Study to develop Alternate Sampling Strategies to measure tacrolimus and creatinine – to facilitate domiciliary care of transplant patients: an interim analysis

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Background: Therapeutic drug monitoring of tacrolimus and assessment of renal function after renal transplantation is paramount at various time point in the post transplant period. Patients travel long distances from all over India and incur huge financial burden for travel, stay and loss of work during the regular review visits to the nodal transplant centres. Literature has reported using alternate sampling strategies such as dried blood spots (DBS) for both tacrolimus and creatinine. Volumetric absorptive microsampling (VAMS), though expensive, may be the best alternative to eliminate bias created by hematocrit and blood spotting variability. Therefore, we aimed to compare which sampling alternative would give the most accurate result in comparison to the gold standard, whilst being practical for use in India

Methods: Renal transplant patients were recruited after obtaining informed written consent. On the day of the test, blood sample was collected for measurement of whole blood tacrolimus, serum creatinine and hematocrit. Immediately, from a finger prick blood drop, blood was first wicked into two samplers of the Mitra Microsampler VAMS (20 ul each) and blood was allowed to freely drop into two spots of the Whatman 903 filter paper card. Whole blood, serum, DBS and VAMS concentrations for tacrolimus and creatinine was measured and compared.

Results:

Of the152 patients recruited, four were not included for the DBS and one for the VAMS analysis. The intraclass correlation (95% CI) between mean DBS concentration and whole blood tacrolimus concentration was 0.969 (0.929-0.984), between mean VAMS concentration and whole blood tacrolimus was 0.978(0.964-0.986), between mean DBS concentration and serum creatinine was 0.913(0.207-0.973) and that between mean VAMS concentration and serum creatinine was 0.926(0.388-0.976). Both haematocrit and spot size did not improve the correlation between DBS and serum creatinine, by regression analysis. From the Bland Altman, the mean (sd) bias was -0.24 (0.18) and -0.22(0.18) mg/dl for DBS and VAMS creatinine respectively. Including this correction factor better predicted the serum creatinine, when the serum creatinine was >1.0 mg/dl.

Conclusion: Both DBS and VAMS can be used to measure tacrolimus. Measurement of serum creatinine using both DBS and VAMS needs to be interpreted with caution.

Keywords: Dried Blood Spot; VAMS Microsampler; Tacrolimus; Creatinine