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P221 -Body weight based initial dosing of tacrolimus post renal transplant- Is this an ideal approach?

Dr Rajkumar Chinnadurai[1], Dr Sara Taha Ibrahim[1], Dr Shiv Bhutani[2], Prof Philip Kalra[1]
[1]Salford Royal NHS Foundation Trust, Salford, United Kingdom, [2]Central Manchester University NHS Foundations Trust, Manchester, United Kingdom

Introduction
Tacrolimus has a narrow therapeutic index and dosing can be challenging due to its high intra- and inter-individual variability. The current FDA recommendation for tacrolimus dosing immediately post-transplant is based on body weight (0.1mg/kg/day in two divided doses). Recent studies have highlighted that the dosing of tacrolimus purely based on weight may not be appropriate, particularly in obese individuals, as this can lead to very high trough levels due to decreased activity of the hepatic cytochrome P450 metabolising enzyme (CYP 3A4) and suppressed intestinal transporter activity.
Objective
This study aims to estimate the effect of body mass index (BMI) and the weight-based dosing on tacrolimus trough levels in renal transplant recipients.
Methods
This study was conducted on 88 of the 177 Salford Kidney Study patients who had renal transplantation between 2010 and 2017 and who had complete datasets. Data including demographics, BMI, drug history, and tacrolimus trough levels with corresponding doses were collected at baseline (first trough level after transplantation), at one month and six months post-transplantation. Data on delayed graft function and transplant biopsy details were also gathered. The cohort was split into three groups based on BMI (Kg/m2) (group-1 >30, group-2 >25-30, and group-3 < /= 25) and compared with tacrolimus dose, levels and concentration/dose (C/D) ratio at the three time points.
Results
The median age of our cohort was 57 years with a predominance of males (57%) and Caucasians (83%). 67% received a deceased donor transplant and 33% were transplanted from live donors. The standard induction immunosuppression regime included basiliximab (96%) and methylprednisolone followed by tacrolimus dosed based on dry weight (0.1 mg/Kg/day in two divided doses), myfortic 720 mg bd (91%) and prednisolone 20 mg od for 5 days. The median time for the first tacrolimus level was 3 days post-transplant. Patients with higher BMI received a significantly higher dose at baseline (p=0.001), however their C/D ratio was not significantly different in comparison with the normal BMI group (p=0.22). Similarly, there was no difference observed between the BMI groups in the C/D ratio at one month and at six months post-transplant. Also, there was no clear correlation between BMI and the baseline C/D ratio (Pearson's correlation coefficient r= -0.116, p=0.28) (figure). 5/88 patients had kidney biopsy for delayed graft function, and this was not attributed to tacrolimus dosing or concentrations.
Conclusions
Our study showed that there was no clear correlation between BMI and tacrolimus levels. The standard dosing of tacrolimus based on body weight in obese individuals did not adversely affect their tacrolimus concentrations or transplant functions. Until further evidence from large scale studies is available, the current dosing practice based on body weight with close monitoring of trough levels should be the adopted approach.