Tumori, 97: 243-247, 2011

Concurrence of *UGT1A* polymorphism and end-stage renal disease leads to severe toxicities of irinotecan in a patient with metastatic colon cancer

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ABSTRACT

Aims and background. Colorectal cancer is one of the most common malignancies in the world, and irinotecan (CPT-11) is useful in its treatment. However, the safety and pharmacokinetics of irinotecan in dialysis patients with metastatic colorectal cancer are unclear.

Case report. We report the case of a 74-year-old man receiving chronic hemodialysis who had metastatic colorectal cancer. Palliative chemotherapy with irinotecan (80 mg/m^2 weekly) was administered after hemodialysis. Blood samples were collected before and 1.5, 3, 6, 9, and 15 hours after administration of irinotecan. The peak serum concentrations (C_{max}) of irinotecan and SN-38 in this patient were 1,480 and 17.8 ng/mL, respectively, which were similar to the reported values in patients with normal renal function after a similar dose of irinotecan (75 mg/m^2). The area under the serum concentration-time curve ($AUC_{0-\infty}$) was 8,240 ng×h/mL for irinotecan and 619 ng×h/mL for SN-38. The $AUC_{0-\infty}$ for SN-38 was markedly higher than that for patients with normal renal function. Sequencing analysis of the *UGT1A* genes found that the patient had variant alleles of UGT1A1*28, UGT1A1*60 and UGT1A9*22, which may lead to decreased glucuronidation and excretion of SN-38, and may account for increased irinotecan-related toxicity. The patient developed febrile grade 4 neutropenia on day 7 after chemotherapy and died of septic shock on day 14.

Conclusions. *UGT1A* polymorphisms and renal failure may lead to accumulation of SN-38, which may have played a role in the death of this patient. Irinotecan should be used cautiously in dialysis patients with metastatic colorectal cancer and screening for *UGT1A* polymorphisms may help in identifying patients with lower SN-38 glucuronidation rates and greater susceptibility to irinotecan-induced toxicity.

Key words: hemodialysis, irinotecan, colorectal cancer, *UGT1A*.

Acknowledgments: This work was supported by grant number NSC 98-2314-B-075-029 from the National Science Council, Taiwan, grant number VGH 99C1–107 from Taipei Veterans General Hospital, Taipei, Taiwan, and grant number DOH 99-TD-C-111-007 from the Department of Health, Taiwan, and assisted, in part, by the Division of Experimental Surgery of the Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan.

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Received May 18, 2010;
accepted October 29, 2010.