Effect of Viscosity of Cooled Blood-free Solutions on Perfusion Dynamics and Function of Kidney Transplants

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The use of a donor kidney prepared in an optimum manner is decisive for the post-operative course and the success of kidney transplantation.

The aim of the experiments under discussion was to study to what extent the perfusion of an isolated kidney is affected by the varying viscosity of a perfusate, and whether there is a correlation between the viscosity-conditioned change in the renal perfusion dynamics in artificial circulation and the functional behaviour of the kidney after re-implantation.

METHODS

The investigations were carried out on 27 freshly removed heparinised dog kidneys of an average weight of 71 g, which were connected in a blood filled state to a semi-closed pulsatile pump system with electronic cooling. The average perfusion pressure was 90 mm Hg and the cooling temperature 50°C. Three perfusates with identical electrolyte content and a concept resembling that of the formulation of Collins (Table I) were tested. By means of different concentrations of glucose and glycocoll and by gradual addition of mannitol and dextran (Molecular weight 40,000), viscosities of 1.9, 3.2 and 4.2 centipoise were obtained. At the same time the osmotic and the colloido-osmotic pressures changed; 10,000 U/l heparin and 0.1 g/l procaine hydrochloride were added to each solution.

The duration of perfusion was thirty minutes. During this period the venous flow was checked at one minute intervals and the respective flow resistance was calculated according to Ohm’s law.

After perfusion the kidneys were re-implanted and urine and blood samples were taken at intervals of ten to twenty minutes. The clearance of mannitol and PAH, sodium and potassium as well as the concentrations of lactic acid dehydrogenase and leucine aminopeptidase were determined.

After completing the measurements the kidneys were stored for histological assessment.
**Table I. The substitution of the three different perfusates tested**

<table>
<thead>
<tr>
<th>Perfusates</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identical for I-III</td>
<td>K$_2$HPO$_4$ · 3H$_2$O 85 mM</td>
<td>K$_2$HPO$_4$ 15 mM</td>
<td>K$_2$HPO$_4$ 15 mM</td>
</tr>
<tr>
<td></td>
<td>KH$_2$PO$_4$</td>
<td>KCl 15 mM</td>
<td>NaCl 75 mM</td>
</tr>
<tr>
<td></td>
<td>MgSO$_4$ · 7H$_2$O 25 mM</td>
<td>NaHCO$_3$ 10 mM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>glucose 25.0</td>
<td>glucose 2.5</td>
<td>glucose 25.0</td>
</tr>
<tr>
<td></td>
<td>glycoll 25.0</td>
<td>glycoll 2.5</td>
<td>glycoll 25.0</td>
</tr>
<tr>
<td></td>
<td>mannitol 50.0</td>
<td>dextran 40 50.0</td>
<td>mannitol 50.0</td>
</tr>
<tr>
<td></td>
<td>aqu. ad 1000.0</td>
<td>aqu. ad 1000.0</td>
<td>aqu. ad 1000.0</td>
</tr>
</tbody>
</table>

**Viscosity (5°C) (cP)**
- I: 1.9
- II: 3.2
- III: 4.2

**Osmotic pressure (mOsm)**
- I: 1150
- II: 430
- III: 1150

**Colloid-Osmotic pressure (mm Hg)**
- I: ~0
- II: 22
- III: 22

**pH (5°C)**
- I: 7.3
- II: 7.3
- III: 7.3

**Figure 1. The average values of the renal flow resistance**
RESULTS

Figure 1 shows the change with time of the average values of the renal flow resistance using the perfusates I to III. From the course of the curves it can be seen that with perfusate I the increase in resistance was most distinct differing significantly from the other solutions after only ten minutes. When comparing the statistical mean values the $p = 0.01$ for the difference in resistance between the perfusates I and III, and 0.05 for the difference between the perfusates I and II. There was no significant difference between the average values of perfusates II and III at that time. After 30 minutes the kidneys perfused with perfusate II also showed a marked increase in resistance as compared with perfusate III. The probability of error is 0.01.

While perfusate I regularly produced degeneration of the kidneys, five out of nine kidneys perfused with perfusate II showed only an increase in weight due to oedema. Perfusate III, however, did not cause any perceptible formation of oedema.

![Figure 2. The urinary values of lactic acid dehydrogenase](image)

Figure 2 compares the urinary values of lactic acid dehydrogenase determined in the transplant with the renal flow resistances taking into account only analyses related to a minimum urine flow of 0.1 ml per min/100 g kidney. These comparisons show a statistically established correlation between both parameters.

When the renal function tests were assessed, a reciprocal relation
between the flow resistances and the mannitol clearance was striking (Figure 3), i.e., kidneys with a high flow resistance during hypothermic perfusion showed, in most cases, strongly reduced clearance values after re-implantation as compared with the initial values supposed to be 100 g. When comparing the individual groups, a significant difference in the mannitol clearance values between perfusates I and III was observed.

The results of the PAH clearance as well as those of the sodium and potassium excretion also showed different mean values for the three groups, the worst values having been obtained from perfusates with low viscosity. Histologically, the kidneys perfused with perfusate I and some of the kidneys perfused with perfusate II showed signs of granular degeneration and of interstitial cortical oedema. The Arteriae radiatae corticales and the glomerular capillary loops were insufficiently filled or not filled at all. Bowman's capsules and the renal tubules were markedly enlarged. Some of the kidneys perfused with the dextran-containing perfusate III showed finely granulated structured casts of the capsules and tubules. In some kidneys the peritubular capillaries of the medulla were well supplied with blood, while in others they were insufficiently supplied with blood or even ischaemic. Such contradictory pictures were also observed in some of the kidneys perfused with perfusate III.

CONCLUSIONS

The increase in renal resistance when using perfusates is conditioned by oedematous renal degeneration. The increase in the extravascular fluid
volume and the renal tissue pressure result in a narrowing of the cross-section of the terminal vascular system and in the mechanical lesion of the cell membranes.

The considerable decrease in mannitol clearance is caused by a poor blood supply to the oedematous cortical substance. The high enzyme values of the urine, the deviations of the PAH clearance as well as the sodium and potassium excretion ensue from the destruction of the membrane potential of the highly differentiated tubule cells.

As we see it, the variance of the PAH clearance and electrolyte excretion values is caused by the different circulatory conditions within the kidney after extracorporeal kidney perfusion and re-implantation.

The most favourable results were observed when perfusates with a high viscosity similar to that of the blood and high osmolarity were used.

The formation in perfused kidneys of oedema reducing the functional capacity can be reduced by using such perfusates.

OPEN DISCUSSION

R W LAWTON (Iowa City, Iowa): I wondered if you fractionated the LDH into its five isoenzymes?

ERDMANN: Yes, we have done it in this manner.

LAWTON: Is one or more of the isoenzymes elevated to account for your elevation in the total LDH?

ERDMANN: No, we found that the LDH was higher.

LAWTON: Why did you use a temperature of 5°C? At that temperature, the sodium pump in the membrane begins to leak out potassium.

ERDMANN: We thought that 5°C was the best temperature for our research.