Simultaneous pancreas kidney recipients have a lower tacrolimus exposure for a similar c0 as compared to kidney only recipients

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Background

Current guidelines recommend similar target trough levels (C_0) for Simultaneous Pancreas Kidney Transplant recipients (SPKTR) and kidney transplant recipients (KTR). Thus, the assumption is made that SPKTR and KTR have a similar area under the concentration versus time curve ($AUC_{0\text{-}12h}$) for a given target C_0. However, it could be hypothesized that SPKTR have a different $AUC_{0\text{-}12h}$ for the same target C_0, from e.g. diabetic gastroparesis or enteral surgery.

Methods

In this cohort study, we investigated whether SPKTR differed in their tacrolimus pharmacokinetics from KTR. The ratio of the $AUC_{0\text{-}12h}$ and the target trough level (AUC/C_0) was used as a marker for the pharmacokinetics of tacrolimus. The $AUC_{0\text{-}12h}$ and the C_0 were routinely measured at week one, week six, month six and year one post-transplant. At week one, the AUC_0-12h was determined using samples obtained at 0, 1,2,3,4,5 and 6 hours. At week six, month six and year one, the AUC_0-12h was determined using samples obtained at 1,2,3 hours. We included all SPKTR and KTR that were transplanted between 2011 and 2023 at our center. KTR with type 1 diabetes were not excluded from the primary analysis. Mean AUC/C_0 ratios were compared using the student's t-test between weeks 0-6, weeks 6–26. and weeks 26 - 52. A sensitivity analysis was performed using a univariate linear mixed effects model to address potential bias introduced by repeated measurements.

Results

A total of 528 measurements were performed for 198 SPKTR and 4428 measurements were performed for 1659 KTR during the first-year post-transplant. For SPKTR the mean AUC/C_0 ratio was 14% lower ($p<0.001$) between weeks 0 - 6, 11% lower ($p<0.001$) between weeks 6 - 26 and 12% lower ($p<0.001$) lower between weeks 26 - 52, as compared to KTR. Differences remained similar after correction for repeated measurements.

Conclusions

SPKTR have a lower $AUC_{0\text{-}12h}$ for a given C_0 as compared to KTR that persists over time and is thus not readily explained by postoperative opioid use or enteral drainage. Future guidelines should take into account that SPKTR are on average pharmacokinetically different from KTR.