

急性腎不全家兎の血漿蛋白とフロセミドの結合

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Plasma Protein-Furosemide Binding in Acute Renal Failure Rabbit

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ABSTRACT Acute renal failure (R.F.) rabbits induced by the muscular injection of HgCl_2 (10 mg/kg) produced a significant increase of blood urea nitrogen concentration (BUN) and plasma creatinine concentration (Cre) after a few days. However, no significant change was observed for free fatty acid level. The pharmacokinetic of furosemide in acute renal failure rabbit was also studied. The apparent volume of tissue compartment slightly increase. The elimination rate constant from central compartment significantly decreased, and mutually correlated with BUN or Cre.

It was found from results of *in vitro* equilibrium dialysis measurement that the protein binding of furosemide significantly decreased in the plasma obtained from R.F. rabbits as well as that from patients with acute renal failure. Calculation made according to Sandberg-Rosenthal's formula revealed that the maximum binding concentration (nP) was not changed but binding constant (K) decreased in the R.F. rabbit. The presence of endogenous substances that inhibited the plasma protein-furosemide binding competitively may be suggested from the above results.

抄録 塩化第二水銀の筋注により惹起した急性腎不全家兎において、血中尿素窒素 (BUN) と血中クレアチニン (Cre) の濃度は大きく増加したが、遊離脂肪酸濃度に変化はなかった。腎不全家兎では、フロセミドの見かけの組織分布容積は若干増加し、中央分画からの消失速度定数 (k_{10}) は小さくなった。 k_{10} の値と BUN 及び Cre 値との間には相関性が認められ、腎不全時のフロセミドの体内挙動を予測することが可能である。*In vitro* 平衡透析の結果、腎不全家兎血漿蛋白とフロセミドの結合は、正常時と比べて大きく低下し、ヒト腎不全の場合と同様の傾向を示した。この際の蛋白結合の低下は、結合定数が見かけ上小さくなったことによるものであり、腎不全時に血中に増加するある内因性物質の競合阻害によるものと推定される。

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