INFLUENCE OF THE LEWIS BLOOD GROUP SYSTEM ON CLINICAL KIDNEY TRANSPLANTATION

Elisabeth Fischer, V Lenhard, W Römer, K Dreikorn, K Schärer, D Roelcke

University of Heidelberg, FRG

Summary

The different Lewis phenotypes were determined prospectively in 201 kidney transplant recipients. Transplant survival rates in Lewis compatible recipients were significantly higher (p < 0.0005) than in Lewis incompatible recipients. The improvement of transplant prognosis by matching for Lewis antigens was confirmed by a prospective study comprising 55 donor/recipient combinations. HLA matching had little benefit on transplant survival whereas survival rates are strikingly increased by Lewis compatibility. In the Lewis compatible but HLA mismatched group, graft survival was definitely higher than in the HLA matched but Lewis mismatched group. Our data indicate that Lewis antigens play an important role in transplant prognosis. Compatibility in the Lewis system should therefore be considered when recipients are selected.

Introduction

Except for ABO other blood groups have not been considered so far in the procedure for selecting donor and recipient. However, recent findings indicate that compatibility in the Lewis antigen system and transplant survival are correlated [1–4]. Lewis antigens are very close to ABH antigens in chemical structure. The biosynthesis of these antigens is controlled by independent genes; Le genes act by adding one (Le^a) or two fucose molecules (Le^b), ABH genes by adding fucose (H), fucose and galactosamine (A) or galactose (B) to the same precursor molecule [5]. The objective of the present study was to examine the influence of the Lewis blood group system on transplant survival. In addition, we have investigated whether the results of kidney transplantation are improved to a greater extent by compatibility in the Lewis system or by matching for HLA antigens.
Patients and Methods

We analysed retrospectively 201 kidney transplantations performed in Heidelberg. One hundred and ninety patients were transplanted for the first time (170 cadaver and 20 living related donors), 11 patients received second cadaver transplants. Only patients no longer under our care or patients who died before the beginning of the study were excluded. The recipients were classified according to the Lewis phenotypes Le (a- b+), Le (a+ b-) and Le (a- b-). In addition, we analysed prospectively 55 kidney transplantations. In this study, donors as well as recipients were typed for Lewis antigens. The patients were subdivided into those who had received Lewis compatible and those with Lewis incompatible transplants.

The Lewis phenotypes were determined in duplicate by the usual haemagglutination technique. In Le (a- b-) patients typing was repeated at least once. HLA typing was performed according to the two-stage NIH technique with few minor modifications [6]. To provide adequate numbers for analysis the patients were only classified in an HLA matched (≥ B locus identity; n = 71) and in an HLA mismatched group (< B locus identity; n = 120). All possible mismatches (e.g. only one B locus antigen defined in the donor) were considered as mismatch.

Actuarial graft survival rates were calculated by the method of Merrell and Shulman [7]. Statistical significances in comparison of graft survival rates were computed by the log-rank test [8].

Results

Actuarial graft survival rates in 136 Le (a- b+), 33 Le (a+ b-) and in 32 Le (a- b-) recipients are shown in Figure 1. Graft survival in the Le (a-b+) recipients was significantly higher (p < 0.0005) than in the combined group of Le (a+ b-) and Le (a- b-) patients. Two-year graft survival in Le (a- b+) recipients was 79%, whereas in Le (a+ b-) patients only 53% and in Le (a- b-) recipients only 58% of the transplants were functioning after two years. In the prospective study, too, Lewis matched transplants had significantly higher (p < 0.01) survival rates than Lewis mismatched transplants. Graft function in 33 recipients who had received Lewis compatible transplants was 81% after one year whereas it was only 46% in 22 patients with Lewis incompatible transplants (Figure 2).

When the influence of the HLA and Lewis antigen systems are compared separately, HLA matching slightly improved the two-year graft survival (HLA mismatched transplants: 67%; HLA matched transplants: 76%). When Lewis compatible were compared with Lewis incompatible groups, the differences were more striking (p < 0.0005). In Le (a- b+) recipients 79% of the transplants survived after two years as against only 54% in the combined Le (a+ b-) and Le (a- b-) group (Figure 3). Analysing the influence of HLA matching in the three Lewis phenotype groups, transplant survival is not significantly improved by HLA matching in the Le (a+ b-) and in the Le (a- b-) patients. In Le (a- b+) recipients, however, we found significantly higher (p < 0.005) survival rates in the HLA matched (two-year graft survival: 88%) than in the HLA mismatched transplants (two-year graft survival: 73%). That implies that best results could be obtained in the Lewis compatible and HLA matched group (Figure 4).
Figure 1. Actuarial transplant survival rates in 201 recipients with the different Lewis phenotypes Le (a− b+), Le (a+ b−) and Le (a− b−)

