Association of Capecitabine pharmacokinetic parameters with cutaneous adverse events in Iranian cancer patients

Sepideh Hassanlou, Minoo Afshar, Mehdi Rajabi

Department of Clinical Pharmacy, Islamic Azad University of Pharmaceutical Sciences Branch (IAUPS), Tehran, Iran

Abstract: Capecitabine, a prodrug of 5-FU, is converted into the main drug by thymidine phosphorylase, existing in high amount in tumor tissues. The efficacy of this medicine in treatment of colon, colorectal and breast cancers is evident. However, one of the most common side effects of treatment is hand-foot syndrome (HFS), which is not life-threatening, but is the most frequent dose-limiting toxicity—often leading to discontinuation of therapy due to a marked decrease in quality of life.

The aim of this study was evaluation of the relationship between pharmacokinetic parameters of Capecitabine and the HFS induced by this drug in Iranian cancer patients.

After providing informed consent, nine patients with histologically proven cancer treated by Capecitabine (1500mg twice daily) were included in this study. Serial blood samples were collected before and from 0.5 to 4 hours after the morning dose. Plasma Capecitabine concentrations were measured using a validated HPLC-UV method, with a lower limit of quantitation of 50ng/mL. Pharmacokinetic parameters were determined using noncompartmental methods.

All 9 subjects (2 men, 7 women; mean age, 52 years; mean weight, 76.33 kg) completed the study. All subjects reported HFS. Mean (SD) pharmacokinetic parameters observed were as follows: $C_{\text{max}}$, 6070 (5279) ng/mL; $t_{\text{max}}$, 0.58 (0.20) h, AUC, 458.75 (370.90) ng·h/mL and $t_{1/2}$, 0.48 (0.10). Inter-patient variation in plasma concentration was high and $C_{\text{max}}$ within individuals varied by 10 fold. Interestingly, grade 3 of HFS was observed in 2 out of 9 patients with higher plasma concentrations.

Although no relationship between Capecitabine plasma concentration and adverse drug reactions was found in previous reports, a positive association between pharmacokinetic parameters and occurrence of HFS in Iranian patients was observed in this study.

Keyword: Capecitabine, Hand-foot syndrome, pharmacokinetic