Clinical Evaluation of Patients Dialysed with Double Gambro 4 hours, three times per week

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Summary

To reduce the hours and cost of each dialysis and/or to increase adequacy of haemodialysis treatment 14 chronic dialysis patients were dialysed with two Gambro dialysers, 4 hr for 3 days per week. General well-being, anaemia, and nerve conduction velocity improved in some patients during the study period. Increasing dialysis surface area by using two Gambro dialysers enabled reduction of hours of dialysis, which was favourably accepted by all patients and decreased cost of dialysis, mainly by increasing the capacity of a unit to dialyse more patients with the same personnel and equipment.

Introduction

Babb et al (1971) introduced the square-metre hour hypothesis and in 1972 appropriately called it the middle molecule hypothesis. This hypothesis has stimulated investigation into the clinical application of different haemodialysers and haemodialysis schedules. Various clinical studies have been devised to test or prove this hypothesis. Christopher et al (1971) reported that a low dialysate flow ($Q_D = 100 \text{ ml/min}$) will result in elevation of pre-dialysis concentrations of smaller molecules (urea, creatinine) but will have no significant effect on the clearance of middle molecule uraemic toxins. Nerve conduction velocity and haematocrit have been reported to be stable with this method of haemodialysis.

Ginn et al (1971) reported that use of high-efficiency dialysers with small surface areas result in reduced nerve conduction velocity in some patients, possibly due to increased accumulation of small and middle molecule uraemic toxins. In order to improve the dialysance of middle molecules without compromising the
clearance of smaller molecules, duration of dialysis could be reduced by 30% providing that the surface area of the dialyser is increased by 100%. The following study was designed to evaluate the efficiency, feasibility and cost of this method.

MATERIALS AND METHODS

Fourteen male patients, of ages between 29 and 62, (mean 45.6 yr) with chronic renal failure of various aetiologies were selected (Table I). Residual renal function measured by creatinine clearance was 1.0 ml/min or less in thirteen patients. All patients were considered stable, free of infection or hepatitis-associated antigen (HAA).

Table I

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (Years)</th>
<th>Etiology</th>
<th>CCR (ml/min)</th>
<th>Weight (Kg)</th>
<th>Control Period (CP)</th>
<th>Study Period (SP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. W.V.</td>
<td>42</td>
<td>Alport's Syndrome</td>
<td>&lt;1</td>
<td>80</td>
<td>6*</td>
<td>13</td>
</tr>
<tr>
<td>2. R.B.</td>
<td>40</td>
<td>CGN</td>
<td>&lt;1</td>
<td>70</td>
<td>6*</td>
<td>7</td>
</tr>
<tr>
<td>3. W.T.</td>
<td>45</td>
<td>MNS</td>
<td>0</td>
<td>60</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>4. H.W.</td>
<td>45</td>
<td>CGN</td>
<td>0</td>
<td>80</td>
<td>6*</td>
<td>10</td>
</tr>
<tr>
<td>5. J.H.</td>
<td>50</td>
<td>MNS</td>
<td>0</td>
<td>80</td>
<td>9*</td>
<td>7</td>
</tr>
<tr>
<td>6. W.J.</td>
<td>59</td>
<td>Analgesic nephropathy</td>
<td>&lt;1</td>
<td>60</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>7. J.P.</td>
<td>62</td>
<td>Polycystic</td>
<td>&lt;1</td>
<td>65</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>8. B.P.</td>
<td>45</td>
<td>MNS</td>
<td>1</td>
<td>80</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>9. N.P.</td>
<td>29</td>
<td>Diabetic</td>
<td>6</td>
<td>120</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>10. C.W.</td>
<td>48</td>
<td>CGN</td>
<td>&lt;1</td>
<td>80</td>
<td>10*</td>
<td>8</td>
</tr>
<tr>
<td>11. F.M.</td>
<td>46</td>
<td>CGN</td>
<td>&lt;1</td>
<td>85</td>
<td>9*</td>
<td>8</td>
</tr>
<tr>
<td>12. H.S.</td>
<td>43</td>
<td>MNS</td>
<td>&lt;1</td>
<td>90</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>13. E.C.</td>
<td>52</td>
<td>Polycystic</td>
<td>&lt;1</td>
<td>70</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>14. W.B.</td>
<td>36</td>
<td>CGN</td>
<td>&lt;1</td>
<td>70</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Mean</td>
<td>45.6</td>
<td>77.8</td>
<td>6.6</td>
<td>6.6</td>
<td></td>
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</tr>
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</table>

