Blood Loss During Haemodialysis: an Evaluation of the Ab Gambro System

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The regular dialysis patient remains anaemic in spite of efficient haemo- dialysis. During dialysis it is inevitable that some blood is trapped in the dialyser and its blood lines and is, thus, lost to the patient aggravating the anaemia. It is important that this iatrogenic blood loss should be minimised as blood transfusion is undesirable in this group of patients because of the risks of hepatitis (Drukker et al, 1968) and because of the possible development of leucocyte antibodies which could jeopardise subsequent renal transplantations (Batchelor, 1969).

The advantages of a new disposable parallel flow dialyser made by the Swedish firm, AB Gambro have been separately described by Alwall (1968) and Kulatilake (1969). Neither author, however, seriously considered the blood lost to the patient by this system. We have, therefore, measured the blood loss in the AB Gambro dialyser and compared it with the Travenol 'Ultra-Flo' 100 coil as routinely used in this hospital. We, also, have determined the reason for blood being trapped in the AB Gambro dialyser by examining used membranes and by studying the nature of the blood flow and the linear blood velocity through this dialyser.

MATERIALS AND METHODS

The AB Gambro dialyser has a dialysis area of one square meter made from Cuprophane membrane arranged in eleven compartments. An exploded diagram of this dialyser is shown in Figure 1. Three and six layer paediatric dialysers with correspondingly smaller dialysis areas are also produced by AB Gambro and were studied.

The Travenol Ultra-Flo 100 coil contains two cellophane or cuprophane membrane tubes, with a dialysis area of one square meter, which are wound into a coil configuration and supported by plastic mesh backing.
Figure 1. Exploded view of the Gambro dialyser – the stippled area shows site of trapped blood within the blood manifold

PATIENTS

During dialysis all patients were heparinised using an initial dose of 2,000 units at start of dialysis and 1,500 units per hour of dialysis. The clotting time at 37°C was always in excess of 40 minutes with this regime.

ESTIMATION OF BLOOD LOSS

The blood trapped in the two types of dialyser was measured as follows:-

In five patients, red cell labelling with $^{51}$Cr as for the technique of red cell survival (Dacie, 1963) was carried out using a total of 120 $\mu$Ci $^{51}$Cr. Towards the end of each dialysis a venous sample of blood was withdrawn to provide a standard for each assay. At the end of dialysis the dialyser was completely dismantled and cut separately into small pieces. The fragments were placed in identical 1 gallon (4 litre) cans containing 100 ml of pure alcohol and granite chips. The volume was made up to 1 gallon (4 litres) with tap water and the cans were sealed. The standard blood sample was handled identically. To achieve uniform dispersion of the isotope the cans were agitated in a paint shaker for 5 minutes. Counting was carried out in a scintillation counter with a 2$\frac{3}{4}$" (7 cm) sodium iodide crystal and a 2" (5 cm) lead shield according to the method used by Watson (1964) for the estimation of faecal blood loss. The volume of blood trapped was computed by a comparison with the standard.

Initially three of the patients were dialysed alternately by the AGBambro and Travenol systems until ten estimations were made on each system. The technical details of these dialysers are shown in Table I. The 'wash-back' procedures employed were as follows:-

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Table I. Technical Data of Dialysers

<table>
<thead>
<tr>
<th>Dialyser</th>
<th>Duration of Dialysis</th>
<th>Blood Flow Rate</th>
<th>Dialysate Flow Rate</th>
<th>'Venous' Pressure (in Dialysate)</th>
<th>Dialysate Pressure mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Travenol Ultraflo 100</td>
<td>10 hr</td>
<td>225–275 ml/min</td>
<td>250 ml/min</td>
<td>50–100 mm Hg</td>
<td>0 mm Hg</td>
</tr>
<tr>
<td>AB Gambro 10</td>
<td>250 ml/min</td>
<td>500 ml/min</td>
<td>80 mm Hg</td>
<td>-100 mm Hg</td>
<td></td>
</tr>
</tbody>
</table>

* Roller type flow inducers used on arterial side

1. Travenol System:
At the end of each dialysis the arterial side of the patient's shunt was closed and blood in the arterial tubing was allowed to enter the coil. The blood was then pushed through the coil by 500 ml normal saline which was pumped into the arterial side of the coil at a flow rate of 150 ml/minute and minimum venous pressure possible (0 – 20 mm Hg) in these circumstances. During 'wash-back' the coil was lifted from the container and, free from its cuff, was placed on its side above the container to facilitate drainage of the blood.

