GRAFT SURVIVAL AND BLOOD TRANSFUSION

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Summary

The outcome of primary kidney transplantation in 244 patients was studied with reference to pre-transplant blood transfusions. Fifty-eight patients received kidneys from living related donors with one shared HLA-haplotype, 186 patients received kidneys from cadaveric donors. Graft survival was found to be significantly poorer in non-transfused patients, especially in patients receiving kidneys from living related donors. The degree of uraemic intoxication did not seem to influence the outcome.

Introduction

For many years blood transfusions were considered to have an unfavourable influence on graft survival after kidney transplantation because of the risk of sensitising the patients against a graft. This was supported by the poor outcome of transplantation in patients with preformed cytotoxic antibodies1,2.

During recent years, however, several groups have observed poorer graft survival in patients who have not been transfused prior to transplantation, compared with transfused patients3,4,5.

The purpose of this study was to investigate the influence of blood transfusions on the outcome of primary renal transplantation and to evaluate the possible importance of the degree of uraemia at the time of transplantation in this respect.

Patients and Methods

Two hundred and forty-four recipients of primary kidney grafts were studied, 238 males and 6 prepubertal girls. They were transplanted between 1966-1976 at the Transplant Unit in Gothenburg, Sweden. The study was limited to males and children in order to avoid the possible influence of pre-sensitisation due to
pregnancies. ‘High risk’ patients and patients receiving low quality grafts were excluded from the study. Data on pre-transplant transfusions were obtained retrospectively, and in patients receiving living donor grafts, all earlier medical records were checked and, when necessary, surviving patients were questioned. One hundred and eighty-six patients received kidneys from cadaveric donors, 144 patients were trans fused prior to transplantation, 42 were not transfused. Fifty-eight patients received kidneys from living related donors with one shared HLA-haplotype; HLA-identical siblings were thus not included. Forty-two of these patients were transfused prior to transplantation and 16 were not transfused. In the living donor group the time for, type of and number of transfusions were registered. The distribution of age and causes of uraemia, donor sex, recipient blood group and presence of HLA-antibodies were noted. Factors supposedly related to the degree of uraemia at transplantation were studied; rate of progress of uraemia, mean time on dialysis prior to transplantation, significant uraemic complications, serum creatinine and haemoglobin concentration.

The actuarial graft survival was calculated according to Merrell and Schulman. Grafts lost due to non-immunological causes were treated as cases lost from observation. Differences between groups were tested with Student’s t-test.

Results

The graft survival was poor in the non-transfused patients compared with those transfused, as seen from Figure 1. In recipients of kidneys from living related donors, the graft survival was 95% at 6 months in the transfused group compared with 59% in the non-transfused group (p < 0.01), at 12 months 89% compared with 25% (p < 0.0005) and at 2 years 78% compared with 17% (p < 0.005). In the cadaveric donor group, the graft survivals at 12 months were 63% and 38% in the transfused and non-transfused groups respectively (p < 0.01) and at 3 years 47% compared with 25% (p < 0.01).

A more detailed analysis was performed in the living related donor group. The quantity of blood, the time of transfusion or the kind of blood component given did not correlate with graft loss due to rejection, but the numbers in the different groups were small. Only three of the 42 transfused patients in the living donor group had HLA-antibodies and these were not multispecific. Donor sex or recipient blood group did not correlate with graft loss. Age and original disease were found to be evenly distributed in the two groups, as seen from Table I, as were the factors supposedly related to the degree of uraemia, as seen from Table II. None of these factors or combinations of factors influenced graft survival.

Discussion

An analysis of the influence of pre-transplant blood transfusions on graft survival showed poor graft survival in non-transfused recipients. In the living related donor group only recipients sharing one HLA-haplotype with the donor were included. This group of 58 patients was therefore quite homogeneous regarding
Graft survival (non-immunol. causes excl.)

Figure 1. Graft survival in 244 recipients of primary kidney grafts correlated with pre-transplant transfusions. (LD: Living donors; CD: Cadaveric donors)

TABLE I. Original Disease and Age in Living Donor Recipients

<table>
<thead>
<tr>
<th>Cause of uraemia</th>
<th>Transfused (n:42)</th>
<th>Non-transfused (n:16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CGN</td>
<td>59%</td>
<td>56%</td>
</tr>
<tr>
<td>CPN</td>
<td>17%</td>
<td>13%</td>
</tr>
<tr>
<td>Others</td>
<td>24%</td>
<td>31%</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>25.0</td>
<td>28.4</td>
</tr>
<tr>
<td>Range</td>
<td>(6–59)</td>
<td>(10–56)</td>
</tr>
</tbody>
</table>
TABLE II. Parameters Related to Degree of Uraemia in Living Donor Recipients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Transfused (n:42)</th>
<th>Non-transfused (n:16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb-concentration at trpl (g/L)</td>
<td>70.7 ± 17.4 (SD)</td>
<td>69.3 ± 14.9 (SD)</td>
</tr>
<tr>
<td>S-creatine at trpl (μmol/L)</td>
<td>986 ± 301 (SD)</td>
<td>1260 ± 421 (SD)</td>
</tr>
<tr>
<td>Progress rate of uraemia (months)</td>
<td>13 ± 9.9 (SD)</td>
<td>16 ± 7.2 (SD)</td>
</tr>
<tr>
<td>Range</td>
<td>(3w - 3y)</td>
<td>(3m - 3y)</td>
</tr>
<tr>
<td>Mean time on dialysis (months)</td>
<td>3.5 (n:39)</td>
<td>3.8 (n:4)</td>
</tr>
<tr>
<td>Significant uraemic complications</td>
<td>21%</td>
<td>13%</td>
</tr>
</tbody>
</table>

*Time in months from s-creatine of 450 μmol/L to start of dialysis or transplantation

HLA-matching, organ viability and the general condition of the patients.

