Development and validation of a method for epidermal growth factor receptor tyrosine kinase inhibitors quantification in dried blood spots: practices of pharmacist assisted self-blood sampling

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Background

Epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) are key drug for treatment of non-small lung cancer patient harboring EGFR mutations. In this study, we developed and validated a liquid chromatography tandem mass spectrometry method for the quantification of EGFR-TKIs (gefitinib, erlotinib, and afatinib) in dried blood spots (DBSs). This study also demonstrated pharmacist assisted self-blood sampling with DBS on patient taking EGFR-TKIs.

Methods

EGFR-TKIs was extracted with methanol from DBS of 3 mm in diameter and detected using a quantum triple quadrupole mass spectrometer (QTRAP4500, ABSCIEX). The method was validated by evaluating its precision, accuracy, selectivity, carryover, matrix effect, recovery, and stability. For clinical validation, paired DBS and plasma concentrations were compared for 22 patients taking EGFR-TKIs (gefitinib: 10 patients, erlotinib: 7 patients, and afatinib: 5 patients). All DBS sample were obtained by pharmacist assisted self-blood sampling using BD Microtainer Contact-Activated Lancets (BD Biosciences). Before collecting and analyzing the samples, we obtained written informed consent from all patients. The study protocol was approved by the Institute of Biomedical Research and Innovation Research Ethics Committee.

Results

The calibration linear range was 37.5-2,400 ng/mL, 78.125-5,000 ng/mL, and 1.953125-1,000 ng/mL, encompassing the therapeutic concentrations of gefitinib, erlotinib, and afatinib respectively. The accuracy and precision were within 15% of the quality controls on each drugs. The lower limit of quantification was determined to be 40 ng/mL, 100ng/mL, and 2ng/mL on gefitinib, erlotinib, and afatinib respectively. Gefitinib and erlotinib were stable in DBSs for 1 months at room temperature and - 20 degree However afatinib was only stable at - 20 degree for 1 months. A good correlation was observed between the blood levels of EGFR-TKIs measured by the DBS method and plasma concentrations in the 22 patients.

Conclusions

This method provides a simple, fast, and accurate approach to quantitative analysis of EGFR-TKIS in DBSs. The method can be used for minimally invasive evaluation of the EGFR-TKIs blood concentration and the DBS samples can be obtained by pharmacist assisted self-blood sampling.