Therapeutic drug monitoring of imatinib in Chinese gastrointestinal stromal tumor patients by an HPLC method

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Background:

Imatinib (IM) is the first-line medication for treating gastrointestinal stromal tumors (GISTs). Due to the large inter-individual variability, the trough plasma concentration of IM should be monitored to ensure the efficacy and safety of IM therapy, which should be over 1100 ng/mL. A simple HPLC-UV method was developed and validated for quantitating IM in the plasma of Chinese GIST patients. The dose-concentration relationship was analyzed.

Methods:

The samples collected from 241 GIST patients were processed by protein precipitation, neutralized, and finally analyzed by High-Performance Liquid Chromatography (HPLC).

Results:

The plotted calibration curve of the HPLC method was linear in the range of 50 to 10000 ng/mL. The retention time of IM was approximately 9 min. The intra-day and inter-day inaccuracies and imprecisions ranged from -5.81 to 6.53 %. The extraction recoveries were all over 90 %. All the results of stability studies were within ± 15 % of nominal concentrations. The percentages of the concentrations below 1100 ng/mL in the 300, 400, and 600 mg daily groups were 18.75, 26.64, and 11.11 %, respectively. For the concentrations over 2000 ng/mL, the percentages of the three dose groups were 12.5, 22.90, and 55.56 %, respectively. 121 patients were determined the genotype, 70.26 % of whom were cKit11 genotype. 29.75 % and 23.14 % of the 121 patients showed low concentrations below 1100 ng/mL and high concentrations above 2000 ng/mL, respectively. Doses of 13 patients were switched from 400 to 300 mg daily due to drug-related toxicities, with the concentrations still over 1100 ng/mL. Doses of 4 patients were increased from 400 to 500 or 600 mg per day to elevate the efficacy according to the concentrations. The dose of 1 patient was decreased from 400 to 300 mg daily because of a serious rash with high trough concentrations.

Conclusions:

The HPLC method was simple, reliable, economical, and reproducible. The concentration distribution displayed in Chinese GIST patients differs from that in Caucasian patients, 73.20 % of whose concentrations were below 1100 ng/mL. Therapeutic drug monitoring of IM, combining genotype detection with blood concentration monitoring, is a useful tool to increase efficacy and guarantee the safety of IM therapy.