Experimental and Clinical Results of Continuous Hypothermic Albumin Perfusion

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Continuous perfusion has previously been shown to be the method of choice in renal preservation at least when the storage time exceeds 10 hours (Belzer, Claes et al., 1971). Previously most perfusions have been performed with cryoprecipitated milli-pore filtered plasma as perfusate. There are however, several drawbacks with plasma: it is time consuming and laborious to prepare, it is poorly standardised, there is a potential risk of contamination with hepatitis virus and of the presence of cytotoxic antibodies which may damage the kidney. We have therefore tried albumin as perfusate in the Gambro perfusion machine.

MATERIAL AND METHODS

The experimental studies were performed in five series of consecutive dogs. The left kidney was removed. If warm ischaemia was included, the kidney was left in the abdomen after division of the renal artery and vein. Thereafter the kidney was initially perfused with 5 ml 1% xylocaine at room temperature followed with 100 ml of cold low molecular weight dextran and then connected to the perfusion machine. After storage the kidneys were autotransplanted to the neck where the vessels were anastomosed to the carotid artery and the jugular vein respectively. The urine was channelled through a skin ureterostomy. Immediate contra-lateral nephrectomy was performed at the time of retransplantation. Function of the kidney was studied by daily measurements of serum creatinine during the first week, and three weeks after transplantation inulin- and PAH-clearances were performed. The perfusate used was either cryoprecipitated milli-pore filtered plasma according to Belzer or 4.5% human albumin solution (KABI) with additives as recommended by Belzer. The following experiments were performed:

Group I: 30 minutes warm ischaemia, 24 hours plasma perfusion, (n=5);
Group II: 30 minutes warm ischaemia, 24 hours albumin perfusion, (n=5);
Group III: No warm ischaemia, 72 hours plasma perfusion, \((n=5)\);
Group IV: No warm ischaemia, 72 hours albumin perfusion, \((n=3)\);
Group V: No warm ischaemia, 96 hours albumin perfusion, \((n=5)\).

In the human material we have compared plasma and albumin perfused kidneys with previous results using hypothermically stored kidneys. This comparison was made in order to evaluate different preservation methods on kidneys of the same type. Most of our kidneys were damaged both by warm ischaemia and by prolonged hypotension before death. The human material was divided into four groups:

Group I: Kidneys stored by simple hypothermia for less than 10 hours, mean 6 hours;
Group II: Kidneys stored by simple hypothermia for more than 10 hours, mean 12 hours;
Group III: Kidneys stored by plasma perfusion, mean 15 hours;
Group IV: Kidneys stored by albumin perfusion, mean 18 hours. (Figure 1)

Most of the machine perfused kidneys had a considerable time of cold storage prior to preservation, sometimes up to 10 hours. The quality of preservation was judged from the frequency of immediate function after transplantation. Immediate function means the immediate onset of diuresis with a decrease of serum creatinine during the first 24 hours after transplantation.

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**Figure 1.** Preservation time in the material of human kidneys
RESULTS

In the experimental groups I and II exactly the same results were obtained. One of the five dogs in each group had a renal artery thrombosis on day four, rise in serum creatinine to slightly above 2 mg/100 ml was highest in the second or third day and most had normalised the serum creatinine within the first week (Figure 2).

In group III two dogs had renal artery thrombosis, three dogs survived. The serum creatinine rose to a maximum of 7 mg/100 ml but returned to normal for the three survivors after 14 days.

In group IV all three dogs survived, the maximum rise in serum creatinine was up to 5 mg/100 ml with return to normal after one week (Figure 3).

Figure 2. Serum creatinine of dogs in group II

Figure 3. Serum creatinine of dogs in group IV
In group V all dogs survived the first two weeks but with a marked increase in serum creatinine three dogs had normal serum creatinines after three weeks (Figure 4).

Clearance studies performed in group I, II, IV and V three weeks after storage revealed the following values expressed as ml/min/g kidney tissue.

