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A prospective, randomized trial of pretransplant blood transfusions in cadaver kidney transplant candidates

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Abstract To assess the effect of pretransplant blood transfusions on the outcome of cadaveric kidney transplantation, a single-centre analysis was performed of 171 patients randomly assigned to receive no pretransplant transfusion ($n = 85$) or to receive at least three random blood transfusions ($n = 86$). After transfusion 18 of the latter patients developed circulating lymphocytotoxic T-cell antibodies, but the sensitization was only transient. At the time of transplantation, none was still sensitized. In both groups 60 patients have been transplanted. Patient and graft survival rates were significantly higher in the transfused group than in the non-transfused group. In the non-transfused patients the higher mortality was due to complications related to repeated anti-rejection therapy. Non-transfused patients had more repeated acute rejection episodes than the transfused patients. The present study indicates that pretransplant blood transfusions still facilitate graft acceptance even in the setting of good HLA matching and with cyclosporine as the basic immunosuppressant. The risk of sensitization is very low.

Key words Kidney transplant
Blood transfusion, pretransplant
Sensitization

Introduction

Based on multiple single-centre as well as international registry studies, pretransplant blood transfusions have generally been accepted as a powerful prognostic factor in cadaver kidney transplantation [1–5]. However, at the 1986 Congress of the Transplantation Society in Helsinki, Opelz reported that the favourable effect of pretransplant blood transfusions could no longer be seen when analysing the graft survival of patients transplanted in 1984 and 1985, irrespective of whether or not cyclosporine was used as the basic immunosuppressant [6]. The disappearance of this strong effect was due to an improvement of graft survival in the non-transfused group. For this reason a prospective randomized study was started by Opelz. However, as the overall results of cadaver kidney transplantation have improved even further, graft survival may not be a sufficiently sensitive indicator to detect the effect of any prognostic factor, and more sensitive parameters such as the incidence of rejection and the degree of renal function are needed. Other factors such as differences in immunosuppressive protocols between different centres may further interfere with the results. As it is too early for this kind of analysis of the CTS data, and since a substantial number (more than one-quarter of the total group of randomized patients) was randomized in our centre, we decided to analyse this group separately. The aim of the present study was to assess the effect of

pretransplant blood transfusions not only on patient and graft survival, but also on the incidence of rejection and renal function.

Patients and methods

Between December 1986 and September 1993, 171 candidates for a first cadaver renal transplant who had never been transfused before were randomized to the non-transfused group (85 patients) or to the transfused group (86). The latter received at least 3 units of packed cells before transplantation.

Of the 85 non-transfused patients, one patient died while on the waiting list, one patient was excluded soon after inclusion as it was discovered that in fact he had received blood transfusions before randomization, one patient inadvertently received blood transfusions after randomization, one patient was transplanted elsewhere from a living unrelated donor, and one patient was transferred to another centre. Sixty patients were transplanted, while 20 patients are still on the waiting list. Of the 86 patients in the transfused group, one patient died before transplantation, one patient was transplanted before having received blood transfusions, and one patient was transferred to another centre. Sixty patients were transplanted, and 24 are still on the waiting list.

Up to December 1992, the basic immunosuppression consisted of cyclosporine and low-dose steroids (starting dose 20 mg methylprednisolone). Cyclosporine was started at a dose of 10 mg/kg body weight daily. The daily dose was adapted according to the whole blood trough levels (between 250 and 300 ng/ml during the first 3 months, and between 150 and 250 up to 1 year after transplantation). From January 1993 to September 1993 patients were included in a randomized, double-blind controlled trial in which the additive effect of mycophenolate mofetil (Syntex) was tested. As shown in Table 1, recipient age, HLA matching and ischaemic times were not different between the two groups.

Results

Sensitization

Of the non-transfused transplanted patients, two had a low titer of lymphocytotoxic T-cell antibodies (10%) at the time of transplantation. Two of the non-transfused and not yet transplanted patients have at present 10% and 25% circulating T-cell antibodies, respectively. Of the transfused patients 18 developed lymphocytotoxic T-cell antibodies ranging from 10% to 85% panel reactivity. In all of these patients, antibody formation was transient, and at the time of transplantation only one patient had a low titer of circulating antibodies (10%). Of the not yet transplanted patients in this group, no patient is sensitized at present.

Patient and graft survival

Patient survival in the transfused group is 100% up to 3 years after transplantation versus 98.2% at 1 year and 89% at 3 years for the non-transfused patients ($P = 0.04$ (Fig. 1)). In the latter group three patients died from infectious complications, two following repeated anti-rejection therapy. One patient with limited renal function died after 6 months from a cerebral haemorrhage, and one patient also with impaired renal function died from a myocardial infarction. Graft survival in the transfused group at 1 year and at 3 years is 93.3% and 87.5% at 1 year and 76.5% at 3 years in the non-transfused group ($P = 0.05$).