2. AB Gambro System: – Procedure 1 –
Thirty minutes prior to the cessation of each dialysis the venous pressure was reduced to a minimum (0 – 40 mm Hg) and the dialysate pressure to – 50 mm Hg and the dialyser was tilted at 60° to the horizontal with the venous end lowermost. The arterial line was emptied as described above and 'wash-back' was carried out using 1 litre of 0.9 g/100 ml saline at a flow rate of 150 ml/minute.

   The fourth patient with 51Cr labelled red cells was then dialysed on five occasions by Gambro dialysers and the blood loss again was measured. In these experiments, however, a different 'wash-back' procedure was employed, the details of which are as follows:–

   – Procedure 2 –
Thirty minutes prior to the cessation of each dialysis the venous pressure was reduced to a minimum (0 – 40 mm Hg) and the dialyser was tilted as described previously. During the 'wash-back' the flow rate was maintained at 250 ml/minute and the dialysate negative pressure was increased to – 150 mm Hg. The 'wash-back' volume of 0.9 g/100 ml saline was 1 litre.

   The actual dialyses were conducted as previously (Table I).

   The fifth patient was dialysed by the Gambro system on six occasions. On four occasions paediatric dialysers were used. In these experiments the duration of dialysis was varied but, otherwise, the dialyses were as shown in Table I. The three layer dialyser was used for a two-hour and a six-hour dialysis and the six-layer dialyser for a two-hour and a ten-hour dialysis.

The adult (eleven layer) dialyser was used on two occasions for two and six
hours respectively. The 'wash-back' was conducted using the second procedure, as described above, except that 600 ml of 0.9 g/100 ml saline was used when the paediatric dialysers were employed.

**Examination of membranes after dialysis**

On several occasions the Cuprophane membranes of the Gambro dialyser were examined after use. To fix the red cells and any thrombus formed during dialysis a buffered glutaraldehyde solution was pumped slowly through the dialyser blood manifolds immediately after the 'wash-back' procedure had been completed. Care was taken not to allow air to enter the dialyser between the N/saline 'wash-back' and the filling with glutaraldehyde. The blood ports were sealed and the dialyser was then left for two hours to allow fixing to take place. The dialyser was then dismantled and the blood compartments examined. Membrane samples, 0.25" x 0.25" (0.6 x 0.6 cm) were removed from the arterial and venous ends of the blood compartments and these were examined by the scanning electron microscope. Other samples were further fixed in 10% formalin and, after routine staining, were examined by light microscopy.

**Investigation of dialyser internal blood flow pattern**

Blood and dialysate pressure readings were taken at the respective inlets and outlets. At a given dialysate negative pressure, of approximately 100 mm mercury, blood flow rates through the dialyser were varied between 80 and 300 ml/minute and the corresponding pressures were measured. The blood flow rates were obtained by using an occlusive pump (Sarns, Travenol) calibrated with a Nycotron electromagnetic blood flow meter.

These pressure readings were made for the three, six and eleven layer Gambro dialysers.

**Estimation of blood velocity**

The blood velocity through each compartment or manifold was calculated from the blood flow rates and the appropriate manifold cross-sectional area.

The values for manifold cross-sectional areas were calculated from the wet priming volume of each dialyser's blood compartment, as measured at atmospheric pressure, and from the dimensions of the blood compartment. Errors due to the blood inlet and outlet tubes were minimised by subtracting the tube volumes from the apparent priming volumes. The blood velocity was calculated for all three Gambro dialysers and for the Ultra-Flo 100 Cuprophane and Cellophane Coils.

**RESULTS**

The volumes of blood trapped in the dialysers under the varying conditions studied are shown in Tables II and III.

Macroscopic examination of the blood compartments of the AB Gambro
Table II. Volume of blood trapped in the 11-layer AB Gambro and Travenol Ultra-Flo coil dialysers

<table>
<thead>
<tr>
<th>Dialyser</th>
<th>'Wash-Back' Procedure</th>
<th>Residual Blood Volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB Gambro (n=10)</td>
<td>No. 1</td>
<td>29.6 ± 4.06</td>
</tr>
<tr>
<td>AB Gambro (n=5)</td>
<td>No. 2</td>
<td>29.2 ± 2.13</td>
</tr>
<tr>
<td>Travenol U. F. 100 Cellophane (n=10)</td>
<td>-</td>
<td>6.58 ± 0.77</td>
</tr>
<tr>
<td>Travenol U. F. 100 Cuprophan (n=5)</td>
<td>-</td>
<td>6.60 ± 0.63</td>
</tr>
</tbody>
</table>

Results expressed as mean ± s.e.m.

Table III.