Our finding of a markedly reduced graft survival in this group thus seems to be quite conclusive and is in accordance with previous reports.3,4,5.

The possible mechanism by which transfusions prolong graft survival is hard to explain. Recently, van Es et al.8 published data on four-fold prolongation of kidney allograft survival in rhesus monkeys transfused with blood from unrelated animals. These experiments suggest a non-specific immunological phenomenon. This is corroborated by similar findings in the dog.9.

The possible role of the degree of uraemic intoxication at the time of transplantation was studied by retrospectively obtained parameters supposedly related to uraemia. Some of the chosen parameters might be questionable as indicators of the degree of uraemia but taken together they serve to show that no difference in this respect existed between transfused and non-transfused patients.

Acknowledgment

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References

Open Discussion

CHAIRMAN (ROHL, Heidelberg) We would like from the clinical point of view to hear how we should pre-treat our transplantation patients. Are we going to give them blood, what amount of blood, what kind of blood, frozen whole blood or packed erythrocytes?

BRUNNER (Basel) I would like to take issue with the data of Dr Mebel. He gave us the impression that the larger the number of blood transfusions the better the outcome of the renal graft. Now looking at the figures, you can see that with the small number of grafts that were performed one cannot make any meaningful comparisons of graft survival beyond one year. We should not conclude that a high number of blood transfusions is better than just five or ten blood transfusions.

MEBEL The slide shows that for this relatively small number of patients, the data are highly significant (p < 0.05).

BRUNNER I do not think it is permissible to construct a survival curve out to five years with such small numbers of cases.

PERSIJN (Leiden) Dr Brynger, in your non-transfused group, did you take into account the number of pregnancies?

BRYNGER There were only male patients so there were no biological possibilities for pregnancies in any patient in these groups.

PERSIJN Do you have any idea about the outcome for patients who received only one blood transfusion?

BRYNGER We have no such patient. We have patients who had only two blood transfusions, and they worked as well as the other ones, but of course the numbers were too small when we divided the patients into subgroups. We have an impression that you should give at least two transfusions and it may be that they should be administered about one month prior to transplantation, but this is a personal opinion and I have no adequate data today.

BROUMAND (Teheran) Almost four years ago Dr Terasaki made the same remarks and observations. He concluded that whole blood is better than frozen blood and frozen blood was worse than no transfusion.

THAYSEN (Copenhagen) Like Dr Brunner and Dr Parsons I feel that the clinical material is too multifactorial to give a final answer to the problem of a possible beneficial effect of blood transfusions and of time on dialysis on graft survival. Animal experiments, which can be much more clearly designed, are still too few. Therefore, in reply to the question of our Chairman, I do not
feel that time has come to change our current therapeutic approach. Such a change would involve a heavy burden on patients as well as on limited dialysis facilities. We need more knowledge, not hasty changes.

TIILIKAINEN (Helsinki) We analysed the patients transplanted in Helsinki according to pregnancy and transplantation so that we got groups who had been both pregnant and had transplantations. All the groups which had been immune-triggered behaved quite similarly. So it is not only transfusions, but also pregnancies that may condition the patient for transplantation.

PARSONS (Leeds) I think I was responsible from the findings of the Transplant Registry in 1969 for the idea that blood transfusions were harmful to a kidney graft. We had on the Registry at that time about 500 patients and were only able to undertake an analysis for the first post-transplant month. This was an unselected group: we did not then have tissue typing or cross-matching.

KLINKMANN (Rostock) Do not forget the dialysis people. I think Dr Brunner has shown quite clearly in his overall review that the so-called 'other causes', other than HLA and blood transfusions, did play an important role, and I think if we look at the time of survival compared to the time of dialysis we should be aware that at least nephrologists have learned how to dialyse patients a little bit better and how to rehabilitate them. In comparison with the time Frank Parsons was talking about, we are able to give much better prepared patients to the transplant surgeons. Professor Hess Thaysen has stressed the multifactorial issues. As a nephrologist I would say that blood transfusion does not do any harm but I would be hesitant to state that this is really the only factor we have to consider.

ANDREUCCI (Napoli) I am just wondering about your policy now in Sweden. Are you not doing transplantation in people who have not had any blood?

BRYNGER As a transplant surgeon I hesitate to transplant a living donor of the type we just described who has not been transfused. From a 'satellite unit', with patients in good shape, although the figures are small, seven out of seven non-transfused patients have rejected kidneys within one year. And when you work with these patients and you have these kinds of early rejections which are irreversible, you are very reluctant to transplant non-transfused patients. Our personal opinion is that if you have patients who have never been transfused you might have to change the state of the patient before transplantation.