Rejection incidence

In the non-transfused group the mean number of rejections per patient during the 1 year was 0.8 ± 1.0 compared with 0.58 ± 0.79 in the transfused group (NS). Of the 60 non-transfused patients 12 had more than one rejection episode versus only 5 of the 60 transfused patients ($P = 0.06$).

Renal function

Serum creatinine at the last measurement was 2.1 ± 1.6 mg/dl in the non-transfused group and

Table 1 Comparison of transfused and non-transfused patients. Data are presented as mean ± standard deviation

	Non-transfused	Transfused	*P*
Number of patients	60	60	
Number of transfusions	0	3.5 ±2.7	<0.0001
Age (years)	44.8 ±13.5	46.1 ±13.1	NS
HLA-DR mismatches	0.46±0.54	0.42±0.5	NS
HLA-B DR mismatches	1.30±0.76	1.37±0.72	NS
HLA-A compatibilities	0.70±0.65	1.00±0.66	<0.02
HLA-B compatibilities	1.12±0.57	1.05±0.50	NS
HLA-DR compatibilities	1.44±0.53	1.46±0.50	NS
Warm ischaemic time (min)	0.32±1.99	1.49±7.55	NS
Cold ischaemic time (h)	19.6 ±4.5	21.0 ±5.6	NS
Follow-up (days)	1008 ±634	959 ±591	NS

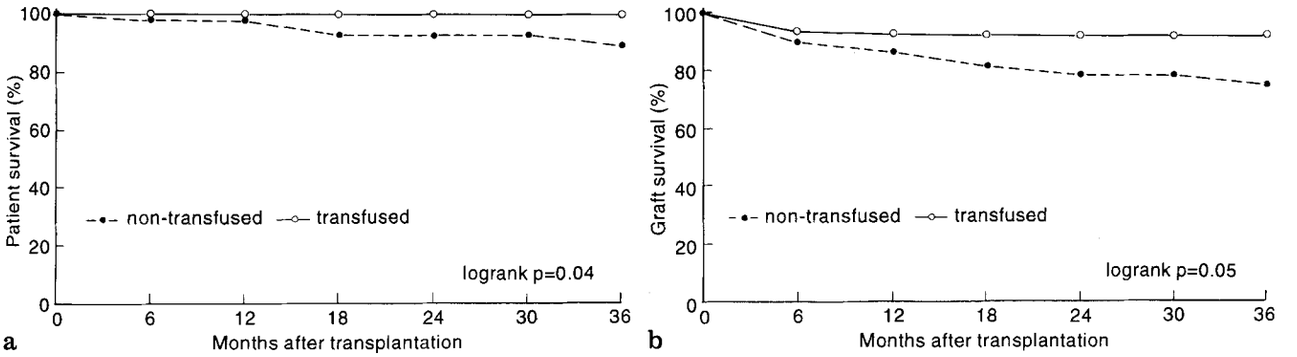

Fig. 1a, b Actuarial patient (**a**) and graft (**b**) survival of the transfused ($n = 60$) and non-transfused ($n = 60$) patients

2.4 ± 2.3 mg/dl in the transfused patients (NS). The last creatinine clearance value was 54 ± 21 ml/min in the non-transfused group and 59 ± 28 ml/min in the transfused patients.

Discussion

The present single-centre analysis indicates that the patient and graft survival of cadaver kidney transplant recipients is significantly improved by three more pretransplant blood transfusions. Although the lower graft survival in the non-transfused patients is related to the higher patient mortality in this group, a detailed analysis of the causes of death reveals that this higher mortality is mainly due to complications related to repeated antirejection therapy. Non-transfused patients are more at risk of developing recurrent rejections than transfused patients. Our findings are in agreement with earlier reports showing the favourable effect of pretransplant blood transfusions in cadaver kidney transplant recipients [1–5]. In our experience this effect is not blunted by the use of potent immunosuppressive drugs such as cyclosporine and is still present in the setting of good HLA compatibility. The degree of HLA matching in our patients was rather high, especially for the HLA-B and -DR locus antigens.

A major disadvantage of pretransplant blood transfusions is the risk of sensitization. Our study indicates that this risk is very low when only a small number of pretransplant blood transfusions are given. Although transfused patients developed circulating antibodies after transfusion, severe sensitization was only transient. The waiting time for transplantation was comparable in both groups, and of the patients still waiting for transplantation, none is highly sensitized.

Recently, it was suggested that pretansplant blood transfusions have a favourable effect on graft acceptance only if they share at least one HLA-DR antigen with the recipient [7, 8]. As systematic HLA typing of the transfused blood was not performed in the present study, we cannot contribute to this topic. All transfused patients received at least three random transfusions, so it is conceivable that at least one of them shared one HLA-DR antigen with the recipient.

We conclude that pretransplant blood transfusions facilitate graft acceptance, even in the setting of good HLA matching and with cyclosporine as the basic immunosuppressant. The risk of sensitization is very low when a small number of transfusions is given.

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