CGN = Chronic glomerulonephritis
MNS = Malignant nephrosclerosis
* = Dialysis for more than 3 years.
CCR = Creatinine Clearance

The patients were dialysed with an EX-01 or EX-03 coil dialyser for 15–18 hr per week during a control period (CP) of 1–15 months (mean 6.6 months). At the end of CP all patients were dialysed with two Gambro dialysers, four hours each day on three days a week, (24 m² hours per week) for 3–13 months during a study period (SP) averaging 6.7 months.

The diet consisted of 80 g protein, 1.2 g potassium and 3000–4000
calories/day throughout the CP and SP. Multivitamins one tablet and folic acid 1 mg were given daily to all patients. Aluminium hydroxide in doses of 1.8 to 7.2 g/day was used to maintain pre-dialysis phosphorus level below 6 mg%. Iron dextran (‘Imferon’) 30 ml (1500 mg) in 150 ml of 5% Dextrose and water was given to all patients with less than 20% saturation of total iron binding capacity. All patients received intramuscular injections of testosterone enanthate 200–400 mg/week.

Pre-dialysis weight, blood pressure and haematocrit were recorded for each dialysis. Blood chemistries (BUN, creatinine, etc.) were evaluated twice each month. Nerve conduction velocities, measured one day after the day of dialysis, were evaluated every four months. Mean values for median and ulnar nerves in both upper extremities and peroneal nerves in both lower extremities were compared at the end of CP and SP.

Two Gambro dialysers were connected in series with counter current flow dialysate using a Drake-Willock proportioning delivery system with slight modification of the location of blood leak detector. A blood pump was used on all patients, blood flow and dialysate flow being maintained at 200 ml/min and 500 ml/min respectively. Gambro dialysers were discarded after a maximum of 12 dialyses with an average reuse of 8 times. Reasons for discarding dialysers before the twelfth reuse included accidental breakage, blood leaks and pyrogen reactions.

Clearance of BUN and creatinine was measured in vivo at \( Q_B = 200 \) and \( Q_D = 500 \text{ ml/min} \), with venous resistance close to zero, using the formula

\[
\text{Clearance} = \frac{Q_B}{C_{B1}} \frac{C_{B1} - C_{B0}}{C_{B1}}
\]

Clearance of crystalline Vitamin B\(_{12}\) was measured by the method described by Shideman et al (1973) modified for a single-pass test fluid flow of 200 ml/min and single-pass dialysate flow of 500 ml/min at test fluid out-flow pressure of zero, 100, and 200 mm Hg using the following formula:

\[
\text{Clearance} = \frac{Q_{B1} \times C_{B1} - Q_{B0} \times C_{B0}}{C_{B1}}
\]

\( Q_{B1} \) = Blood flow in (test fluid), ml/min
\( Q_{B0} \) = Blood flow out (test fluid), ml/min
\( C_{B1} \) = Concentration of blood in (test fluid B\(_{12}\) concentration)
\( C_{B0} \) = Concentration of blood out
\( Q_{B1} \) = Volume in first container at zero time, minus the volume after 10 min, divided by 10
\( Q_{B0} \) = Volume in second container after 10 min minus the volume at zero time, plus 60 cc drawn for B\(_{12}\) levels, divided by 10
\( UF = Q_{B1} - Q_{B0} \text{ ml/min} \)
Duration of each test was 10 min. Samples of 10 ml for B_{12} levels were drawn from arterial and venous sides at 5th, 6th and 7th minutes of the study.

