Symposium

[S-16] S-16: TDM of 5-FU

Chairs: Edward Chu, USA / Yasutsuna Sasaki, Japan
Wed. Sep 27, 2017 10:30 AM - 12:00 PM Room D (1F)

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[S-16-2] Study on the relationship among gene polymorphism, 5-FU plasma concentration and adverse reactions in the chemotherapy of colorectal cancer

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Keywords: colorectal cancer, 5-Fu, plasma concentration, gene polymorphism, individualized drug therapy

Background

5-FU is the first-line medicine for colorectal cancer chemotherapy. Gene polymorphism is a pivotal factor for predicting the adverse reactions of 5-FU. However, most studies focus on the relationship between the genetic polymorphism of a specific metabolic enzyme and the adverse reactions of 5-FU, which often cause conflicting conclusions. This study aims at detecting the polymorphisms of 5-FU metabolism enzymes , and blood concentration, as well as collecting the clinical toxicity data, and then performing the correlation analysis among them. This research will provide the basis for individualized treatment of 5-FU.

Methods

Detect the polymorphisms of 5-FU metabolic enzymes (DPYD and MTHFR) of the CRC patients treated with mFOLFOX6 using pyrosequencing. Blood samples were collected after 18-30h infusion of 5-FU after the second cycle to detect the serum concentration and calculate AUC value. WHO adverse reaction assessment method was used to evaluate toxicity.

Results

1. 57 CRC patients included 1 case of DPYD*2A heterozygous and homozygous mutation separately, 2 case of DPYD c.1679TG, 26 cases of MTHFR 677CT, 6 cases of MTHFR 677TT, 21 cases of MTHFR 1298AC, 5 cases of MTHFR 1298CC; the incidence of myelosuppression, vomiting, and diarrhea in patients with DPYD heterozygous mutation plus MTHFR mutation, and DPYD homozygous mutation was 100%.
2. The AUC of 5-FU was normally distributed in 57 CRC patients ranging from 4.9 to 38.4 mg·H /L, with the median level of 21.6 mg·h/L. There were 35 cases with AUC<22 mg·h/L, 14 cases with AUC 22-27 mg·h /L and 8 cases >27 mg·h/L. The incidence of grade Ⅲ-Ⅳ toxicities in the 3 groups were 10.5%, 12.4% and 62.5%, respectively. 5-FU is effective and safe in the AUC range of 20-27 mg·h/L.
3. The AUCs of patients with DPYD heterozygous mutation plus MTHFR mutation, and DPYD homozygous mutation were >27mg·h /L.

Conclusions

DPYD heterozygous mutation plus MTHFR mutation, and DPYD homozygous mutation, can be used as predictive factors of 5-FU toxicity; there is no significant relationship between MTHFR polymorphisms and 5-

FU adverse reactions.