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DAOSUANG TOLEANG : PHARMACOKINETICS OF GENTAMICIN AND EFFECT ON GLOMERULAR FILTRATION RATE IN PATIENTS WITH HEPATIC DISEASES. THESIS ADVISOR : ASSO.PROF. PANPIT SUWANGOOL,M.D. THESIS CO-ADVISOR : ASSO.PROF. SOPIT THAMAREE , 115 pp. ISBN 974 - 584 - 928 - 6

This study aimed at comparing the pharmacokinetics for gentamicin in female infected patients with hepatic disease (N=8) and without hepatic disease (N=10). Eighteen female had normal renal functions (Scr $\leq$ 1.5 mg/dl). Hepatic patients were diagnosed in according to Moore method. Gentamicin was infused over a 30-minute peroid. In the third day of treatment, blood samples were collected before the infusion of gentamicin and at the following times from the finishing of infusion:15,30,45 min.,1,4,8,12 and 23.5 hr. Assays for determination of gentamicin were performed by use of TDx analyzer. Pharmacokinetics parameters for gentamicin including $K_{e\alpha}$,$K_{e\beta}$,$T_{\frac{1}{2}\alpha}$,$T_{\frac{1}{2}\beta}$,Vc,Vp,V_β ,Cl and AUC were determined by use of MK model fitted with 2-compartment model. Blood collections for serum creatinine were also performed before the beginning of gentamicin treatment and at the day 3,5 and7 of daily gentamicin infusion. The results showed the decrease of $K_{e\beta}$ and the increase of $T_{\frac{1}{2}\beta}$ significantly ($p < 0.05$) in the hepatic patients compared to non-hepatic patients.

Although the hepatic patients did not show the significant decrease in gentamicin Cl but the elimination of gentamicin tended to be decreased. The AUC determined during a 12 hour-period was not significantly different between the 2 groups of patients. However the AUC determined during a 23.5 hr period showed a significant increase in the hepatic patients.

It was founded that serum bilirubin in hepatic patients was closely related to elimination half life of gentamicin ($r=0.86, p < 0.05$) whereas other hepatic parameters had no relation to $T_{\frac{1}{2}\beta}$.

After 5-7 days of continuous treatment , the 2 subjects of hepatic patients observed as high serum bilirubin were determined to have marked increase in Scr compared to the pre - treatment level.

The results from our study indicated that the elimination of gentamicin, a drug excreated almost entirely by glomerular filtration , was decreased in hepatic patients. This was presumably due to a decrease in GFR. Moreover,an increase in tubular reabsorption of gentamicin might come into account and resulted in accumulation of gentamicin and persistently elevated concentration of gentamicin in plasma. This might contribute to the nephrotoxicity induced by gentamicin observed in 2 hepatic patients who developed high Scr. Interestingly, bilurubin might play a role in facilitating gentamicin nephrotoxicity by decrease delivery of calcium to the kidney. As calcium is postulated to be a competitive inhibitor of gentamicin induced nephrotoxicity. The exact mechanism should be further elucidated.

In conclusion, gentamicin therapy should be cautioned in hepatic patients. Laboratory findings of serum creatinine and bilirubin may be used as guideline in adjusting the dosage regimen and monitoring of therapeutic drug effect.