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ORIGINAL ARTICLE

Comparative Routine Therapeutic Drug Monitoring of Mycophenolic Acid in human Plasma with HPLC-UV and Isotope Dilution LC-MS/MS

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SUMMARY

Background: **Therapeutic drug monitoring (TDM) of the immunosuppressant mycophenolic acid (MPA) is especially recommended for the control of personalized immunosuppressive therapy. Various test systems are available for MPA monitoring, including high performance liquid chromatography combined with UV detection (HPLC-UV) and isotope dilution liquid chromatography tandem mass spectrometry (ID-LC-MS/MS).**
Methods: **In the present work, commercially available kits for MPA monitoring with HPLC-UV and ID-LC-MS/MS were subjected to routine use TDM. Following method verification according to the Clinical and Laboratory Standards Institute (CLSI) guidelines, 105 native sample duplicates from patients under therapy with mycophenolate mofetil were assayed with both procedures for comparative testing.**
Results: **Using bi-level quality controls, the estimate of repeatability, within-laboratory imprecision and inaccuracy were ≤ 5.18%, ≤ 5.95% and ≤ 3.86% for all MPA measurements. Weighted Deming regression analysis yielded a slope of 0.93, an intercept of 0.04, and Pearson's correlation coefficient (r) of 0.99, while Bland-Altman analysis showed a combined relative bias of 4.93% (± 1.96 SD: -16.68 - 26.54%). Plasma samples taken from a patient repeatedly showed the presence of an interferent only in HPLC-UV analysis.**
Conclusions: **Based on these results, HPLC-UV testing can be considered suitable for routine TDM of MPA in the clinical setting with high precision. Due to the risk of unforeseen analytical interference in ever-increasing multimorbidity and polypharmacy, highly selective ID-LC-MS/MS methodology should be given preference over HPLC-UV analysis whenever feasible.**
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Supplemental Table

Table S1. Mass spectrometry parameters: multiple reaction monitoring (MRM) transitions with precursor and product ions for quantifier and qualifier.

Analyte	Rt (min)	Precursor ion (m/z)	Quantifier		Qualifier		CV (V)	Dwell time (s)
			Product ion (m/z)	CE (eV)	Product ion (m/z)	CE (eV)		
MPA	1.08	321.2	207.2	20	275.2	13	30	0.055
MPAG	0.77	514.2	275.2	25	207.2	35	20	0.055
MPA -d_3	1.08	324.2	210.2	20	-	-	30	0.055
MPAG -d_3	0.77	517.2	278.2	25	-	-	20	0.055

MPA - mycophenolic acid, MPAG - mycophenolic acid β-D-glucuronide, Rt - retention time, CV - cone voltage, CE - collision energy.