<table>
<thead>
<tr>
<th>Dialyser</th>
<th>Residual Blood Volume (ml) after Varying Durations of Dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB Gambro 3 layer</td>
<td>7.5 6.3 -</td>
</tr>
<tr>
<td>AB Gambro 6 layer</td>
<td>42.8 - 18</td>
</tr>
<tr>
<td>AB Gambro 11 layer</td>
<td>36 46 29.6*</td>
</tr>
<tr>
<td>Duration of Dialysis (hr)</td>
<td>2 6 10</td>
</tr>
</tbody>
</table>

* n=10
Other results are those of single estimations

dialyser showed that the trapped blood lay mainly at the venous or outlet end of the dialyser – (Figure 1). Scanning electronmicrographs and histological examination on light microscopy showed that there existed a thrombus in this region – the trapped red cells being caught in a mass of fibrin (Figure 2).

In Figure 3 the internal pressure drop (mm Hg) through the blood compartment is shown plotted against the blood flow for the three types of Gambro dialyser.

The dimensions of an AB Gambro blood compartment (manifold) are 53 cm in length and 13 cm in width. The Travenol coil has two blood tubes each of 5.8 m in length and 4.5 cm in width. From the wet priming volume the average blood manifold height and cross-sectional area were calculated. These results are given in Table IV. The average linear velocities of blood travelling through the manifolds of the different dialysers at varying machine blood flow rates are shown in Table V.

DISCUSSION

The results show that the amount of blood trapped in the AB Gambro dialyser is over four times that trapped by the Travenol coil. This difference is
Figure 2. Photograph taken with the scanning electronmicroscope showing a fibrin meshwork on the dialysis membrane. Magnification x 3400

<table>
<thead>
<tr>
<th>Dialyser</th>
<th>Wet Priming Volume</th>
<th>Average Manifold Height cm</th>
<th>Blood Manifold Cross Sectional Area cm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gambro 3 layer</td>
<td>63 ml</td>
<td>0.030 cm</td>
<td>1.17 cm²</td>
</tr>
<tr>
<td>Gambro 6 layer</td>
<td>104 ml</td>
<td>0.025 cm</td>
<td>1.95 cm²</td>
</tr>
<tr>
<td>Gambro 11 layer</td>
<td>130 ml</td>
<td>0.0172 cm</td>
<td>2.46 cm²</td>
</tr>
<tr>
<td>Travenol coil</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultraflo 100</td>
<td>274 ml</td>
<td>0.0525 cm</td>
<td>0.4725 cm²</td>
</tr>
<tr>
<td>Cellophane</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Travenol coil</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultraflo 100</td>
<td>282 ml</td>
<td>0.054 cm</td>
<td>0.486 cm²</td>
</tr>
</tbody>
</table>
Figure 3. The internal pressure drop (mm Hg) along the length of the blood manifold is shown plotted against the blood flow for the three types of Gambro dialyser.

Table V. Average blood linear velocity in dialyser manifold

<table>
<thead>
<tr>
<th>Machine Blood Flow ml/min</th>
<th>Gambro 3 layer</th>
<th>Gambro 6 layer</th>
<th>Gambro 11 layer</th>
<th>Travenol Coil Ultraflo 100 (PT 300)</th>
<th>Travenol Coil Ultraflo 100 (Cuprophan)</th>
</tr>
</thead>
<tbody>
<tr>
<td>QB</td>
<td>1.43</td>
<td>0.85</td>
<td>0.68</td>
<td>3.52</td>
<td>3.42</td>
</tr>
<tr>
<td>200</td>
<td>2.86</td>
<td>1.70</td>
<td>1.36</td>
<td>7.05</td>
<td>6.84</td>
</tr>
<tr>
<td>300</td>
<td>4.29</td>
<td>2.55</td>
<td>2.04</td>
<td>10.5</td>
<td>10.26</td>
</tr>
</tbody>
</table>

statistically highly significant (P<0.001). A blood loss of nearly 30 ml/ dialysis is, in our view, undesirable for the regular dialysis patient. This view is shared by Kerr (1969) who states that a new dialyser is only acceptable if the total (that is, dialyser plus blood lines) residual blood volume is well below 20 mls. The blood losses recorded in this paper do not include that blood trapped in the blood lines. An attempt to lessen the blood loss by adopting a different 'wash-back' technique failed. This, however, is not surprising as we have shown that the red cells lost to the patient are part of
a thrombus formed on the dialysis membrane during dialysis (Figure 2). It would be unlikely, therefore, that different 'wash-back' techniques or even larger 'wash-back' saline volumes would be able to return significantly more blood to the patient.

