Poster: Immunosuppression

THERAPEUTIC DRUG MONITORING OF CYCLOSPORINE A IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS USING VOLUMETRIC ABSORPTIVE MICROSAMPLING WITH LC-MS/MS TECHNIQUE – CROSS- AND CLINICAL VALIDATION OF THE BIOANALYTICAL METHOD

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Background: Cyclosporine A (CSA) is one of the main immunosuppressive drugs used in the pediatric population after solid organ transplantation (SOT). Due to the narrow therapeutic index and relatively high inter- and intraindividual variability in pharmacokinetics, therapeutic drug monitoring (TDM) of CSA is strictly needed. In routine clinical practice, frequently uncomfortable venipuncture is necessary for whole-blood (WB) collection to determine trough CSA levels. Volumetric absorptive microsampling (VAMS) is an alternative strategy to WB collection. In this study, we aimed to cross- and validate a method for CSA quantification in WB and VAMS clinical samples.

Methods: Whole blood (classic venous collection) and VAMS samples (finger puncture by a lancet) for this study were obtained during regular follow-up visits between January 2023 and February 2024 from 50 pediatric renal transplant recipients treated at the Children's Memorial Health Institute (CMHI) in Warsaw. The CSA levels were measured in VAMS samples using LC-MS/MS technique, while in the WB samples, CSA was determined using EMIT and LC-MS/MS techniques. The correlation between the developed and validated methods was evaluated using Passing–Bablok and Pearson correlation coefficient calculations.

Results: The correlation between methods was acceptable only in the case of WB versus VAMS results. The correlation between methods was 0.987 (0.961-0.996), 0.990 (0.813-0.997) and 0.919 (0.769-0.973) for WB/EMIT, WB/VAMS and VAMS/EMIT paired results. The mean percentage bias was evaluated as 17.65%, 2.28% and 5.22% for mentioned pairs, respectively. Evaluation of Passing-Bablok regression results was satisfactory only for WB/VAMS paired samples – both intercept and slope fulfilled acceptance criteria.

Conclusions: This study demonstrated and confirmed the utility of VAMS-based CSA monitoring in the pediatric population. Cross validation was only successful for the VAMS and WB methods, and as a consequence, both methods are equivalent in clinical practice. The VAMS method is patient-friendly and rearranges TDM; subsequently, it may minimize non-compliance with helpful regimens because of the straightforwardness of blood collection.

Key Words: Cyclosporine A, VAMS, TDM, EMIT, LC-MS/MS, renal transplantation