

Is matching for human leukocyte antigen-DR beneficial in pediatric kidney transplantation?

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SUMMARY

This Practice Point commentary discusses the findings and limitations of a report by Gritsch *et al.*, in which the authors concluded that human leukocyte antigen (HLA)-DR-mismatched kidneys from deceased donors aged 35 years or less are suitable for use in pediatric patients. We highlight the issues to be considered before adopting such an allocation policy. Gritsch *et al.* reported that the 5-year survival rates of grafts with zero HLA-DR mismatches were identical to those of grafts that were completely mismatched for HLA-DR; however, the report did not provide information about the immunosuppressive regimens used or the frequency of rejection episodes and their treatment. Children who receive HLA-DR-mismatched kidneys will ultimately be exposed to more-intensive immunosuppression in order to overcome the potentially increased risks of acute rejection, graft failure and sensitization. In spite of recent improvements in immunosuppressive therapy, we believe that HLA matching remains crucial for the survival of kidney transplants.

KEYWORDS deceased donors, HLA matching, kidney transplantation, pediatric

COMMENTARY

Kidney transplantation is well accepted as the optimal therapy for children with end-stage renal disease. By analyzing large databases, many investigators have found that recipients of human leukocyte antigen (HLA)-matched kidneys experience superior outcomes—as defined by lower rates of rejection and higher rates of graft and patient survival—than recipients of HLA-mismatched kidneys.¹

The report by Gritsch *et al.*² addresses a critical question regarding the relevance of HLA-DR matching in pediatric transplantation. The authors performed a retrospective analysis of data from the Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients to examine the influence of HLA-DR matching on allograft survival and sensitization rates in children receiving kidneys from deceased donors. They analyzed data from 1,585 children who had received kidneys between 1996 and 2004 from deceased donors aged 35 years or less. The 5-year graft survival rates reported by Gritsch *et al.* were identical in the grafts with zero HLA-DR mismatches and in those with two HLA-DR mismatches (71%). In addition, the authors showed that the odds of

developing a panel-reactive antibody titer greater than 30% by the time of a second transplantation did not increase significantly in the presence of HLA mismatches. Accordingly, Gritsch and colleagues urge the transplantation community in general and pediatric transplantation programs in particular to accept HLA-DR-mismatched kidneys from deceased donors aged 35 years or less for transplantation into children with end-stage renal disease.

Reduced use of HLA matching in kidney transplantation has recently been advocated. As argued by Su and co-workers,³ if immunosuppression has improved to a degree that enables transplantation of well-HLA-matched and poorly HLA-matched kidneys with identical success rates, HLA typing and matching should indeed be abolished from kidney allocation algorithms. However, the notion of comparable success rates has been challenged recently by a report by Opelz and Döhler,⁴ which examined the outcomes of 135,970 deceased-donor transplantations performed over two decades (1985–1994 and 1995–2004). The data were provided by 363 transplantation centers in 41 countries, and 7,315 recipients (11%) were under the age of 18 years. In this report, the number of mismatches correlated significantly with the

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rates of graft survival and rejection. Furthermore, multifactorial analysis of 1,252 pediatric cadaveric renal transplantations performed in the UK and Ireland between 1986 and 1995 also revealed that HLA matching was one of the most important determinants of outcome.⁵

The paper by Gritsch *et al.*² refers to a study by our group⁶ in order to support the authors' contention. However, all the kidneys offered to our pediatric recipients were retrieved from living-related donors and we did not accept any HLA-DR-mismatched grafts. In addition, mismatches in HLA-A or HLA-B were a significant predictor of graft loss in our series. Furthermore, Gritsch *et al.* did not provide information regarding the immunosuppressive regimens used in their analysis. Children who receive HLA-DR-mismatched kidneys will probably undergo more-intensive immunosuppressive treatment in order to overcome the potentially increased risks of acute rejection, graft failure and sensitization. Finally, the frequency of rejection episodes, antirejection treatment and the adverse effects of such treatment (to which pediatric patients are particularly vulnerable) were not reported by Gritsch and colleagues.

Magee *et al.*⁷ reviewed recent trends in and important issues currently facing pediatric organ transplantation. The authors argued that the 5-year follow-up time in the analysis by Gritsch *et al.*² was insufficient to enable a meaningful analysis of long-term outcomes.

Although Gritsch *et al.*² should be congratulated for conducting a study with the aim of

shortening the waiting time on dialysis of pediatric renal transplant candidates and hence minimizing the morbidity of these individuals, their suggestion to use HLA-DR-mismatched grafts should be cautiously analyzed. The increased risks of acute rejection, graft loss and sensitization should be considered, and weighed against the problems associated with longer exposure to dialysis.

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PRACTICE POINT

Acceptance of human leukocyte antigen-DR-mismatched kidneys from young deceased donors would shorten the waiting time of pediatric kidney transplant candidates on dialysis; however, the increased risks of rejection, graft loss, sensitization, and exposure to potent immunosuppressive agents should be seriously considered before adoption of such a policy.

Competing interests

The authors declared no competing interests.