Clinical Kidney Preservation With and Without Continuous Perfusion

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In the Scandia-transplant material good correlation has been found between tissue typing and graft survival (Kissmeyer-Nielsen et al., 1971). However, tissue typing and subsequent transport of kidneys to the most suitable recipient has caused a marked increase in storage time of the kidneys (Figure 1). Before introduction of tissue typing one or two patients waiting for a transplant could be kept on haemodialysis at the transplantation centre and could be prepared for operation within a very short period of time. Since tissue typing was introduced the organ storage time has increased progressively: 50% of the last 50 kidneys had to be stored for more than 10 hours. The purpose of the present paper was to study if a prolonged cold ischaemia had any harmful effect on the organ viability and, if so, if storage by continuous perfusion could decrease or eliminate this harmful effect.

MATERIAL AND METHODS

The material includes 223 consecutive cadaveric renal transplants performed in Gothenburg. 194 kidneys were stored by simple hypothermia after initial perfusion and cooling with low molecular weight dextran in balanced electrolyte solution (Perfadex). The kidneys were stored in bicarbonate - invert sugar solution in refrigerator (Brunius et al., 1967). Reperfusion was performed every 4th hour. These kidneys were separated into two groups. One with a storage time of less than 10 hours and one group with a storage time of more than 10 hours. 29 kidneys (Group III) were preserved by continuous hypothermic perfusion in the Gambro perfusion machine. This system includes continuous hypothermic perfusion with plasma which is cooled, oxygenated in a membrane oxygenator and pumped into the organ with a pulsatile flow. The method was originally described by Belzer et al in 1967. The viability of the kidneys was in most instances decreased before preservation started. Most of the donors were victims from traffic accidents coming in to the hospital dead or dying at the emergency entrance. Severely
Figure 1. Preservation time in 200 consecutive cadaver renal transplants before and after introduction of tissue-typing. The kidneys were stored by simple hypothermia.

Figure 2. Preservation time for kidneys stored by hypothermia for less than 10 h (n 150 group I), more than 10 h (n 44 group II) and machine perfused kidneys (n 29 group III).

\[ C = \text{cold ischaemia} \quad P = \text{perfusion} \]

brain damaged patients were kept on respirators until cardiac arrest occurred. Almost all kidneys therefore had a warm ischaemia time up to 1 hour before nephrectomy and many donors had a considerable period of hypotension and oliguria before death.

The warm ischaemia time, ie the time from cardiac arrest until the kidney was removed and cooled was the same in the 3 groups, mean 30 minutes. The preservation times as shown in Figure 2 for Group I 6 hours, Group II 12 hours and Group III 14.5 hours. Most of the kidneys stored by continuous perfusion had a cold ischaemia time prior to perfusion. The longest perfusion time was 22.5 hours.

Evaluation of the results was based on the frequency of kidneys showing immediate function and on graft survival and function 6 months after trans-
plantation. Immediate function was assessed as urine production and a fall in the serum creatinine within the first 24 hours after transplantation. Follow-up studies after six months were performed for 100 kidneys stored by hypothermia and 13 kidneys stored by continuous hypothermic perfusion.

RESULTS

Kidneys with a cold ischaemia time less than 10 hours functioned immediately in 19% of the cases (Figure 3). There was no correlation within this group between the length of cold ischaemia and frequency of immediate function. Seven per cent of kidneys stored for more than 10 hours functioned immediately, while kidneys stored by continuous perfusion functioned immediately in 27.5% of cases.

![Figure 3. Frequency of grafted kidneys with immediate function. Mean warm ischaemia time in all groups 20 min](image)

At follow-up six months after transplantation 55% of the kidneys with a storage time of less than 10 hours were still functioning, 25% had a serum creatinine of less than 2 mg/100 ml. Thirty-six per cent of the kidneys with a cold ischaemia time of more than 10 hours were still functioning, 8% with a serum creatinine of less than 2 mg/100 ml. Forty-six per cent of the machine perfused kidneys were still functioning, all with a serum creatinine of less than 2 mg/100 ml.

