Poster: Oncology

CLINICAL COMPARISON OF EMIT AND QMS ASSAYS WITH LC-MS/MS METHOD FOR METHOTREXATE DETERMINATION – APPLICATION FOR THERAPEUTIC DRUG MONITORING

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Background: Methotrexate (MTX) is a crucial cytostatic drug used both in autoimmune diseases (low doses) and cancer chemotherapy, especially in the lymphatic system and neurological tumours (high doses). MTX is considered a highly toxic drug, and prevention of side effects using leucovorin and/or glucarpidase is necessary. High-dose methotrexate (HDMTX) is administered as an intravenous bolus with a body surface area of > 500 mg/m^2. During pharmacotherapy with MTX, routine monitoring of MTX and serum creatinine concentrations is performed, while the dose of leucovorin infusion, with the possible addition of glucarpidase, is adjusted simultaneously. According to MTX measurements, immunochemical assays are currently more popular than chromatographic techniques. On the other hand, potential cross-reactivity with metabolites (e.g. 7-OH-MTX) speaks in favour of more selective techniques such as LC-MS/MS. The aim of the study was to evaluate three methods of MTX level determination in plasma samples from pediatric patients treated with HDMTX during chemotherapy.

Methods: To study the 53 triplicated plasma samples from pediatric patients under MTX treatment due to neurological cancers. For MTX determination in clinical plasma samples, the three methods have been used: Syva EMIT (Enzyme Multiplied Immunoassay Technique; Siemens Healthineers), QMS (Quantitative Microsphere System; ARK Diagnostics) and ESI(+)-LC-MS/MS (validated in our laboratory). The obtained results have been evaluated statistically, using correlation tools, Passing-Bablok regression, and Bland-Altman bias as well.

Results: The correlation between methods were: EMIT vs QMS (0.934; 0.887 to 0.962), EMIT vs LC-MS/MS (0.981; 0.967 to 0.989) and QMS vs LC-MS/MS (0.971; 0.950 to 0.983). The Passing-Bablok regression equation was: QMS=1.073(EMIT)-0.004 for EMIT vs QMS, EMIT=0.9323(LC/MS)+0.0078 for EMIT vs LC-MS/MS and QMS=1.005(LC/MS)+0.01013 for QMS vs LC-MS/MS, respectively. The mean percentage bias, calculated using the Bland-Altman method, was 3.10%, 8.26% and 11,49% for EMIT/QMS, EMIT/LC-MS and QMS/LC-MS, respectively. The criteria for slope and intercept according to regression were acceptable.

Conclusions: After cross-validation, we may consider both immunochemical methods and LC-MS/MS equal in laboratory and clinical practice (test results have been acceptable according to acceptance criteria). The sensitivity and selectivity of immunochemical methods seem acceptable in clinical practice during TDM of HDMTX treatment.

Key Words: methotrexate, EMIT, QMS, LC-MS/MS, TDM