RESULTS

The general feeling of well being improved during SP. Patients’ acceptance of this new dialysis schedule was excellent, especially among working patients. Values for BUN, creatinine, serum albumin and lean body weight during the CP and SP are shown in Table II.

<table>
<thead>
<tr>
<th></th>
<th>Control Period Mean ± SEM</th>
<th>Study Period Mean ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN mg%</td>
<td>81 ± 2.3</td>
<td>80 ± 2.6 NS</td>
</tr>
<tr>
<td>Creatinine mg%</td>
<td>16 ± 0.98</td>
<td>16 ± 1.06 NS</td>
</tr>
<tr>
<td>Serum albumin g%</td>
<td>3.6 ± 0.10</td>
<td>3.8 ± 0.08 NS</td>
</tr>
<tr>
<td>Body weight kg</td>
<td>77 ± 3.6</td>
<td>74 ± 6.2 NS</td>
</tr>
<tr>
<td>Hematocrit %</td>
<td>25 ± 0.76</td>
<td>29 ± 1.9 &lt;0.05</td>
</tr>
<tr>
<td>NCV upper ext.</td>
<td>45 ± 2.3</td>
<td>45 ± 2.0 NS</td>
</tr>
<tr>
<td>NCV lower ext.</td>
<td>36 ± 1.6</td>
<td>35 ± 1.7 NS</td>
</tr>
</tbody>
</table>

SEM = Standard error of mean  
NCV = Nerve conduction velocity  
NS = Not significant

The haematocrit improved significantly (p < 0.05) during the study period in 13 patients. Transfusion requirements decreased from 2.7 units per month during the CP to 1.5 units per month during the SP in one patient. The mean transfusion requirement for the group was 0.4 units per patient per month during the CP and 0.35 units per patient per month during the SP.

Although the mean value for nerve conduction velocity (NCV) of the upper and lower extremities did not change significantly during the SP, in patients 1, 4, 5 and 14 there was some improvement (>4 m/sec) in the mean NCV of the upper extremities and in patient 6 in the lower extremities. In patient 3 progressive neuropathy arrested during the SP and in patient 6 neuropathy progressed during the SP. NCV in the lower extremities in patients 5, 9 and 10 was zero throughout the study. For patients 9 and 13 NCV data was incomplete. Clearance, BUN and creatine clearance for two Gambro dialysers were 166 ± 12 ml/min and 130 ± 6 ml/min (Mean ± SD) respectively and did not change in multiple reuse. Vitamin B_{12} clearance for two Gambro at TFOFP of zero, 100 and 200 was 33 ± 1, 43 ± 1, and 46 ± 3 respectively.
DISCUSSION

Reduction of the dialysis hours by increasing the surface area with two Gambro dialysers has been the most encouraging and important aspect of this study. Patients were able to work longer hours and spend more time with their families. The capacity of the dialysis unit was increased and the total cost of dialysis per patient was reduced. A relatively high clearance of small and middle molecule uraemic toxins was not significantly reduced with multiple reuse. This, combined with low leak rate, made the double Gambro arrangement the most feasible dialyser for this study.

The patients accepted the new dialysis schedule enthusiastically and their general feeling of well-being improved. Serum albumin and dry body weight increased during the study period in some patients, indicating improved nutritional status. Mean Haematocrit was significantly higher during the study period (p<0.05), perhaps attributable to more adequate dialysis.

The reuse procedure is uncomplicated, safe and takes 15–30 min to perform. The leak rate was 2% in reused Gambro units, and the pyrogen reaction rate was less than 0.1 per patient per month. Reuse was not practised in patients with intercurrent infections or in HAA-positive patients. Because of the shorter dialysis time, three patients could be dialysed in a two-nursing-shift work schedule on one day. This resulted in 30% saving in the cost of space, equipment and personnel salaries—which are the major cost of haemodialysis. The cost of dialysers was significantly reduced by reusing up to 10–12 times.