<table>
<thead>
<tr>
<th>Group</th>
<th>Inulin ml/min/g</th>
<th>PAH ml/min/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I: 30 min warm ischaemia 24 h plasma perfusion</td>
<td>0.59</td>
<td>1.81</td>
</tr>
<tr>
<td>Group II: 30 min warm ischaemia 24 h albumin perfusion</td>
<td>0.62</td>
<td>3.05</td>
</tr>
<tr>
<td>Group IV: No warm ischaemia 72 h albumin perfusion</td>
<td>0.79</td>
<td>2.43</td>
</tr>
<tr>
<td>Group V: No warm ischaemia 96 h albumin perfusion</td>
<td>0.48</td>
<td>2.17</td>
</tr>
<tr>
<td>Control material</td>
<td>0.65 - 0.90</td>
<td>1.8 - 2.6</td>
</tr>
</tbody>
</table>

In the human material immediate onset of function in group I was obtained in 22%, in group II in 7%, in group III 35% and in group IV 60% (Figure 5). In the albumin perfused group we also compared kidneys stored in the machine between 10 and 20 hours and kidneys stored between 20 and 35 hours. There
was no difference in onset of function between these two groups.

Of two kidneys stored for 35 hours both had immediate onset of function.

DISCUSSION

The use of albumin for continuous hypothermic perfusion has previously been described by Collste et al (1970) and Johnson et al (1971). They also performed comparative studies with plasma perfusion and also obtained the same results with the two perfusates used. Albumin is commercially available, standardised and can be stored in the refrigerator which makes the starting up of a perfusion a very rapid procedure. It takes about 30 minutes to load the machine with a pre-sterilised disposable set, fill it with perfusion fluid and connect the kidney to the machine.

The differences in the experimental series between albumin and plasma perfused dog kidneys were not significant. It has been shown that continuous perfusion with albumin is possible even up to 96 hours. In the human material considerably better results were obtained after albumin, compared to plasma perfusion. This may partly be explained by a slightly lower warm ischaemia time in this group. Twenty minutes compared to 30 minutes in the plasma perfused group and the groups stored by simple hypothermia. In the plasma perfused group three kidneys underwent hyperacute rejection although cross-matching was negative. We suspect those hyperacute rejections to be due to cytotoxic antibodies in the plasma but it has not been possible to obtain definite proof for this mechanism. In the albumin perfused group no hyperacute rejection occurred.
CONCLUSIONS

The use of albumin in perfusate for continuous hypothermic perfusion has been shown to give as good results as plasma. Storage of dog kidneys up to 3 - 4 days and of ischaemically damaged kidneys up to 24 hours is possible. Better results were obtained in the human material after albumin than after plasma perfusion. Perfusate containing albumin is easy to prepare, there is no risk of contamination with hepatitis or presence of cytotoxic antibodies. We therefore advocate albumin instead of plasma for use in continuous hypothermic perfusion.

REFERENCES


OPEN DISCUSSION

C M KJELLSTRAND (Minneapolis, Minnesota): When you perfused dog kidneys, did you use dog albumin or human albumin?

CLAES: We used only human albumin both in the animal and in the human experiments.

J TRAEGGER (Lyon, Chairman): You always used the same preparation of albumin? Did you have trouble with other preparations?
CLAES: No we have only used one type of albumin that was commercially available in Sweden, so I have no experience of other types of albumin, but I think there might be a difference between them.

R W LAWTON (Iowa City, Iowa): I would like to ask if you measured the weight gain in your kidneys during the perfusion, what that weight gain was, and whether you were using a 4.5 g/100 ml solution of albumin.

CLAES: In the animal experiments we measured the weight gain and found it was exactly the same as in the plasma perfusion, about 10 to 15%. In Stockholm they have made similar experiments where they have used 6% albumin solution, and with a higher concentration of albumin they have no weight gain at all.