LONG-TERM HAEMODIALYSIS — AN ENHANCING FACTOR FOR CADAVERIC GRAFT SURVIVAL

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Summary

In 220 consecutive cadaveric kidney transplants, graft survival in patients dialysed for a period of two years or longer was significantly greater than in those dialysed for less than two years. More blood transfusions were received and the formation of HLA antibodies was greater in the group dialysed for more than two years. A positive cross match was the basis for excluding 21% of the HLA positive patients from transplantation during a one year period of observation. When these same HLA positive patients had more than two subsequent opportunities for donor-recipient selection the exclusion rate dropped to 2%. The longer period of dialysis with more blood transfusions had a favourable influence on cadaveric graft survival whereas the formation of HLA antibodies had a negative influence. Even in HLA positive patients graft survival was better in the long-term dialysis group when compared with the group dialysed for a shorter period. These results suggest that longer dialysis with more blood transfusions represents an enhancing factor for cadaveric kidney grafts.

Introduction

An analysis was undertaken in 220 consecutive patients receiving their first cadaveric kidney transplant at the Berlin transplantation centre between 1968 and 1976 to determine whether a long period of pre-operative dialysis therapy influences graft survival. The presence of HLA antibodies and a gradual deterioration in the clinical status of long-term maintenance dialysis patients as a result of inadequate dialysis were factors which might be considered to have an unfavourable influence on graft survival. The retrospective analysis of the transplanted patients did not, however, support this.

Patients and Methods

The selection of 220 consecutive patients for first cadaveric grafts for transplan-
tation was determined according to the clinical guidelines of Dutz et al. and ABO and HLA matching. Since 1974 patients with three or more mismatches were not considered for transplantation, hence the overall average of 1.5 mismatches. HLA and crossmatching was done according to the NIH standard method. Blood transfusions were administered to all patients in the form of once washed packed red blood cells. The average number of leucocytes was $3 \times 10^8$ per unit of packed red blood cells. Cumulative survival was calculated according to Parsons et al. significances were calculated using $\chi^2$ test.

Results

**Graft Survival, Blood Transfusions and Dialysis Duration**

Comparison of patients dialysing less than one year, one to two, two to three and more than three years pre-transplantation shows a correlation between graft survival and length of dialysis. This correlation was significant after three years. Transfusions of packed red blood cells were administered regularly to

<table>
<thead>
<tr>
<th>TABLE I. Cumulative Graft Survival, Blood Transfusions and Percentage of HLA Antibody Carriers in 220 Cadaveric Graft Recipients, Divided into Four Groups of Differing Pre-transplant Dialysis Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years on RDT</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>&lt; 1</td>
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<tr>
<td>1 - 2</td>
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<tr>
<td>2 - 3</td>
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<tr>
<td>&gt; 3</td>
</tr>
</tbody>
</table>

* $p < 0.01$

dialysis patients (Table I). Since, in all patients, length of dialysis and number of blood transfusions parallel one another, it is impossible to determine which factor is responsible for enhancement of graft survival.

**HLA-antibodies, Graft Survival and Consideration for Transplantation**

The percentage of HLA antibody carriers in dialysis patients increased in proportion to the increase in blood transfusions they received. Graft survival in patients with HLA antibodies was significantly worse both in patients dialysed for two years or less and those dialysed two years or longer. Graft survival, however, in the group of dialysis patients treated for more than two years with HLA antibodies was comparable with the group dialysed for less than two years without HLA antibodies (Figure I).
In one year 28% positive cross matches were observed in 1000 potential donor-recipient considerations, as a result of the high percentage of HLA antibody carriers among potential graft recipients. The possibility of kidney transplantation in 112 HLA antibody-positive patients was calculated on a one year basis in a recipient pool of 196 patients. Of these, a positive cross match precluded transplantation in 27 patients. Of another 85 patients with two opportunities to be matched, only 10 had positive cross matches. If a cross match positive patient had three or more chances of consideration in donor-recipient matching the likelihood of a negative cross match was 98%. Despite the high incidence of antibody-positive patients within the potential recipient pool, when considered on a yearly basis, only 20% of these patients had to be kept on a waiting list longer than one year.

*Distribution of HLA matching, Patient Age, and Ischaemic Time Among Patients on Dialysis for Varying Years*

No significant differences were found in graft survival in differing patient age groups, average number of HLA mismatches, warm or cold graft ischaemic times, onset of function and number of non-functioning kidneys (Table II). To determine whether length of time on dialysis with increasing numbers of blood transfusions had an effect on graft survival regardless of poor HLA matching patients were considered in groups based on the number of transfusions while on dialysis. Seventy-seven patients with two or more mismatches were divided into the following groups: 22 patients with less than 10 transfusions; 41 patients with 10–49 transfusions and 14 patients with 50 or more
TABLE II. Age, Ischaemia Time, Graft Function and Mismatch in Four Groups of Patients Dialysed for Varying Durations Before Transplantation

<table>
<thead>
<tr>
<th>Years on RDT mean</th>
<th>warm ischaemia time (min)</th>
<th>cold ischaemia time (min)</th>
<th>% grafts without function</th>
<th>average onset of function (days)</th>
<th>mismatches (average)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>33</td>
<td>18</td>
<td>560</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>1-2</td>
<td>30</td>
<td>24</td>
<td>490</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>2-3</td>
<td>34</td>
<td>16</td>
<td>680</td>
<td>26</td>
<td>12</td>
</tr>
<tr>
<td>&gt;3</td>
<td>35</td>
<td>19</td>
<td>725</td>
<td>20</td>
<td>21</td>
</tr>
</tbody>
</table>

transfusions. The four year graft survival of 16%, 35% and 64% respectively strongly suggested that the transfusions had a favourable effect on graft survival even in poorly-matched patients.

Discussion

The development of HLA antibodies following blood transfusions resulted in a policy in many haemodialysis centres not to transfuse prospective transplant recipients.

The negative effects of omitting transfusions on graft survival in such patients has been reported by Williams, Briggs, Festsenstein and Opelz. The results reported here confirm these observations. The mechanism of the enhancing effect of blood transfusions on graft survival is unclear since only in experimental animals have blocking antibodies been demonstrated.

For practical reasons cross matching has an important role in donor-recipient selection. Single case reports have demonstrated excellent graft function despite a positive cross match. Most active transplant centres have also experienced acute or hyperacute rejections despite negative cross matches. The appearance of rejections in cross match negative patients might be explained by inadequate sensitivity of the NIH technique. Good graft function without rejection in positive cross matched patients may be due to the development of protective antibodies during extended periods of dialysis. Time could also be a helpful factor for the development of cytotoxic antibodies, leading to a clearcut cross match instead of a falsely negative one. This possibility may explain the near equal graft survival among the HLA antibody-positive patients dialysed for longer periods compared with the shorter term dialysis patients who were antibody-negative. Increasing numbers of HLA antibody positive patients in the longer dialysed patients’ recipient pool does not reduce the likelihood of successful transplantation. Most HLA antibodies have a limited specificity, therefore an HLA antibody positive patient waiting long enough has a fair chance of being transplanted. Once transplanted, his chances are good of retaining that kidney for years. The observations reported here of favourable graft survival in multi-transfused but poorly matched patients is not in keeping with the statement of the 5th EDTA Combined Report9.
Conclusion

Good graft survival is possible in patients dialysed for long periods of time with multiple blood transfusions, even in the presence of HLA antibodies.

References