Poster: Immunosuppression

LC-MS/MS DETERMINATION OF RAPAMYCIN (SIROLIMUS) IN WHOLE BLOOD AND VOLUMETRIC ABSORPTIVE MICROSAMPLES – ASSESSMENT OF THERAPEUTIC DRUG MONITORING IN IMMUNOSUPPRESSIVE THERAPY AND COMPARISON WITH APPLICATIONS OF IMMUNOCHEMICAL TECHNIQUES

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Background: Rapamycin (sirolimus, SIR) is a widely used mTOR inhibitor in transplantology, neurology, and oncology. Routinely, due to narrow therapeutic range and high inter- and intraindividual variability, therapeutic drug monitoring of SIR is required. The recommended matrix for SIR determination is whole blood (WB), and several analytical methods are used in the clinical laboratories, such as immunochemical (e.g. EMIT, Enzyme Multiplied Immunoassay Technique) and chromatographic (e.g. LC-MS/MS, Liquid Chromatography-Tandem Mass Spectrometry) as well. Volumetric absorptive microsampling (VAMS; Mitra™, Trajan, USA) is a recent approach for sample collection, particularly during therapeutic drug monitoring (TDM). This technique is attractive, especially in the pediatric population, where the amount of collected material should be reduced. The aim of the study was to perform a cross- and clinical validation of the new VAMS-based LC-MS/MS method for SIR determination compared with reference WB-LC-MS/MS and routinely used EMIT methods.

Methods: Whole-blood (classic venous collection) and VAMS samples (finger puncture by a lancet) were obtained during regular follow-up visits between January 2022 and February 2024 from 150 pediatric renal transplant recipients treated at the Children's Memorial Health Institute (CMHI) in Warsaw. The SIR levels were measured in VAMS samples using LC-MS/MS technique, while in the WB samples, SIR 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. Additionally, potential hematocrit effects (HE) were evaluated.

Results: The correlation between methods was acceptable in the case of WB versus VAMS and VAMS and EMIT results. The mean percentage bias was evaluated as 0.96%, 19.84% and -10.02% for WB/VAMS, WB/EMIT, and EMIT/VAMS pairs, respectively. Evaluation of Passing-Bablok regression results were satisfactory only for WB/VAMS and EMIT/VAMS paired samples – both intercept and slope fulfilled acceptance criteria (0 i 1 in 95% CI). No hematocrit effect was observed during validation and clinical samples determination.

Conclusions: Cross-validation confirmed the potential implementation of VAMS-based assay in routine clinical practice. The mentioned microsampling technique is equal according to the reference WB-LC-MS/MS method and, interestingly, to the EMIT immunochemical assay.

Key Words: rapamycin, VAMS, TDM, EMIT, LC-MS/MS