INFLUENCE OF LEWIS AND OTHER BLOOD GROUP SYSTEMS IN KIDNEY TRANSPLANTATION

V Lenhard, B Hansen, D Roelcke, K Dreikorn, P Wernet, H Bockhorn, W Fassbinder, R F Fetta, H Wilms, B Gumbel, F W Albert, R W Ewald, I Sprenger-Klasen, S F Goldmann

Universities of Heidelberg, Tübingen, Frankfurt, Freiburg, Kaiserslautern, Mannheim, Ulm, FRG

Summary

In 167 first cadaver kidney recipients and their donors the blood groups ABO, Rhesus, Lewis, MN, Ss, P, Kell and Duffy were determined. The influence of incompatibility in each system as well as of simultaneous presence of several mismatches was analysed. Whereas one-year graft survival of Lewis-compatible grafts was 67 per cent, Lewis-incompatible grafts functioned in only 53 per cent ($p = 0.02$). The other blood groups showed no significant effect on graft outcome. Cumulative red cell incompatibilities, however, led to decreased survival rates. One-year graft survival in the group with $\geqslant 4$ incompatibilities was only 51 per cent versus 69 per cent in transplants with < 4 incompatibilities (18% difference, $p < 0.01$). When the Lewis system was excluded from analysis, the difference in survival rates was reduced to only six per cent. These data indicate that cumulative incompatibilities of red cell antigens have an unfavourable effect on graft survival. Of the different blood groups, the Lewis system is of major importance.

Introduction

ABO compatibility between donor and recipient is an absolute prerequisite in kidney transplantation. Other blood groups have not been so far considered in the selection of donor and recipient. However, an influence on kidney graft survival has been described for the Lewis [1–4], Rhesus [5, 6], and P system [7]. Furthermore, the results of the International Transplant Workshop Study [8] indicated that cumulative red cell incompatibilities are associated with a marked decrease in graft survival rates. This multicentre study investigates the separate influence of Lewis and other blood group antigens and the effect of combined red cell incompatibilities on cadaver graft outcome.

Patients and methods

In 167 first cadaver kidney recipients and their respective kidney donors the blood groups ABO, Rhesus, Lewis, MN, SS, P_1, Kell and Duffy were determined

by the usual haemagglutination techniques. Compatibility in each system was defined as the presence of a given antigen in donor and recipient. Combinations in which the donor and recipient had different antigens were considered incompatible. Graft survival rates were calculated by actuarial methods [9]; the statistical significances were computed by the log-rank test [10]. Non-immunological failures were not excluded.

Results

In Figure 1 the separate influence of several blood group systems on cadaver graft survival is shown. Only Lewis compatibility had a significant effect on graft outcome. In Lewis-compatible transplants, the one-year survival rate was 67 per cent, whereas Lewis-mismatched grafts functioned only in 53 per cent (p=0.02). For the other blood group systems, e.g. ABO, RhD, MN, Ss, P, Kell and Duffy a significant effect was not observed, although RhD, MN, and Ss incompatibilities tended to be unfavourable.

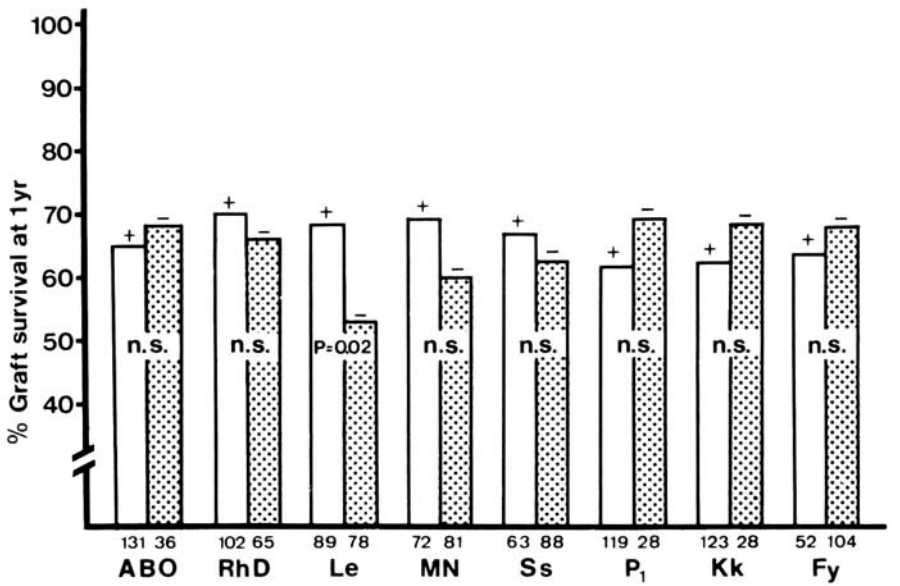

Figure 1. Influence of several red cell systems on graft survival rates; + : presence of a given antigen in donor and recipient; – : donor and recipient have different antigens. The number of combinations studied for each system is indicated

The effect of cumulative red cell incompatibilities on graft survival is depicted in Figure 2. Transplants with a total of four or more mismatches were compared to those with less than four mismatches. The simultaneous presence of several red cell incompatibilities was indeed associated with unfavourable graft survival.