DISCUSSION

Earlier investigations by Bergentz et al (1968) and Sells and Pena (1970)
have shown that storage of kidneys by simple hypothermia is safe for up to 8-10 hours. The results obtained in this study showed, however, that if this time limit was exceeded there was a considerable decrease in organ viability as judged from the frequency of immediate kidney function. There are many factors influencing the frequency of immediate function, such as pre-mortem condition and warm ischaemia. These factors were, however, evenly distributed in the groups. The reason for a lower frequency of kidneys showing immediate function in the group stored by simple hypothermia for more than 10 hours was therefore probably due to the prolonged storage time. If the advantage gained by tissue typing should not be completely vitiated by decreased organ viability from prolonged ischaemia there is an urgent need for a better preservation system for kidneys where a long storage time can be expected. This led to the introduction of continuous perfusion into the clinical transplantation programme. Since this introduction the frequency of immediate function has increased although the preservation time has been prolonged considerably. Up to now only 13 kidneys have been observed for more than 6 months. Graft survival rate for machine perfused kidneys was slightly lower than the rate for kidneys stored for less than 10 hours. The number is, however, too low to draw any definite conclusions (Figure 4). In most cases there was also a very long cold ischaemia time before the machine perfusion started. An interesting fact is that all machine perfused kidneys which survived 6 months had an almost normal function at the follow up investigation. This was not due to better matching in the machine perfused group since the match grades were evenly distributed within the 3 groups. It may, however, be due to a more efficient removal of passenger leucocytes.

Figure 4. Graft survival and kidney function 6 months after transplantation in 100 consecutive cases stored using hypothermia and 13 cases stored by continuous perfusion.
in kidneys stored by continuous perfusion since these cells have been shown
to be able to immunise the patient against the graft (Stuart et al., 1971).

Besides these advantages we have, after introduction of continuous per-
fusion, been able to schedule all operations in the daytime, and investigate
and treat the patient more thoroughly before operation, in some instances
with a preoperative haemodialysis. It has also been possible to use kidneys
which otherwise would have been discarded because of too long cold ischaemia.
The machine is transportable and we have transported kidneys in the machine
to other transplantation centres such as Copenhagen, Helsinki, London and
Brussels. We think that this preservation system will allow an even wider
exchange thereby increasing the chance for better matched kidneys.

CONCLUSION

Kidney preservation by hypothermia alone is a simple and effective preser-
vation method for kidneys up to 10 hours. After this time limit viability
seems to decrease. The harmful effect of prolonged ischaemia can be elimi-
nated by continuous hypothermic perfusion.

REFERENCES

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OPEN DISCUSSION

W J KOLFF (Salt Lake City, Chairman): As Dr Gelin is one of the authors
of this paper, I would not be surprised if there were some dextran in your
fluid. Is that so?

CLAES: No, actually we have used the plasma described by Belzer and we
have recently made a perfusion study using a 4% albumin solution and the
results were as good as with the plasma perfusion.

KOLFF: Do you filter your plasma?

CLAES: Yes, the plasma was filtered with a millipore filter but the albumin
solution was not treated in any way before perfusion.
KOLFF: Do you freeze and thaw it and freeze and thaw it repeatedly the way Belzer does?

CLAES: We freeze and thaw the plasma once and filter it after thawing.

KOLFF: Is Dr Gelin there – does he want to explain why he does not use Dextran instead of albumin.

L-E GELIN (Gothenburg): I think Dr Claes can explain that.

CLAES: Initially we did use Dextran but the results were very poor. Since then the machine has been improved considerably and I think it is now time to try using Dextran for continuous perfusion again. The early results were so bad that we have only just decided to do this.

KOLFF: At a recent meeting in the United States, Schreiner got up and said that it was perhaps not accidental that the cross section of the glomerular capillaries was such that when the red blood cells went through they swept the walls clear. This reminds me of what happens in some artificial kidneys, for example in the one designed by Lavender which spreads the blood flow over a very large surface area and in which you get deposition of proteins on the inside. This suggests that it might be useful if you added a few red blood cells, not too many, to your perfusate. Have you ever considered this?

CLAES: Well, we are quite satisfied with our preservation technique. I presented mostly clinical results. We have, of course, a lot of other experimental results after 72 hours. There has not been any clinical need for a longer preservation time than this but of course if you want to go up to one week or more I think you will have to alter the preservation technique by adding different substances to the perfusate.