramps</td>
<td>20</td>
<td>1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Tiredness</td>
<td>50</td>
<td>21</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Nausea</td>
<td>17</td>
<td>3</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td>Thirst</td>
<td>9</td>
<td>25</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Remaining complaints</td>
<td>88</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>184</strong></td>
<td><strong>105</strong></td>
<td><strong>&lt; 0.001</strong></td>
</tr>
</tbody>
</table>

* $X^2$-test with Yates' correction

dialysate, than during the period with glucose-containing dialysate. In the reports made by the staff there were no further significant differences between the patients' behaviour during the two periods.

Table III shows the mean concentrations of blood sugar, sodium and osmolality in plasma before and after dialysis treatments in the two trial periods A and B. Thus during treatments the blood sugar was increased even if the dialysate contained no glucose. However, the increase was not as pronounced as when glucose-containing dialysate was used.

No difference was found between the mean concentrations of urea-N and creatinine in plasma before dialysis between periods A and B. The osmolality in the dialysate containing 900 mg/100 ml glucose was 306 mosm/kg water (Table I) and in the dialysate without glucose 294 mosm/kg water. Thus, there was a difference of 12 mosm/kg water. In the dialysis equipment used, ultrafiltration was controlled by a variable negative pressure in the dialysate. In the calculations concerning ultrafiltration pressure and weight reduction in patients, but where food intake was not taken into consideration, it was shown that about 50 mmHg higher ultrafiltration pressure was needed to attain desired weight reduction in the use of a glucose-free dialysate than in glucose-containing dialysate.

The complete EEG records showed slight or moderate abnormalities of a diffuse nature. One-channel curves from each patient showed no constant differences either between recordings made during each separate dialysis, or between corresponding recordings from the two periods A and B. The results of the quantitative frequency analysis is shown in Figure 1. It reveals good correspondence between the means of the EEG frequency spectra of the six patients before, in the middle of and after dialysis treatment. This is also the case for corresponding spectra from the periods with and without glucose in the dialysate. The EEG frequency index calculated on the basis of the respective frequency spectra shows no significant differences.
Table III. The mean concentrations of blood sugar, osmolality and plasma sodium before and after the dialysis treatments in the periods with and without glucose in the dialysate

<table>
<thead>
<tr>
<th></th>
<th>Dialysate with glucose</th>
<th></th>
<th>Dialysate without glucose</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment Mean ± S.E.</td>
<td>After treatment Mean ± S.E.</td>
<td>Difference</td>
<td>Before treatment Mean ± S.E.</td>
</tr>
<tr>
<td><strong>Blood sugar</strong></td>
<td>88.4 ± 5.2</td>
<td>141.7 ± 8.8</td>
<td>+53.3 ± 7.5</td>
<td>82.6 ± 3.5</td>
</tr>
<tr>
<td>mg/100 ml</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Osmolality</strong></td>
<td>325.2 ± 2.6</td>
<td>296.3 ± 2.0</td>
<td>-28.9 ± 3.6</td>
<td>323.5 ± 3.7</td>
</tr>
<tr>
<td>mosm/kg H₂O</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Plasma sodium</strong></td>
<td>138.7 ± 0.6</td>
<td>135.9 ± 0.8</td>
<td>-2.9 ± 0.7</td>
<td>141.0 ± 0.7</td>
</tr>
<tr>
<td>mEq/l</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**DISCUSSION**

The glucose-free dialysis fluid B contained 10 mEq/l more sodium than the glucose-containing fluid A. This meant that the sodium concentration in plasma was somewhat increased with the use of the dialysis fluid first mentioned (Table III). During the 3-week trial period B an increased thirst was noted, but no other unfavourable effects, neither in the form of increased blood-pressure nor an increased inclination for fluid retention. However, out of fear that the higher concentration of sodium in the long run should bring these complications the concentration of sodium was decreased to 135 mEq/l when we later began using glucose-free dialysate in all haemodialyses, after which no bothersome thirst was noted.

The presence of tonic muscle cramps was significantly lower during period B, when a glucose-free dialysate was used, than during period A. Hagstam et al (1969) found support for the fact that decrease of the extracellular osmolality drop during dialysis through mannitol infusion could decrease the appearance of such cramps. Dialysis against the glucose-free dialysate B in the present study meant an osmolality drop of 15 mOsm/kg water compared with a decline of 29 mOsm/kg water in dialysis against the glucose-containing dialysate A. This can be seen as remarkable against the background of the fact that the osmolality in dialysate A was 12 mOsm/kg water higher than in dialysate B. The explanation could be that glucose is metabolised and thus gives only a short lived osmolality increase, as opposed to the higher content of sodium and chloride in the glucose-free dialysate.

Present data admits no certain conclusions concerning the cause of the
decreased occurrence of muscle cramps during period B, but against the background of the above mentioned findings in mannitol administration it is possible that the osmolality factor is of the greatest importance.

At the EEG supervision during both trial periods no certain changes of the type described in the disequilibrium syndrome could be shown (Kennedy et al, 1963; Kennedy et al, 1964). The transition to glucose-free dialysis fluid brought no change of the EEG picture in this study. These results correspond to observations, both by others and by ourselves, that graver clinical and electroencephalographic symptoms of the type referred to dialysis disequilibrium are relatively uncommon in patients treated with regular dialysis and who are in a stable phase (Maher & Schreiner, 1965; Edel et al, 1965).

Leonards et al (1961) found, in using glucose-free dialysate in dogs, that significant hypoglycaemia induced convulsions. The difference between these experimental and our clinical observations seems partly to be explained by the fact that Leonards et al conducted more rapid dialyses in relation to the body weight of animals than we did in our patients. The most important factor could be, however, that our patients were allowed to eat freely both before and during treatment, while the animals in their experiment fasted. A risk of hypoglycaemia could exist when the condition of the patient does not allow oral nutrition during dialysis. In such cases prophylactic intravenous carbohydrate infusion should be considered.

CONCLUSION

To ascertain advantages and disadvantages of a glucose-free dialysate compared with dialysate containing 900 mg/100 ml glucose, six patients from our regular haemodialysis programme have been studied closely over a period of six weeks. During the first half of the period glucose-containing fluid was used and during the second, glucose-free dialysis fluid whose sodium concentration was increased by 10 mEq/l.

The EEG was followed during all dialyses without showing any change. No decrease in blood sugar was noted. Totally, less subjective symptoms were recorded during the glucose-free trial period. Among the single symptoms during this period nausea, tiredness, and muscle cramps were less frequent and thirst more frequent. Whether these differences were caused by the absence of glucose or the increased concentration of sodium, can not be determined.

Glucose-free dialysate brought no serious side effects in this series, however, we want to stress that patients should eat during dialysis. In regular haemodialysis treatment we now use solely glucose-free dialysate.

ACKNOWLEDGMENT

This investigation was supported by grants from the Swedish Medical Research Council (to Professor Nils Alwall, project B68-19X-763-03).
REFERENCES

Bergström, J. (1969) Personal communication
Bosiche, M. van den and Kolff, W. J. (1948) Geneeskunde gids, 26, 284
Potter, D. J. (1966) Annals of Internal Medicine, 64, 399