The cumulative dose-dependent benefit of metformin in kidney transplantation recipients

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Background: The status of metformin as a primary treatment of choice is concrete, moreover it has recently been recommended for advanced chronic kidney disease patients. Although, the evidence of metformin usage in kidney transplant recipients is lacking. We investigated the effect of metformin in kidney transplant recipients.

Methods: The primary outcomes were all-cause mortality and death censored graft survival (DCGS) and secondary outcome was biopsy proven acute rejection (BPAR). Cox analysis and propensity score (PS) matching were done. Time-varying cox and marginal structural cox regression was conducted for HbA1c. A defined daily dose (DDD) of the WHO Collaborating Centre and penalized spline curve based on DDD was used cumulative effect of metformin.

Results: In 2,048 diabetic KTRs of six tertiary center, 1,199 patients were metformin user and 849 patients were non-metformin user. Most patients were pre-existing diabetes mellitus (DM) before transplantation (78.7%; new-onset diabetes mellitus after transplantation [NODAT], 21.3%) and pre-existing DM tends to be less prescribed metformin than NODAT (pre-existing DM: 902 patients, 56.0%; NODAT: 297 patients, 68.0%; $P<0.001$). The metformin user had a lower risk of all-cause mortality (adjusted hazard ratios [aHR], 0.57; 95% confidence interval [CI], 0.34–0.94; $P=0.028$), graft failure (aHR, 0.45; 95% CI, 0.29–0.69), and BPAR (aHR, 0.57; 95% CI, 0.44–0.73). The trend was consistent after PS matching. Even after time varying adjustment of HbA1c with other covariates, metformin usage was associated with significant reduction in all target outcomes. In addition, the more cumulative metformin exposure was correlated to the less risk of all-cause mortality, DCGS and BPAR in whole and PS matched population.

Conclusions: In conclusion, metformin can be also considered as first-line anti-diabetic treatment of choice in KTRs, not only from the benefit of lower mortality, graft survival and acute rejection, but also cumulative dose dependent protective effect of metformin.

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