Heptaplatin의 신독성 : 진행성 위암에서 Cisplatin과의 무작위 비교연구

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Nephrotoxicity of Heptaplatin : A Randomized Comparison with Cisplatin in Advanced Gastric Cancer

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Heptaplatin is a newly developed platinum derivative, which has been reported to be less toxic than cisplatin. However, after the widespread use of heptaplatin, we experienced a few cases of severe proteinuria and/or acute renal failure. This study was designed to evaluate nephrotoxicity of heptaplatin by comparing it with cisplatin in patients with advanced gastric cancer (AGC).

Previously untreated stage IV AGC patients with normal renal function were randomly assigned into either group I (heptaplatin 400 mg/m^2 1-hour IV on day 1 + 5-FU 1,000 mg/m^2/day, continuous IV from day 1 to 5), or group II (cisplatin 60 mg/m^2 1-hour IV on day 1 + 5-FU 1,000 mg/m^2/day, continuous IV from day 1 to 5), with the cycles repeated every 4 weeks. A uniform hydration procedure was followed for the prevention of nephrotoxicity in both groups. Baseline renal function parameters including serum creatinine and amount of 24-hour urinary protein excretion were obtained before chemotherapy. Follow-up measurement was repeated at day 5 of the first cycle to evaluate acute nephrotoxicity, and before each new cycles to evaluate cumulative nephrotoxicity.

From April 2000 to May 2001, total 99 patients were enrolled; 51 in group I and 48 in group II. Baseline characteristics were similar in the 2 groups. When the renal function parameters measured at day 5 of the first cycle were compared with those of pretreatment, 24-hour proteinuria much more increased in group I (97$\pm$107 mg/day (mean$\pm$ S.D)-> 8,998$\pm$4,621 mg/day) than in group II (104$\pm$148 mg/day -> 149$\pm$101 mg/day), and serum creatinine also more increased in group I (0.79$\pm$0.2 mg/dL-> 1.26$\pm$0.3 mg/dL) than in group II (0.85$\pm$0.2 mg/dL-> 0.95$\pm$0.3 mg/dL)(P-value<0.05). Although severe proteinuria and

elevated serum creatinine were improved before the start of next cycle, significant differences between 2 groups were statistically persistent through the subsequent cycles. Two cases of acute renal failure developed only in group I during the study period.

Our data shows that nephrotoxicity is more severe in patients treated with heptaplatin 400 mg/m^2 than cisplatin 60 mg/m^2 when it is combined with 5-FU. Measures to prevent nephrotoxicity more effectively should be developed for the safe use of heptaplatin.