Figure 2. Actuarial transplant survival in 55 cadaver kidney transplantations depending on Lewis compatibility between donor and recipient. Le m = Lewis matched transplants, Le mm = Lewis mismatched transplants; Le m vs. Le mm = p < 0.01
Figure 3. Transplant survival in recipients with different Lewis phenotypes and in recipients with HLA matched (m) or HLA mismatched (mm) transplants. HLA m > B locus identity; HLA mm < B locus identity. HLA m vs. HLA mm: p < 0.001, Le (a− b+) vs. Le (a+ b−) + Le (a− b−): p < 0.0005

Figure 4. Actuarial transplant survival in 191 recipients with different Lewis phenotypes depending on HLA matching. HLA matched (m) > B locus identity; HLA mismatched < (mm) B locus identity. Le (a− b+) and HLA m vs. Le (a−b+) and HLA mm: p <0.005. For details see text.
HLA incompatibility index, ischaemic times of the transplants, the distribution of ABO blood groups as well as pretransplant transfusions did not differ significantly in any of the patient groups.

Discussion

Le (a− b+) individuals constitute about 65%, Le (a+ b−) 25% and Le (a− b−) 10% of the European population [5, 9]. By calculating from this known distribution of Lewis antigens it would be expected that 90% Le (a− b−) recipients and 75% Le (a+ b−) recipients have received a Lewis incompatible transplant. These two groups did in fact have lower graft survival rates than Le (a− b+) recipients, of whom only 35% should be Lewis incompatible. These data were confirmed by the prospective study in which donor and recipients were typed for Lewis antigens. Patients who had received Lewis incompatible transplants had unfavourable transplant prognosis compared with patients who received Lewis compatible transplants.

These data support findings published by Oriol et al [1–3] and Fischer et al [4], who suggested that Lewis compatibility between donor and recipient has a beneficial effect on transplant prognosis.

Furthermore, we tried to find out whether transplant outcome is influenced more by HLA matching or by Lewis compatibility. As is well known, transplantation results are only slightly improved by matching for A and B locus antigens. In our study, two-year graft survival was about 10% higher in HLA matched compared to HLA mismatched transplants. Matching for Lewis antigens, however, strikingly improved the results of kidney transplantations. We found that 79% of Lewis compatible transplants functioned after two years whereas the Lewis incompatible group only had 54% two-year graft survival. Compatibility in both systems, Lewis and HLA, led to the best results. Thus HLA matching additionally improves the positive effect of Lewis compatibility on transplant prognosis, but it seems not to influence graft survival in Lewis incompatible transplants. In contrast to Oriol et al [2, 3], we found that the Lewis compatible but HLA mismatched group had significantly higher graft survival rates than transplants matched for HLA, but mismatched for Lewis antigens.

Our data suggest that the effects of HLA and Lewis matching are not only additive but that Lewis compatibility is the more important for transplant prognosis.

References

Open Discussion

VAN ROOD (Leiden) How do you define HLA matched combination?

FISCHER HLA match means A or B locus identical or one B locus and one A locus identity.

VRIESMAN (Maastricht) Were your patients transfused and if so were they matched for Lewis? For blood transfusions I mean.

FISCHER The percentage of patients that were not transfused were not statistically different in any of the groups. We had about 7% in every group that were not transfused.

VRIESMAN If they were transfused did you match the blood for Lewis, and if not, did you ever find anti-Lewis antibody?

FISCHER We checked about 400 sera of 250 recipients and we could not find any single anti-Lewis antibody.

SELWOOD (Bristol, UK) Your graft survival figures, I guess, are based on all causes of graft failure. Have you identified any association between Lewis compatibility and the frequency of rejection episodes.

FISCHER That is what we tried to show in a prospective study. When we have Lewis compatible transplants, that means an Le\(^b\) positive recipient has received an Le\(^b\) positive donor kidney, graft survival was significantly higher than it was in the Lewis non-matched group.

SELWOOD Yes, but graft-failure can have many causes. I am interested if you looked at just the immunological causes of graft-failure.

FISCHER We did not differentiate the causes of the failure. We have immunological failures as well as any other reasons.

SELWOOD Thank you, that is what I wanted to know.