Transplant Int (1992) 5 [Suppl 1]: S 429–S 432

TRANSPLANT
International

A preliminary report of the HTK randomized multicenter study comparing kidney graft preservation with HTK and EuroCollins solutions

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The main goal of transplantation is to restore good renal function and to improve the quality of life of thousands of dialysis patients, something which can only be achieved by providing them with well functioning grafts. Delayed renal allograft function is a serious problem. It is important to prevent this complication because it makes the diagnosis of acute rejection in the early postoperative period difficult, increases the necessity for diagnostic procedures, introduces dialysis treatments and prolongs hospital stay. The aetiology of delayed graft function (DGF) is multifactorial, and factors including donor management, technique used for organ procurement and preservation, age, anatomical variations in the graft, ischemia periods, use of cyclosporine A (CyA) or recipient immunological reactions have been implicated. Using different preservation solutions DGF rates vary from 30 % to 60 %. Recent clinical data have demonstrated better preservation and improved renal function posttransplant with HTK and University of Wisconsin (UW) solutions compared to EuroCollins solution. In a randomized multicenter study in collaboration with the Eurotransplant organ exchange organization, the efficacy of the HTK solution in renal transplantation was compared to EuroCollins and UW solutions in two parallel prospective randomized trials. The first preliminary results comparing HTK and EuroCollins solutions are reported here.

Key words: HTK solution – Kidney transplantation

Organization of the randomized trial

This randomized trial was organized in collaboration with Eurotransplant. This facilitated a uniform central policy for kidney graft allocation through HLA matching, standardized techniques and reagents for donor and recipient tissue typing and crossmatching. Randomized assignment of the preservation solution for kidney donors and data collection were coordinated by Eurotransplant. The randomized multicenter trials started in July 1990 and the recruitment has progressed steadily since then. Our goal is to randomize 300 donors in each trial i. e. 300 donors in the HTK versus UW trial and 300 donors in the HTK versus EC trial. We need a large number transplants for an appropriate statistical analysis to detect a 10 % difference in delayed graft function (DGF) between HTK and the other solutions. In total, 14 centers are participating in the HTK versus UW preservation part of the trial and 26 in HTK versus EC.

With the efforts of many physicians and transplant coordinators, 529 donors have been randomized up to September 21st, 1991. The randomized donors and their transplants in the participating centers are presented in a Table 1, and the numbers of randomized donors and transplants are presented in Table 2. It is apparant that the number of transplants in the HTK versus EC trial is sufficient to fulfil our goal. Interim results based on all donors and those recipients for whom follow-up information has been returned are presented.

Clinical results

To date, complete information about 338 donors and 307 transplants at 1 month follow-up has been obtained and analyzed. The descriptive information of donor and recipient characteristics which could influence the delayed graft function, as presented in Table 3, show that the HTK and EuroCollins groups are comparable.

Delayed graft function (DGF) of the transplanted kidney was defined as the absence of life-sustaining renal function which required dialysis treatment on two or more occasions within the 1st week after transplantation. This definition of DGF included patients with initial non-functioning kidneys that recovered after dialysis treatment and patients with transplanted kidneys that did not recover and the patient returned to chronic dialysis treatment. The analysis of outcome, limited to the percentage of DGF with

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Table 1. Overview of the number of randomized donors and transplantations

