ASSOCIATION OF HISTORICAL PEAK PRA AND RENAL TRANSPLANTATION OUTCOMES

Alexey Zulkarnaev1, Vadim Stepanov1, Veronika Fedulkina1

1Surgical Department of Transplantation and Dialysis, Moscow Regional Research and Clinical Institute, Moscow, Russian Federation

INTRODUCTION AND AIMS: A routine method of assessing the risk of renal graft loss is using of Panel Reactive Antibody (PRA) test, a surrogate indicator of sensitization. It is well known, that lower PRA score is associated with higher transplant survival rate. Our research shows that sometimes a fall in PRA at the point of transplantation compared to the peak value may lead to an underestimation of the risk.

METHODS: 287 recipients from the waiting list, with anti-HLA antibodies I, II or both classes (PRA>5%) were included in the study. Patients were screened periodically to identify PRA and the specificity of antibodies (identifying the intensity of the immunofluorescence of each antibody specificity). Of these recipients, 142 received a kidney transplant. At the point of the transplantation the patients had no donor specific antibodies. Cross-match (complement-dependent cytotoxicity test) was negative. HLA-genotyping of recipients was performed using the sequence specific primers method (A-, B-, DR-loci), antibodies were analysed using the Luminex platform (single antigen-bead based assay). Endpoints - graft loss and number of AMBR episodes. Poisson regression was used to assess the risk. Median follow up was 6.4 (IQR 3.5; 8.4) years.

RESULTS: In the patients on the waiting list, the PRA, as well as MFI of specific circulating antibodies were not constant in time (fig. 1). Current PRA may decrease over time to 30-40% of the historical peak (maximum value) PRA. This is accompanied by a marked reduction in the MFI of some antibodies - sometimes below the lower threshold (but always higher than MFI of self-antigens!), which in this case was 1000. At times this may lead to an underestimation of the immunological risk. In univariate model, the increase in current PRA, increase in historical peak PRA and a decrease in ΔPRA (difference between peak and current PRA) was associated with an increased risk of ABMR (p<0.001 each) and transplant loss (p<0.001 each) (fig. 2). In our opinion, ΔPRA is a very ambiguous measure. The inclusion of ΔPRA in the multivariate model of Poisson regression shows that an increase in current PRA is associated with increased risk of humoral rejection (p<0.001), but not with transplant survival (p=0.17). Whilst historical peak PRA remains a significant factor for both humoral rejection of the transplant (p<0.001) and for its survival (p<0.001).

CONCLUSIONS: In the selection of donor-recipient pairs it is necessary to consider the spectrum of antibodies at the point of the peak (highest) PRA score. A reduction in this indicator may in some cases be hiding antibodies, which are reactive to donor antigens or to certain epitopes. The using only current PRA value may lead to underestimation of risk.