Implementation of the Toxtyper LC-MS^n instrument in a routine laboratory for drug of abuse screening in urine

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Introduction: Screening of substance misuse and verification of compliance to opioid replacement therapy is usually performed in urine samples. For this purpose immunological drug screens are frequently used. This is mostly complemented by gas chromatography mass spectrometry (GC-MS) or liquid chromatography mass spectrometry (LC-MS) for drugs and metabolites for which immunoassays are lacking. This divided work-flow is sometimes tedious and time consuming in a routine laboratory with a high work load. A step forward would be an instrument which can consolidate the screening approach and an automated sample pretreatment. The ion trap mass spectrometer (IT-MS) Toxtyper^{TM} (Bruker) has the potential to simplify current algorithms. To verify this assumption the Toxtyper protocols based on three spectrum matching libraries were compared to the current approach used at the central laboratory of Klinikum Stuttgart.

Materials and Methods: A selected drug panel was used to investigate the analytical performance of the Toxtyper instrument and concordance between the established approach and the Toxtyper results was investigated with 188 patient urine samples.

Results: For acetylcodeine, amphetamine, benzoylecgonine, methadone, and nordiazepam the lower limits of detection and identification were below the common cut-offs for immunological screening assays and similar to GC-MS. Within- and between-run imprecision as well as accuracy were always better than 25%. For the detection of pregabalin and sufentail Toxtyper protocols were less sensitive compared to targeted LC-MS assays. In patient urine samples concordance met the predefined criterion of >90% for all drugs, except for pregabalin. Due to the very simple and straightforward sample preparation (no extraction) that covers a very comprehensive set of drugs and metabolites the sensitivity of these Toxtyper assay protocols can show limitations for some specific drug classes. Therefore, cannabis misuse could not be reliably detected and would make a more specific sample preparation necessary to enhance the sensitivity. Finally, the automation of the sample pretreatment procedure using a Tecan pipetting robot has been successfully implemented.

Conclusions: The integration of the Toxtyper IT-MS instrument combined with automated sample preparation allowed considerable consolidation of methods and instruments as well as saving of time. It replaced GC-MS screening and targeted LC-MS methods for benzodiazepines, pregabalin, as well as synthetic opioides. The performance of the Toxtyper IT-MS turned out to be as robust as GC-MS with more than 9,000 urine samples analyzed to date.