Clinical validation study to derive conversion factors from capillary blood to plasma concentration for mirtazapine, quetiapine and norquetiapine, Stern M[1], Giebels M[2], Fey T[2], Lübking M[3], Alferink J[3], Hempel G[1],

[1] Department of Pharmaceutical and Medical Chemistry – Clinical Pharmacy, University of Münster, Corrensstraße 48, 48149 Münster, Germany

[2] Geriatric Psychiatry, LWL-Klinik, Friedrich-Wilhelm-Weber-Straße 30, 48147 Münster, Germany

[3] Damian-Klinik, Alexianer Münster GmbH, Alexianerweg 9, 48163 Münster, Germany

Background

Therapeutic Drug Monitoring (TDM) has gotten more important in psychiatric treatment over the past years. With TDM, the therapeutic reference ranges of antidepressants or antipsychotics can be achieved even faster when plasma concentrations are checked and possible drug interactions are averted. The ways of sampling blood have also improved in the near past. Different microsampling devices enable at-home sampling by the patients themselves or sampling as pharmaceutical service in pharmacies. One of these devices are the volumetric absorptive microsampling (VAMS) tools called Mitra.

Methods

In two hospitals in Münster patients in the psychiatric department are asked to give written informed consent and to give an additional drop of blood out of the finger berry during the next routine blood withdrawal. The venous blood, capillary blood and plasma is then sampled with a VAMS device and shipped to a laboratory. There, the device is processed with an optimized extraction method and measured by an LC-MS with single-quadrupole detector. The obtained concentrations in different matrices are checked for linear regression by using Passing-Bablok regression. Afterwards a Bland-Altman analysis according to the cross-validation requirements of the EMA guideline for bioanalytical method validation is conducted.

Results

For mirtazapine and quetiapine a good correlation with a pearson's R of above 0.95 could be achieved. The correlation for norquetiapine is slightly worse with 0.86 what might be caused by the small sample size for this substance. Only mirtazapine passed the cross-validation test. After exclusion of an obvious outlying patient, the cross-validation was passed for quetiapine, but not for norquetiapine. The derived conversion factors are 1.03 for mirtazapine and 1.49 for quetiapine.

Conclusions

The use of VAMS as a sampling device could be tested in the clinical validation study and conversion factors for quetiapine and mirtazapine could be achieved. With these conversion factors, it is possible to collect samples by finger prick and to calculate estimated plasma concentrations. The study showed that the handling of the devices is very easy and intuitive and an introduction of the method to routine healthcare is possible

Key Words

Volumetric absorptive microsampling, clinical study, quetiapine, mirtazapine, conversion factor