Country Center	(Code)	Local HTK trial FUP-coordinator	Number of donors	Number of transplants
Austria				
Innsbruck	(IB)	Fetz/Steurer	9	8
Graz	(GA)[a]	Pogglitsch	0	9
Linz	(OE)[a]	Breitenfeller	0	4
Linz	(OL)	Kaiser	0	2
Vienna	(WM/WG)	Wamser	25	57
Belgium				
Antwerpen	(AN)	van Beeumen	5	5
Bruxelles	(BJ)	Amerycks	6	2
Bruxelles	(BR)	Kinnaert	3	18
Bruxelles	(LA)	Lecomte	4	16
Gent	(GE)	VanderVennet	0	7
Leuven	(LM)[a]	Roels	0	13
Liege	(LG)[a]	Delbouille	0	4
Germany				
Aachen	(AK)[a]	Homburg	0	4
Berlin	(BE)	Passfall	20	33
Berlin	(EB)	Rücker	0	6
Bonn	(BO)	Molitor	1	1
Bremen	(BM)	Grote	12	15
Düsseldorf	(DU)	Schäpers/Westhoff	30	40
Erlangen	(ER/NB)	Neumayer/Hüls	0	21
Essen	(ES)	Walz	19	38
Frankfurt	(FM)	Ernst	13	29
Freiburg	(FR)	Kirste	20	35
Göttingen	(GO)	Werner	6	13
Hamburg	(HG)[a]	Clausen	0	11
Hannover	(HO)	Gubernatis/Heigl	58	66
Hann Munden	(HM)	Schäfer	0	26
Heidelberg	(HB)	Beer	17	19
Homburg/Saar	(HS)	Riegel	0	1
Jena	(JE)	Börner	0	1
Kaiserslautern	(KS)	Nauth	8	15
Kiel	(KI)	Schütt	16	31
Köln Lindenthal	(KL)	Kerp	28	33
Köln Mehrheim	(KM)	Arns	11	23
Lübeck	(LU)	Kopmann	18	26
München	(MH)	Groenewoud	1	20
München	(ML)	Abendroth/Schneeberger	35	47
Münster	(MN)	Mauritz	32	62
Marburg	(MR)	Kuhlman	3	8
Mainz	(MZ)	Kreber	24	15
Mannheim	(MA)	Schnülle	0	5
Rostock	(RO)[a]	Hudemann	0	1
Stuttgart	(ST)	Ziech	11	16
Tübingen	(TU)	Fischer-Fröhlich	13	19
Ulm	(UL)	Grupp	2	7
Würzburg	(WZ)	Goetz	12	16
Luxembourg	(LX)	Duhoux	1	2
the Netherlands				
Amsterdam	(AB)	Oosterlee	18	24
Groningen	(GR)[a]	de Maar	0	18
Leiden	(LB)[a]	van der Woude	0	10
Maastricht	(MS)	Wijnen	8	14
Nijmegen	(NY)	Hoitsma	22	34
Rotterdam	(RD)[a]	Hendriks/Sietse	0	15
Utrecht	(UT)	Hené	9	8
Utrecht	(UW)	Donckerwolcke	0	3
Outside Eurotransplant			18	
		Total	520	994

[a] Not participating in the preservation part of the study

each solution used, is shown in Table 4. A clear-cut difference was observed in the incidence of DGF after transplantation when the treatment groups were compared, but final statistical comparisons await further follow-up. In the HTK group, 24% (37/156) of the recipients had DGF of the transplanted kidney that required dialysis treatment compared to 37% (56/151) in the EuroCollins group. No recovery of the kidney function with a return to chronic dialysis treatment was observed in 5% (8/156) of the HTK group and in 3% (5/156) of the EuroCollins group.

Serum creatinine levels were recorded daily for 1 month. Posttransplant serum creatinine levels decreased more rapidly in the HTK group than in the Euro-

Table 2. Overview of the number of donors and transplantations performed in each arm of the trial

Number of donors		Number of transplants	
HTK versus UW		HTK versus UW	
78	79	152	149
HTK versus EC		HTK versus UW	
181	182	352	341

Table 3. Characteristics of the kidney donor, transplant procedure and kidney recipient

	HTK solution		EC solution	
	(*n*)	%	(*n*)	%
Donor age (years)[a]	45		49	
Donor diagnosis				
- Multi trauma	(14/169)	8%	(16/169)	9%
- Trauma capitis	(32/169)	19%	(50/169)	29%
- Intracranial bleeding	(82/169)	49%	(85/169)	50%
- Others	(38/169)	23%	(18/169)	12%
Before donor nephrectomy				
- Resuscitation	(35/169)	21%	(23/169)	14%
- Hypotensive episodes	(100/169)	59%	(96/169)	57%
Donor drug treatment				
- Plasmaexpanders	(103/169)	62%	(113/169)	68%
- Bloodtransfusions	(59/169)	36%	(59/169)	36%
- Dopamine only	(152/169)	91%	(153/169)	91%
- Diuretics	(51/169)	31%	(53/169)	31%
Oliguria of the donor	(8/169)	8%	(11/169)	10%
Cold ischemia period (h)[a]	24		23	
Anastomisis time (min)[a]	33		33	
Recipient age (years)[a]	47		46	
Prior transplants				
- one or more	(21/156)	14%	(130/151)	14%

