Pharmacokinetic Changes of Carumonam in Patients with Renal Insufficiency

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Background : Carumonam, which has comparable in vitro antimicrobial activity with aztreonam is known to have more favorable pharmacokinetic characteristics such as low protein binding. We intended to evaluate the pharmacokinetic changes in patients with renal insufficiency comparing with normal subjects to deduce appropriate dosing guidelines to such patients.

Method : Eight subjects with normal renal function and sixteen patients with renal impairment were entered in this study. Plasma carumonam concentration and renal excretion of the drug were determined after 20 minutes infusion of 1g carumonam. The data were analyzed by 2-compartmental pharmacokinetic model.

Results : The elimination half life of carumonam significantly increased with decreasing creatinine clearance from 1.6hr in normal subjects to 12.3hr in patients with creatinine clearance less than 10ml/min. Peak plasma concentration and distribution half-life were increased with decreasing cretinine clearance. Total body clearnce showed linear correlation($r=0.95$, $p<0.001$) with creatinine clearance. However, the AUC in patients with renal insufficiency was better correlated with changing GFR in exponential term. The non-renal clearance of carumonam in patients with renal insufficiency was significantly lower than that of normal subjects, which suggested the depressed metabolic clearance of carumonam in those patients.

Conclusion : With regard to dosage, we suggest the following dosing guidelines for the renal dysfunction patients : Patients with Clcr between 30 and 60ml/min should be given the dose every 12hr and those with Clcr between 10 and 30ml/min once a day. Patients with Clcr less than 10ml/min should receive one-half of the standard dose once a day.