急性腎不全がセフォペラゾンの体内動態に及ぼす影響

片山博和、安原眞人*、堀　了平**

J. Pharm. Pharmacol., **51**, 361-366(1999)

Effect of acute renal failure on the disposition of cefoperazone

Hirokazu Katayama, Masato Yasuhara*, and Ryohei Hori**

ABSTRACT The effect of acute renal failure (ARF) on the disposition of cefoperazone (CPZ) was investigated. Rats 3 days after uranyl nitrate treatment were used to model ARF. Although plasma protein binding of CPZ decreased significantly in ARF rats compared to control rats, the plasma clearance of total (bound plus unbound) drug after intravenous administration (50 mg/kg body weight) did not differ significantly between the two groups (5.61 ± 2.37 ml/min for control and 4.75 ± 2.82 ml/min for ARF). Consequently, the plasma clearance of the unbound drug in ARF rats (6.14 ± 1.16 ml/min) was significantly lower than in control rats (15.6 ± 3.7 ml/min, $p < 0.025$). Plasma clearance of the drug (both total and unbound) was also dependent on bile flow, and clearance of the unbound drug in ARF rats was lower than in control rats with identical bile flow rates. To examine the mechanism of reduced unbound CPZ clearance, an *in vitro* experiment using a simultaneous perfusion system of rat liver and kidney was performed. By changing perfusate plasma protein from bovine serum albumin to human serum albumin, the plasma clearance of the total CPZ changed to one-sixth of the unbound fraction in the perfusate plasma. On the other hand, the plasma clearance of the total and unbound drug in ARF rats decreased significantly compared with controls.

These results demonstrate that the plasma clearance of unbound CPZ, which is mainly eliminated by the liver, decreased in ARF rats, probably due to changes in hepatic transport in ARF rats.

抄録　急性腎不全（ＡＲＦ）モデルラットにセフォペラゾン（ＣＰＺ）を投与し、その体内動態について検討した。In vivo 実験によりＣＰＺの血漿蛋白結合率が低下しているにも拘わらず全身クリアランスが同じになることを見い出し、ＡＲＦラットの非結合型クリアランスがコントロールに比べ小さくなることを明らかにした。この原因についてラット肝腎同時摘出灌流法を用いてさらに詳細に検討し、ＡＲＦラットではＣＰＺの肝への輸送能が低下していることを示した。

* Department of Hospital Pharmacy, School of Medicine, Tokyo Medical and Dental University
東京医科歯科大学医学部附属病院薬剤部
** Pharmaceutical Research and Technology Institute, Kinki University
近畿大学薬学総合研究所