

KSN 2017 Abstract

KSN-17-P124

Short-term anti-proteinuric effect of tacrolimus is not related to preservation of glomerular filtration rate during 5 year-follow up period in IgA nephropathy.

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Objectives : It has been known that tacrolimus reduced proteinuria in IgA nephropathy for a short period of time. We investigate persistent effects of proteinuria reduction and improvement of kidney function after discontinuation of the tacrolimus administration.

Methods : Patients with biopsy-proven IgA nephropathy were randomly selected for two treatment groups and control groups for each group; 1) patients treated with tacrolimus (Tac group) and 2) a placebo group with stratification by using a renin angiotensin system blocker (placebo group). The Tac group was treated up to 16 weeks and then stopped administration of tacrolimus at the final visit (trial phase). We tracked patients at 12-, 24-, 52-, and 240-week (observational phase). The primary outcome was the percentage change of time-averaged proteinuria (TA-proteinuria; g/g cr) and estimated glomerular filtration rate (eGFR) between the trial and observational phases. The TA-proteinuria was defined as the average of urine protein to creatinine ratio (UPCR) measured every three month during the two phases.

Results : Significant reduction of UPCR was observed in the Tac group compared to its control group at 4-week and 8-week visits during the trial phase ($p=0.023$ and $p=0.003$, respectively). The difference between Tac and its control group was not evident at the other periods, estimated by repeated measured ANOVA. The percent change of TA-proteinuria in the Tac group was more than the control group ($116 \pm 96\%$ vs. $63 \pm 239\%$, $p=0.004$). Therefore the TA-proteinuria during the observational phase was not significantly different between the Tac and control groups (1.150 ± 0.733 g/g cr vs. 1.455 ± 2.017 g/g cr, $p=0.775$). The levels of eGFR throughout the observational phase were not significantly different between the two groups. Furthermore, the mean rate of eGFR change during the whole phase was -6.4 ml/min/1.73 m²/year in the control group and -5.4 ml/min/1.73 m²/year in the Tac group ($p=0.988$).

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Conclusions : The anti-proteinuric effect of tacrolimus was promptly reversed 3 months after discontinuing the drug. The use of tacrolimus for a short period of time for the patients with IgA nephropathy temporarily reduces proteinuria, but ultimately, there is no long-term efficacy such as reduction of proteinuria and improvement of renal function.

Keywords : Tacrolimus; IgA nephropathy; Proteinuria; Glomerular filtration rate