Oral

[O25-1] O25-1: Biomarkers for transplantation

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[O25-1-4] Urinary miR-155-5p and CXCL10 as prognostic and predictive biomarkers of rejection, graft outcome and treatment response in kidney transplantation

Olga Millan[1], Klemens Budde[2], Claudia Sommerer[3], Irene Aliart[4], Cristina Espinosa[5], Olesja Rissling[6], Beatriz Bardaji[7], Maaren Matz[8], Martin Zeier[9], Irene Silva[10], Lluis Guirado[11], Merce Brunet[12] (1.Hospital Clinic of Barcelona, University of Barcelona, 2.Charité Universitätsmedizin Berlin, 3.University of Heidelberg, University Hospital of Heidelberg and Mannheim, 4.Hospital Clinic of Barcelona, University of Barcelona, 5.Hospital Clinic of Barcelona, University of Barcelona, 6.Charité Universitätsmedizin Berlin, 7.Fundació Puigvert, 8.Charité Universitätsmedizin Berlin, 9.University of Heidelberg, University Hospital of Heidelberg and Mannheim, 10.Fundació Puigvert, 11.Fundació Puigvert, 12.Hospital Clinic of Barcelona, University of Barcelona)

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Background

MicroRNAs (miRNAs) may be useful diagnostic biomarkers of rejection and allograft outcome in kidney transplantation. Elevated urinary CXCL10 levels have been associated with acute rejection (AR) and may prognostic allograft failure. We examined the association between urinary pellet miRNA expression, CXCL10 levels, immunosuppressive drug exposure and AR and graft function in kidney transplant recipients.

Methods

Eighty *de novo* kidney transplant recipients were recruited from four European centres. All patients received tacrolimus (TAC), mycophenolate mofetil, and methylprednisolone. TAC trough concentrations and AUC (completed at 1st week and simplified at 1st, 2nd, 3rd and 6th month post-transplantation) were measured by liquid chromatography/tandem mass spectrometry and mycophenolic acid trough concentrations and AUC (in the same way as TAC) were measured by high-performance liquid chromatography with ultraviolet detector. Urinary pellet expression of miR-142-3p, miR-210-3p, and miR-155-5p was assessed by qPCR and urinary CXCL10 levels were assessed by ELISA at the 1st week and the 1st, 2nd, 3rd, and 6th month post-transplantation.

Results

Eight patients (10%) experienced AR (7 before the end of 1st month). As expected, a high interindividual variability in drug exposure was observed. However, rejectors patients showed a clear tendency towards lower TAC trough concentrations and AUC than non-rejectors, but the difference was not significant (P from 0.073 to 0.052). Before and during AR, patients showed a significant increase of urinary miR-142-3p, miR-155-5p, and CXCL10 levels and a decrease of miR-210-3p levels. Receiver Operating Characteristic curve analysis showed that miR-155-5p (AUC 0.875; $P = 0.046$) and CXCL10 (AUC 0.865; $P = 0.029$) had excellent capacity to discriminate between rejectors and non-rejectors. The optimal cut-off values for the prognosis of AR were 0.51, with 85% sensitivity and 86% specificity for miR-155-5p and 84.73 pg/ml, with 84% sensitivity and 80% specificity for CXCL10. miR-155-5p and CXCL10 levels correlated with glomerular filtration rate. Levels of both biomarkers normalised after recovery of graft function.

Conclusions

The regular early post-transplantation monitoring of urinary pellet expression of miR-155-5p and CXCL10 can help in the prognosis of AR and graft dysfunction. Large prospective randomized multicentre trials are warranted to refine our cut-off values and validate the clinical usefulness of these biomarkers.