Poster

[P25-9] P25-9: Oncologic drugs (1)

Chair: Ryuji Ikeda, Japan

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[P25-9-5] Simultaneous quantification of 5-FU, uracil and tegafur using ultra-performance liquid chromatography coupled to tandem mass spectrometry

Ken Shiraiwa[1], Yosuke Suzuki[2], Motoshi Iwao[3], Tetsuya Kaneko[4], Yuhki Sato[5], Yukio Iwashita[6], Hiroki Uchida[7], Kazuhiro Tada[8], Masafumi Inomata[9], Hiroki Itoh[10] (1.Oita University Hospital, 2.Oita University Hospital, 3.Oita University Hospital, 4.Oita University Hospital, 5.Oita University Hospital, 6.Oita University Hospital, 7.Oita University Hospital, 8.Oita University Hospital, 9.Oita University Hospital, 10.Oita University Hospital)

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Background

Combination therapy of tegafur/uracil (UFT) and leucovorin (LV) is commonly used to treat colorectal cancers. This therapy has significant therapeutic effect, but severe adverse effects appear frequently. Therapeutic drug monitoring (TDM) may be useful to prevent the adverse effects. The aim of this study was to develop and validate an assay for simultaneous quantification of 5-FU, uracil and tegafur in human plasma using ultra-performance liquid chromatography coupled to tandem mass spectrometry (UPLC-MS/MS). This is first report to quantify three compounds in plasma simultaneously.

Methods

After a simple protein precipitation step, plasma samples were extracted with ethyl acetate, evaporated, and reconstituted in 27.5% acetonitrile with 2 mM ammonium formate. 5-FU, uracil and tegafur were analyzed by UPLC-MS/MS in negative electrospray ionization mode with a run time of 11.5 minutes using an ACQUITY UPLC® HSS T3 column. The mobile phase was a gradient of water: acetonitrile. ^{13}C and ^{15}N-labeled 5-FU, uracil and tegafur were used as internal standards. Validation was performed according to FDA guidance.

Results

The calibration curves were linear over the concentration range of 2-500 ng/ml for 5-FU, 20-5000 ng/ml for uracil, and 200-50000 ng/ml for tegafur. The limits of quantification (LOQ) for 5-FU, uracil and tegafur were 2, 20 and 200 ng/ml respectively. Average recovery rates of 5-FU, uracil and tegafur were 79.9, 80.9 and 87.8%, respectively. The precision was below 13.3% and accuracy was within 11.6% for all quality control levels. Matrix effect of 5-FU, uracil and tegafur were more than 43.5%, 84.9% and 100.2%, respectively. This assay was successfully applied to assess the time course of plasma 5-FU, uracil and tegafur concentrations in two patients after administration of UFT.

Conclusions

We have developed a sensitive and robust UPLC-MS/MS method for simultaneous quantification of 5-FU, uracil and tegafur in human plasma. This method may be useful for TDM in patients undergoing UFT/LV combination therapy.