MEMBRANE PLASMA SEPARATION: PROCEDURAL RECOMMENDATIONS

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Introduction

Continuous plasma separation was developed by Nosé et al [1] and first used in humans for the treatment of hepatic coma in 1976 and 1977 [2, 3]. Since 1978 hollow fibre devices have largely replaced centrifuges for plasma separation. With these devices plasma is separated from blood by filtration through microporous membranes.

Plasma separation is an effective method to eliminate high molecular substances and will be used increasingly for a number of reasons: elimination of antibodies and immune complexes, protein bound hormones and toxins and other foreign serum components.

At our institution we have used this procedure since May 1979 and since then performed more than 100 separations on seven patients without complications (one patient with Goodpasture’s Syndrome, one with systemic lupus, one with immune complex vasculitis, three with rapidly progressive glomerulonephritis and one with transplant rejection.

Material and methods

The filters were either from Asahi Med. Co. (surface: 0.65m², and pore width 0.2μ) or from MTS Co., St Wendel (surface 0.8m², pore width 0.2μ).

According to the manufacturers both have a cut-off point at 3 mill. daltons. Balancing and substitution of the filtered plasma was done with the haemofiltration machine of Dialyse Tecknik Co., Karlsruhe. Immune globulins were determined using a laser nephelometer (FA, Behring, Marburg).

Substitution Balancing and substitution of the filtered plasma should be done by using a haemofiltration machine to avoid side effects from volume variations.

In the acute phase of Goodpasture’s Syndrome fresh frozen plasma should be used. With this regime clotting factors are available and diminish the chance of
bleeding into the lung.

For the other indications we used a substitution solution based on a haemofiltration solution with the addition of 20% human serum albumin (HSA) with the following composition listed as 1 in Table I.

TABLE I

<table>
<thead>
<tr>
<th></th>
<th>Na</th>
<th>K</th>
<th>Ca</th>
<th>Cl</th>
<th>P</th>
<th>Fe</th>
<th>Cu</th>
<th>Zn</th>
<th>Mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>159</td>
<td>2.2</td>
<td>3.0</td>
<td>88</td>
<td>0.4</td>
<td>9.8</td>
<td>7.5</td>
<td>12.18</td>
<td>1.1 mmol/L</td>
</tr>
<tr>
<td>2</td>
<td>145</td>
<td>3.5</td>
<td>2.5</td>
<td>105</td>
<td>1.0</td>
<td>15</td>
<td>15</td>
<td>13</td>
<td>1.5 mmol/L</td>
</tr>
</tbody>
</table>

During all treatments serum electrolytes were within normal limits.

A more desirable composition of replacement fluid is listed as 2 in Table I. But this is not yet available.

Heparinisation

For heparinisation the patients were given heparin by an initial IV dose and then by continuous infusion. Dosage should be flexible and coagulation should be controlled by measuring activated partial thromboplastin time (APTT). Generally the initial dose (about 2500–4000IU) and the maintenance dose (1200–2300IU) is 2–3 times higher than in haemodialysis. However the consumption of heparin decreases during the procedure because of loss of clotting factors. For one plasma separation about 4500–7500IU heparin is necessary. If heparinisation is done according to the actual APTT value, APTT values can be held within narrow limits (47–75 sec) without clotting. With this procedure bleeding due to overdosage is avoidable. This is especially useful in patients with bleeding tendencies as with Goodpasture’s Syndrome.

Effectiveness of the procedure

A plasma exchange of 5L can be done in 60 minutes with a blood flow of 225 ml/min and a transmembrane pressure (TMP) of about 150mmHg. This corresponds to a plasma filtrate flow of about 83ml/min. Under these conditions no haemolysis is observed, as shown by plasma haemoglobin determinations.

In contrast to haemofiltration, plasma filtration has to be performed with lower TMP, as higher TMP induces secondary membranes (proteins and platelet layers on the membrane), which lowers filtrate flow.

Lower filtrate flows also result from higher heparinisation, probably because of decreasing separation of plasma and blood cells on the capillary wall with increasing deposition of platelets [4]. With TMP's higher than 200mmHg red blood cells will be deposited on the surface of the filter with consecutive haemolysis.

To calculate the TMP exactly, the resistance on the blood side and the AV difference of the filter, has to be determined in addition to the negative pressure on the filtrate side. Measurement at different blood flow rates showed a linear
increase of the resistance from 40–85 mmHg with blood flow rate from 150–300 ml/min. The AV-pressure difference is therefore in the same range as that of the hollow fibre filters used for haemodialysis.

Figure 1. Mean values for oncotic pressure and blood pressure during six plasma separations with 3% albumin-electrolyte substitution.
Oncotic pressure

To prevent hyper- or hypovolaemia with the possible danger of lung oedema by having the wrong HSA concentration, it is highly desirable to measure the oncotic pressure before the start of treatment. The albumin concentration in the substitution fluid should be chosen, so that the solution has about the same oncotic pressure as that of the patient.

As up to 50% of the albumin can leave the vascular space, deviations of oncotic pressure are still possible. This makes repeated determination of the oncotic pressure necessary.

In Figure 1 the values for oncotic pressure during six plasma separations are shown. With a starting oncotic pressure of 14—17 mmHg and using a 3% HSA-electrolyte solution, parameters are nearly stable throughout the procedure.

Only once was a 2% HSA solution used. Signs of increasing hypovolaemia, like falling blood pressure and increasing pulse rate, made it necessary to increase the HSA concentration. These side effects are due to the unphysiological low oncotic pressure of this solution, which should not be used. This is in contrast to other authors [5—7] who have used 2% or 2.5% HSA solution without measuring the oncotic pressure.

With HSA concentrations of 3—5% corresponding to the oncotic pressure of the patient, no side effects were observed.

A 5L plasma exchange reduces fibrinogen, IgM, IgA, IgG, complement factor C3 to 50—60% of the initial value.

Blood count is not altered substantially during the procedure. There was a reduction in leucocytes of 11 ± 4%, haematocrit (initial value = 100%) of 6 ± 2% and platelets of 13 ± 4%.

Measuring of the sieving coefficients (IgG, IgA, C3 and IgM) shows a falling permeability with increasing molecular weight and duration of treatment.

Acknowledgments

We wish to acknowledge the immunological measurements by Dr G Kratzsch, Division of Internal Medicine I, University of Ulm.

References

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356