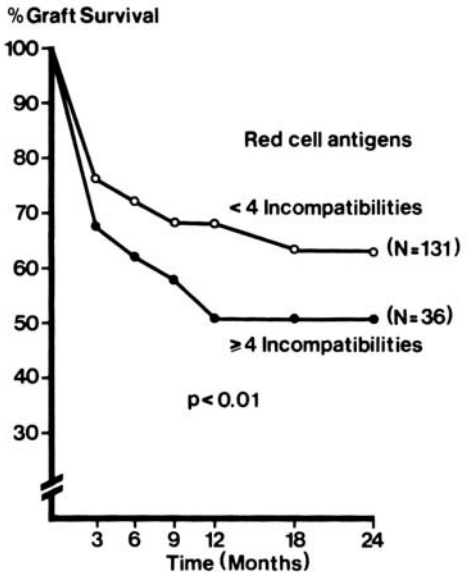

Figure 2. Effect of cumulative incompatibilities of different red cell antigens on actuarial graft survival rates. The difference between transplants with fewer than four as compared to those with four or more red cell antigen mismatches was statistically significant ($p<0.01$)

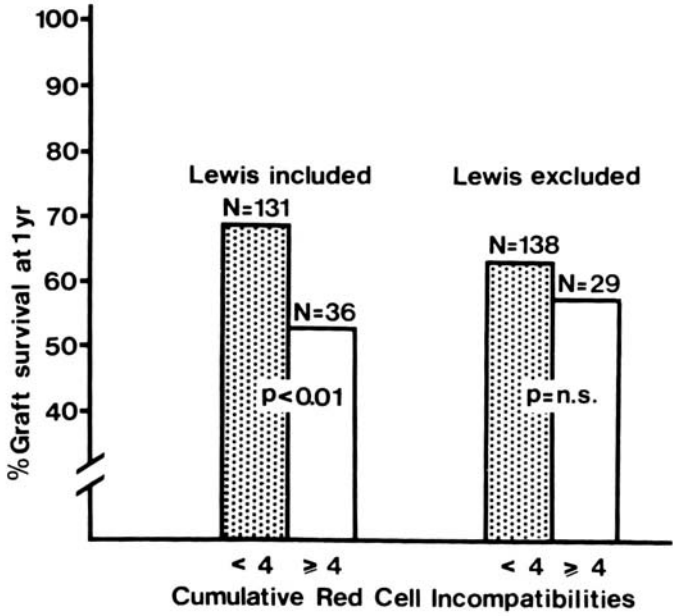

Figure 3. Effect of cumulative red cell incompatibilities on graft survival, including and excluding the Lewis system from analysis. The difference of one-year survival rates (< 4 versus ≥ 4 mismatched red cell antigens) was 18 per cent when Lewis was included, but only six per cent excluding Lewis antigens

Transplants with ≥ 4 incompatibilities functioned in only 51 per cent at one year as compared to 69 per cent of transplants with < 4 incompatibilities ($p < 0.01$).

The Lewis antigens seem to be the most important of the blood group systems studied. We therefore analysed the influence of combined red cell incompatibilities on graft prognosis, including or excluding the Lewis system. When Lewis was included, the difference of one-year survival rates between the two groups (< 4 and ≥ 4 red cell antigen incompatibilities, respectively) was 18 per cent, whereas it was only six per cent when Lewis was excluded (Figure 3). This finding again indicates the greater influence of Lewis than of other red cell antigen mismatches.

Discussion

Since the early 1960s, compatibility between the ABO blood groups of donor and recipient has been considered an absolute requirement for successful transplantation [11]. Transplantation across this barrier has almost always resulted in hyperacute graft rejection, due to the fact that A and B antigens are present on the vascular endothelium of the kidney. The blood group isoagglutinins are responsible for the graft rejection in those cases. However, in a few cases A to O, or B to A grafts have been successful [12, 13].

Interestingly, Oliver et al [14] and van Hooff et al [15] first reported that kidneys from blood group A donors transplanted into A recipients had a lower survival rate than O kidneys transplanted to O recipients. This finding could not be confirmed by others [16]. In addition, the donor's ABO blood type seems to be irrelevant for graft prognosis. In our series a significant adverse effect could not be observed when O kidneys were transplanted in non-O recipients as compared to ABO-identical grafts.

Apart from ABO, other blood group systems were not considered in the selection of donor and recipient, although an influence of some blood group systems on graft prognosis has been described. Oriol et al [1, 3] and our group [2, 4] have recently shown that the Lewis system plays a major role in graft rejection. In this study a significant effect of Lewis compatibility was also seen. Lewis-incompatible grafts had a 15 per cent lower one year survival rate than Lewis-compatible grafts. If this observation can be confirmed by further prospective studies, it will be of great practical importance. Since the determination of the Lewis phenotype is technically rather simple and not time consuming, it should not pose a serious problem to type for Lewis antigens before transplantation and to exclude Lewis-incompatible grafts.