Mean distal nerve conduction velocities of upper and lower extremities improved in five patients; this could indicate better removal of middle molecule uraemic toxins during the study period. In patient 3, with malignant hypertension, neuropathy did not improve during the SP. In patient 12, necrotising vasculitis of malignant hypertension may have been a contributing factor in the deterioration of nerve conduction velocity observed during both control and study period. This patient had developed severe retinopathy and subsequent blindness before dialysis was started.

The disequilibrium syndrome was not seen with four-hour dialyses thrice weekly. Ultrafiltration up to 750 ml/hr or 3 kg in four hours could be achieved without difficulty. In patients with high intrinsic venous resistance, excessive ultrafiltration was replaced with normal saline throughout each dialysis to prevent hypotension and muscle cramps.

CONCLUSIONS

1. Haemodialysis with two Gambro dialysers for four hours, three days each week is safe and adequate for chronic stable dialysis patients.
2. Better removal of middle molecule uraemic toxins may have resulted in
improvement of haematocrit and nerve conduction velocity in some patients.

3. This mode of haemodialysis increases the capacity of a haemodialysis unit
to permit dialysis of 30% more patients with the same space, equipment and
personnel. With reuse, it also decreases the cost of dialysers as well as the total
cost of haemodialysis.

4. This system may represent one more step toward an ideal, safe, adequate,
short, frequent, less expensive haemodialysis with semi-disposable dialysers
available for anyone with chronic renal failure.

5. Efforts should be made toward developing a dialyser with better middle
molecule clearance by increasing the surface area or improving the permeability
of the membrane, or both. If either of these developments could be achieved,
adequate dialysis could be accomplished in two to three hours on alternate days.
These developments might make in-centre dialysis more competitive in terms of
cost compared to home dialysis.

Acknowledgements

We wish to thank all unit personnel, and in particular James Kelly and Gary
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Open Discussion

V CAMBI (Italy) Did you try treating the same patient that you had treated with 2 square meters with 1 square meter? How long did you treat this patient and why do you say that the recent improvement in the well-being of this patient is similar to the results obtainable with 1 square meter dialysis? I would like to heavily criticise the use of motor nerve conduction velocity. Unfortunately it is one of the reasons why for ten years and more we were dialysing 30 hours per week. The variability of motor nerve conduction velocity does not allow judgements of this sort.

MIRAHMADI All fourteen patients were dialysed with a coil dialyser for 15–18 hours a week during the control period which I showed on the first slide. Then they were switched to the 2 square meter dialysis. The object was to see if by increasing the middle molecule clearance we could show any improvement in various parameters. I can say this new schedule was extremely well accepted by most patients, especially working patients. They were able to come to the unit at 5 pm and leave by 9 pm for home.

Thank you for your comments on nerve conduction: I am well aware of the problems with this test.

S SHALDON (France) Kjellstrand, Vittel (Journées International de Néphrologie, Vittel, 1974) recently analysed the increase in symptomatic trauma occasioned by shortening dialysis time. Patients’ symptoms during short dialysis were significantly worse in terms of vomiting, cramps, nausea, and transient episodes of hypotension. Are you sure that short dialysis with its higher ultrafiltration rate and larger extracorporeal blood volume is worthwhile in terms of the patient’s safety and comfort during dialysis compared with longer and perhaps more physiological methods?

MIRAHMADI In the interviews we have had with patients most of them seem to be very happy with the short dialysis, although some of the minor complications might be more than that of long dialysis.

H C BURCK (GFR) An important factor in anaemia in dialysis patients is blood loss. Was blood loss the same in both your groups, and were side effects, such as headache and cramp, the same in both groups?

MIRAHMADI Blood loss was not measured exactly. Blood tests were done twice a month on both patient groups, amounting to 60 ml blood per month. It was the same during the study period and control period.

H BUCHT (Sweden) In Göteborg we have used two Gambro dialysers 4 hours, 3 times a week for a year. The patients complained, so we used one Gambro 5 hours, 3 times a week. The data you mentioned did not change between the two groups and the patients felt better.