Transpl Int (1994) 7 [Suppl 1]: S519–S521

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Comparison of serological and DNA HLA-DR typing results for transplantation in Western Europe, Eastern Europe, North America and South America

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Abstract In a previous study, DNA typing revealed that 25% of serological HLA-DR typings of kidney transplants were incorrect. In the current study, we analyzed whether this error rate had improved in recent years, and whether there were differences according to geographical region. From 1988 to 1991 the error rate of serological typing improved slightly in Western Europe from 19% to 16%, and in North America, from 21% to 16%. In Eastern Europe, the error rate decreased from 49% to 33% in 1991, whereas the rate remained high in South America at 60% in 1988 and 72% in 1991. The high error rates in South America and Eastern Europe reflected a lack of good quality serological typing reagents. The 16% typing errors in Western Europe and North America demonstrated the current limit of serological techniques for cadaver donor typing and underlined the need for prospective DNA typing.

Key words HLA antigens
DNA-typing
Kidney transplantation

Introduction

We have reported previously that serological typing for the HLA-DR antigens is associated with a high error rate of approximately 25% as revealed by retrospective DNA typing [5]. Similar results have been obtained by others [3, 9]. Most of the discrepancies occur with the specificities HLA-DR5, -DR6, -DR8 and their respective splits. In a recent European study, a discrepancy rate between serology and DNA typing of lower than 10% has been reported for typings performed in 1991 [10]. We, therefore, investigated whether the quality of serological typing may have improved during the last 5 years.

Materials and methods

The current analysis was limited to HLA-DR typings of cadaver kidney donors. Donor spleen tissue or peripheral blood lymphocytes were obtained at the transplant centers, frozen at −20 °C, and shipped on dry ice to the study center at the University of Heidelberg where DNA was extracted by routine methods [2, 4]. Aliquots of DNA were distributed to participating laboratories where DNA typing was performed without prior knowledge of the serological typing results using the RFLP technique described by Bidwell et al. [1]. Serological HLA typing results obtained at the laboratories of the individual transplant centers were used for comparison. Analysis of discrepancies between HLA-DR serology and DNA typing was performed for the specificities HLA-DR1–18.

Results

The discrepancy rates observed for typings performed from 1988 to 1991 in different geographical regions are

Table 1 Discrepancies between HLA-DA typing by the RFLP or serological typing methods in different geographical regions

Year	Western Europe	Eastern Europe	North America	South America
1988	18.6% ($n=870$)	48.9% ($n=90$)	21.4% ($n=373$)	59.5% ($n=121$)
1989	18.5% ($n=1072$)	43.8% ($n=105$)	19.2% ($n=328$)	68.9% ($n=106$)
1990	19.9% ($n=923$)	23.3% ($n=73$)	17.2% ($n=279$)	73.4% ($n=64$)
1991	16.3% ($n=827$)	33.3% ($n=93$)	16.1% ($n=217$)	72.2% ($n=36$)

Table 2 Incorrect „blank" assignments for HLA-DR in different geographical regions

Year	Western Europe	Eastern Europe	North America	South America
1988	7.8%	12.2%	11.3%	28.1%
1989	9.4%	12.4%	11.9%	33.0%
1990	7.4%	11.0%	8.6%	26.6%
1991	8.3%	20.4%	8.3%	22.2%

Table 3 Incorrect antigen assignments in different geographical regions

Year	Western Europe	Eastern Europe	North America	South America
1988	11.7%	36.7%	11.0%	36.4%
1989	10.0%	32.4%	7.6%	49.1%
1990	12.1%	12.3%	9.3%	54.7%
1991	9.3%	16.1%	8.3%	63.9%

Table 4 Overall serological error rates for HLA-DR alleles typed in different geographical regions

HLA-	Western Europe	Eastern Europe	North America	South America
DR1	13%	24%	20%	38%
DR2	5%	8%	4%	33%
DR3	4%	10%	5%	25%
DR4	5%	24%	4%	35%
DR5	9%	16%	10%	33%
DR6	22%	39%	21%	73%
DR7+9	5%	8%	1%	21%
DR8	23%	32%	17%	36%
DR10	26%	82%	31%	89%
Average	12.4%	27.0%	12.5%	42.5%

summarized in Table 1. Although improvements with time were evident with the exception of South America, the error rate remained at 16% both in Western Europe and North America.

Table 2 shows the percentage of erroneously assigned blanks within the different geographical regions. The numbers of individuals tested in each year were the same as those indicated in Table 1. The corresponding percentages of discrepancies due to antigen misassignments are listed in Table 3, whereas Table 4 shows the distribution of the discrepancies among the different alleles, summarized for each region.

Discussion

Our results demonstrated a slight improvement in the quality of HLA-DR typing in Western Europe, with the error rate decreasing from 19% in 1988 to 16% in 1991. This 1991 discrepancy rate was considerably higher than the 9.2% rate reported by Verduyn et al. [10] for selected Eurotransplant centers. The European data of our study included results from centers outside the Eurotransplant area (France, Great Britain, Spain, Italy, and Portugal). The 16% error rate for typings performed in 1991 at North American centers was identical to the error rate in Western Europe.

In Eastern Europe, the error rate remained at a high 33% in 1991, and it was an excessive 72% in South America. Clearly, improvements in these areas are urgently needed.

Whereas European laboratories appeared to have slightly more errors due to antigen misassignments than North American laboratories, incorrect blanks were assigned slightly more often in North America (Tables 2 and 3). Antigen misassignments accounted for the majority of typing errors in Eastern Europe and South America (Table 3).

Table 4 confirms previous reports that errors in serological typing were related mainly to a lack of good typing reagents for definition of the specificities DR6, DR8, DR10, and to a lesser extent DR1 and DR5. The results from Western Europe and North America showed a similar pattern. In Eastern Europe, DR4 also appeared to cause problems. In South America, all specificities tended to have high discrepancy rates.

Even assuming that perhaps 2–4% of the discrepancies were caused by "handling or clerical errors" either at the transplant centers or at the typing laboratories, the remaining discrepancy rate of 10–15% (higher in Eastern Europe and South America) calls for improvements as it directly affects graft survival [7, 8]. Recently developed

rapid DNA typing techniques that are suitable for prospective donor typing, such as PCR-SSP [6], would seem suitable for overcoming the current limits of serological typing.

Acknowledgement We thank the centers participating in the Collaborative Transplant Study for their invaluable support. We also thank IBM Germany for providing computer hardware and software. The technical assistance of Ulrich Christ, Susanne Marburg, Ulrike Prüfer, and Claudia Bugert is gratefully acknowledged. This work was supported in part by grants from Transplantationszentrum Heidelberg and Deutsche Forschungsgemeinschaft.

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