[a] Continous variables are shown as median values

Table 4. Kidney graft function after transplantation in both treatment groups

	HTK solution		EC solution	
	(*n*)	%	(*n*)	%
Initial graft function	(119/156)	76%	(95/151)	63%
Delayed graft function	(37/156)	24%	(56/151)	37%
- with recovery	(29/156)	19%	(51/151)	34%
- without recovery	(8/156)	5%	(5/151)	3%

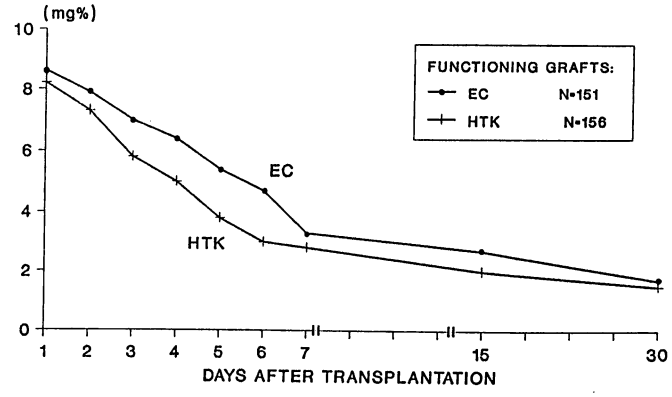

Fig. 1. Comparison of median serumcreatinine decline. Eurotransplant Multicenter Study

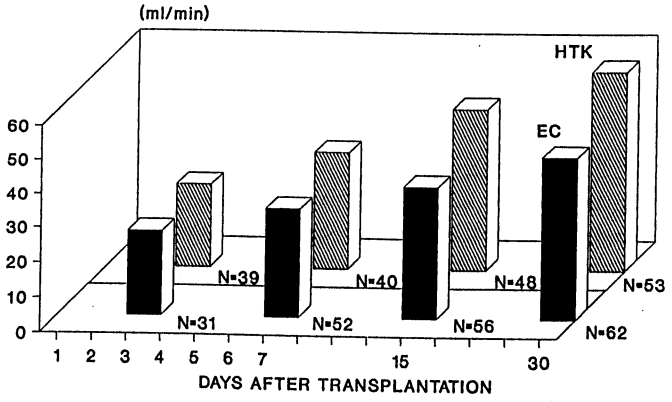

Fig. 2. Comparison of median creatinine clearance increase. Eurotransplant Multicenter Study

Collins group, as shown in Fig. 1. Creatinine clearances were documented on days 3, 7, and 14 and at one month. Higher creatinine clearances were observed at all times posttransplant in the HTK group compared with the EuroCollins group. Since not all centers calculate creatinine clearance values on a routine basis, this variable was obtained in a limited number of patients (Fig. 2).

Conclusions

This study reports the results of the randomized clinical comparison of two preservation solutions in postmortem renal transplantation. The most important preliminary finding in this study was that the incidence of DGF was reduced by 13%, from 37% in the EuroCollins group to 24% in the HTK group, but these percentages do not necessarily reflect the final results. Improved renal function after transplantation was indicated by a rapid decrease in the serum creatinine levels in the HTK group compared to the EuroCollins group. Higher creatinine clearance values were also seen at all time periods posttransplant in the HTK group compared with the EuroCollins group.

We do not wish to prejudge the data of patients yet to be evaluated. A full analysis will be presented when sufficient follow-up information has been returned. We have,

however, been able to demonstrate rapid recruitment and comparability of trial arms through international collaboration within Eurotransplant.

Acknowledgements. The results described in this trial are based upon the data of renal transplant recipients collected and submitted by the medical and administrative staffs collaborating with the Eurotransplant Foundation. The co-operation of the administrative staff and the medical students were of great value in the development of the HTK trial. The conduct of the trials was supported by an International Scientific Committee, in particular, we acknowledge G. Alexandre, H. J. Bretschneider, B. Buchholz, K. Dreikorn, F. Gubernatis, M. Hölscher, F. Isemer, G. Kootstra, R. Margreiter, Y. Vanrentergem, F. Mühlbacher, G. Persijn, J. Wilmink. Without the help of M. Kasterop-Kutz, the clinical data could not have been collected and stored in the computer for analysis.