The influence of other blood group antigens is controversial. No influence of RhD antigens was found by Van Hooff et al [15]; on the contrary Murray et al [5] and Opelz and Terasaki [6] reported a better graft survival in Rhesus-compatible recipients. A possible role of P antigens originally discussed by Gleason and Murray [7] could not be confirmed by others [15]. MN antigens are not considered important as far as kidney transplantation is concerned [15]. In our study, apart from Lewis antigens no other blood group system had a significant influence on graft outcome, albeit kidneys compatible for RhD, MN, or Ss antigens tended to do better. A weak effect of those systems may possibly

only become statistically significant in large series.

In accordance with the International Transplant Workshop Study [8], we observed a significant negative effect of cumulative red cell incompatibilities, that is, if four or more antigens of various red cell systems were mismatched simultaneously, graft survival was markedly decreased. It may be suspected that at least some of the red cell antigen systems represent weak factors having an additive effect on kidney graft outcome. The adverse influence of combined red cell antigen mismatches was, however, strikingly reduced when the Lewis system was excluded from analysis.

In conclusion, the simultaneous presence of different red cell antigen incompatibilities has an unfavourable effect on kidney graft prognosis. Of the different red cell antigens, the Lewis system seems to play a major role.

References

1 Oriol R, Cartron J, Yvart J et al. *Lancet 1978; i:* 574
2 Fischer E, Lenhard V, Römer W et al. *Z Immun-Forsch 1979; 155:* 420
3 Oriol R, Opelz G, Chun C, Terasaki PI. *Transplantation 1980; 29:* 397
4 Lenhard V, Roelcke D, Dreikorn K et al. *Transplant Proc 1981; 13:* 930
5 Murray S, Dewar PJ, Uldall PR et al. *Tissue Antigens 1974; 4:* 548
6 Opelz G, Terasaki PI. *Dial Transplant 1979; 8:* 167
7 Gleason RE, Murray JE. *Transplantation 1967; 5:* 343
8 Opelz G, Terasaki PI. In Terasaki PI, ed. *Histocompatibility Testing 1980;* 592–624. Los Angeles: UCLA Tissue Typing Laboratory
9 Merrell M, Shulman LE. *J Chronic Dis 1955; 1:* 12
10 Peto R, Pike MC, Armitage P et al. *Br J Cancer 1977; 35:* 1
11 Dausset J, Rapaport FT. *Ann NY Acad Sci 1966; 129:* 408
12 Starzl TE, Marchioro TL, Holmes JH et al. *Surgery 1964; 55:* 195
13 Brynger, Blohme I, Lindholm A et al. *Transplant Proc 1982; 14:* 195
14 Oliver RTD, ed. *An assessment of the role of HL-A antigens and the other factors which influence cadaver graft survival. Thesis, Cambridge 1974*
15 van Hooff JP, Hendriks GFJ, van Rood JJ. In van Hooff JP, ed. *The relative importance of HL-A matching in kidney transplantation 1976; Academic Thesis, University of Leiden:* 69–68
16 Opelz G, Terasaki PI. *Lancet 1977; i:* 220

Address for correspondence: Dr Volker Lenhard, Institute of Immunology, Im Neuenheimer Feld 305, D 6900 Heidelberg, FRG

Open Discussion

GLUCKMAN (Paris) But have you looked at Rhesus E compatibility, because in the Pitié hospital where I work we have observed patients with Rhesus E antibodies who all lost their kidneys from rejection within three months. We are very interested to know if anyone else has looked at this problem?

LENHARD Yes, we have looked at this and we have not found any significant effect. We have performed many analyses and only RhD showed a small but insignificant effect. Other groups have reported on a significant effect of RhE incompatibility. We have not seen any effect of RhE.

MOSES (Chicago) You mention that your analysis included incompatibility both ways, in other words, donor positive-recipient negative and the other way round. Have you analysed these separately? In other words, what is the effect when the donor is Lewis positive and the recipient negative, and vice versa. I think you grouped the two together in your analysis.

LENHARD Yes, we have considered each combination in which there were no identical phenotypes as incompatible, irrespective of whether the donor was positive and the recipient for a given antigen or vice versa. We have also analysed other combinations such as donor antigen negative and the recipient positive and we did not find such clear-cut effects.

KREISLER (Madrid) Did you take into account, in your analysis for Lewis incompatibility, the race of the donor or recipient for both groups, incompatible and compatible?

LENHARD This is a German multi-centre study and I think there are only Caucasians in this study. I know that in Negro populations the percentage of Lewis negative individuals is higher than in Caucasian populations.

DIMITRIADIS (Greece) Do you have any information on the effect of incompatibility of Lewis in related donors?

LENHARD No, we have no experience, our data are too small to perform such an analysis.