The volume of blood we estimated to be trapped in the Ultra-Flo 100 coils (Cellophane and Cuprophane) is similar to that reported by Nidus (1969) but slightly higher than that reported by Muth (1969). These authors used a less precise method which involved haemoglobinimetry on the saline 'wash-through'. It is obvious that such a method will grossly underestimate the residual blood volume if thrombus formation has occurred. We suspect that this may explain the discrepancy between our results for that blood volume trapped in the AB Gambro dialyser and the figure of 11 ml quoted by Rastogi and his colleagues (1969). These authors do not give any details of the method used in their investigation. To our knowledge there are no other published figures for the residual blood volume of this dialyser.

The development of thrombus formation on the dialysis membrane during dialysis with adequate heparin anticoagulation appears surprising. Muir (1970), however, has observed by in vitro experiments using the Ross-Muir dialyser that thrombus formation will occur on cellulose-based membranes if the average linear blood velocity falls below 5 cm/sec after running periods of 5 hours. In these experiments the circulating blood was fully heparinised. The pattern of blood flow through this dialyser is in accordance with Poiseuille's Law and the linear plot of pressure drop against blood flow rate indicates that the same is true for the AB Gambro dialyser (Figure 3).

It is seen in Table V that each of the AB Gambro dialysers (3, 6 and 11 layer) will have average linear blood velocities of less than 5 cm/sec under clinical conditions, that is with blood flow rates of 200-300 ml/min. These linear blood velocities are, in fact, so low that thrombus formation occurs even after two hours of dialysis (Table III). The values shown in Table V are the maximum possible since the manifold cross-sectional areas were estimated without negative pressure being applied to the dialysate side of the membrane. The application of negative pressures will distend the membrane and would be expected to increase the blood manifold cross-sectional area which, in turn, would reduce the average blood velocity.

The reason that most of the thrombus formation appears to take place at the venous or outlet end of the blood manifold is not, as yet, fully understood. If the linear blood velocity was constant along the length of the blood manifold and this velocity was less than 5 cm/sec then thrombus formation might be expected to be evenly distributed along the manifold. We can give two possible explanations which may wholly or be partly responsible for this occurrence. These are demonstrated diagrammatically in Figure 4.

In the first place, we have noted a greater pressure drop over the length
of the dialysate manifold than over the length of the blood manifold when the blood flow rate is within the clinically used range. This is explained by the higher dialysate flow rate. This occurrence will lead to a greater transmembrane pressure at the venous or outlet end of the blood manifold. An increase in the manifold cross-sectional area at this end will occur and, in turn, the blood velocity will drop further and lead to the initial thrombus formation. Furthermore, phase separation of red cells and plasma may occur. Muir and Gaylor (1970) have demonstrated such phase separation in an experimental manifold of similar dimensions to the Gambro manifold with blood velocities under 5 cm/sec. If this occurs then the slower moving red cells will tend to be deposited upon the membrane and caught up in the fibrin component of the thrombus.

The linear blood velocities through the Travenol coils (Cuprophan and Cellophane) are in excess of 5 cm/sec providing the blood flow rate is well in excess of 100 ml/minute (Table V) and thrombus formation was not found to occur. It would not be advisable to conduct a coil dialysis with blood flow rates of 100 ml/minute or less as thrombus formation may occur and lead to increased patient blood loss.

We submit that the present design of the AB Gambro dialyser is such that high blood losses are inevitable to the patient. However, if practical comparisons are to be made between this dialyser and the Travenol coil, then consideration of the respective leakage rates must be made. Our current leakage rate with the Travenol coil lies between 2 and 5% and each leaking coil will mean a loss of approximately 350 ml whole blood to the patient. We have not experienced a single leak in 50 Gambro dialyses. Over
a prolonged period, therefore, the difference between Travenol and Gambro
dialyser blood losses will be diminished. We recommend to both manufac-
turers that steps be taken to reduce the blood loss to the patient using their
dialyser. Finally, we would recommend to all dialyser manufacturers to
consider the factors leading to patient blood loss with any new dialyser design.
Amongst these factors we would include the linear velocity of blood travelling
through the membrane manifolds.

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REFERENCES

Page 18. Excerpta Medica, Amsterdam
Batchelor, J. F. (1969) British Journal of Hospital Medicine, 2, 7, 1199
Dacie, J. V. and Lesh, S. M. (1963) In 'Practical Haematology', 3rd
and Transplant Association. Volume V. Page 3. Excerpta Medica,
Amsterdam
Volume VI. Page 319. Pitman Medical & Scientific Publishing Co. Ltd.,
London
Journal, 3. 447
Muth, R. F. and Wells, D. E. (1969) Archives of Internal Medicine, 124, 179
New York Stage Journal of Medicine, 1, 273
Pitman Medical & Scientific Publishing Co. Ltd., London
Watson, W. C. and Dickson, C. (1964) Gut, 5, 488