Sulfadiazine 在慢速乙醯反應型家兔體內之藥物動力學研究

Studies on the pharmacokinetics of sulfadiazine in the slow acetylation rabbits

中文摘要

丙酮酸 (pyruvic acid，PA) 對 sulfadiazine (SDZ) 在快速乙醯化型家兔中，並無藥物動力學之影響。但對慢速乙醯化型家兔，PA 則具有促進 SDZ 消失之能力，而其原因則尚未確立。本實驗之目的在進一步探討慢速乙醯化型家兔體內，PA 對 SDZ 之藥物動力學影響及原因。

以 SDZ 爲標的藥物，檢測家兔之乙醯化表現型，選取其中六隻慢速乙醯化型雄性紐西蘭家兔爲實驗動物。再以靜脈連續輸注法投予 PA，起始劑量 300 mg/kg，維持劑量 7.5 mg/min/kg，將 PA 維持在恆定高血漿濃度 ≒ 100 mg/mL 下，將 SDZ 及其代謝物 acetyl-sulfadiazine (AcSDZ) 分別對實驗動物以每公斤 0.08 毫莫耳的劑量作靜脈投予。抽取血漿，利用高效液相層析法，檢測血漿中 SDZ 及其代謝物之濃度，並以 winnonlin 做 curve fitting，探討 PA 對 SDZ 之藥物動力學之影響。

實驗結果顯示，慢速乙醯化型家兔在 PA 靜脈連續輸注後，對 SDZ 的影響如下:

(1) SDZ 之 t1/2 由 107.75±14.33 min 降爲 75.48±7.21 min，PA 具明顯之加速 SDZ 消失作用 ($P < 0.05$)；

(2) 由 SDZ 生成之 AcSDZ 的 AUC 由 8520±3300 mg min/mL 降爲 3493±1520 mg min/mL，具顯著之減少結果 ($P < 0.005$)，AcSDZ 之生成率由 0.28±0.08 降爲 0.13±0.04 亦爲顯著減少 ($P < 0.005$)；

(3) AcSDZ 靜脈注射後，各項藥物動力學參數均無顯著不同。表示 PA 靜脈連續輸注後，對 AcSDZ 之藥物動力學並無影響。

綜合以上之結果，顯示 PA 可促使 SDZ 之消失加快, 但 AcSDZ 之生成反而減少，而 remained clearance 由 0.0015 ± 0.0003 L/min/kg 增加爲 0.0026 ± 0.0006 L/min/kg (P < 0.005)，其原因可能爲 slow acetylation rabbits 的 SDZ 之腎消除率增加。

英文摘要

There is no influence of pharmacokinetics to sulfadiazine (SDZ) with sod. pyruvate (PA) infused on rapid acetylation rabbits, but it has been proved that PA enhances the elimination rate of SDZ on slow acetylation rabbits. The reason is still unknown. The purpose of this study is to investigate the reason of PA effects to pharmacokinetics of SDZ on slow acetylation rabbits.

Six male slow acetylation rabbits were used in experimental animals. Maintain plasma concentration of PA at 100 mg/ml by I.V. infusion to rabbits (loading dose: 300 mg/kg; maintain dose: 7.5 mg/min/kg), then I.V. administration at 0.08 mmol/kg of SDZ and acetyl-sulfadiazine (AcSDZ) to rabbits. Plasma concentration of SDZ and AcSDZ was detected by HPLC. With winnonlin curve fitting, the pharmacokinetic parameters of SDZ were obtained.

After consecutive PA I.V. infusion on slow acetylation rabbits, the t1/2 of SDZ was significantly decreased from 107.75 ±14.33 min to 75.48 ± 7.21 min (P < 0.05). About the formated AUC of main metabolite of SDZ, AcSDZ, there was also significantly decreased from 8520 ±3300 mg min/mL to 3493 ±1520 mg min/mL (P < 0.005). The formation fraction of AcSDZ formed from SDZ was decreased from 0.28 ±0.08 to 0.13 ± 0.04 (P < 0.005). On the other hand, there were no significant changes in all pharmacokinetic parameters after AcSDZ I.V. administration during PA infusion.

According to the results obtained, it showed that PA enhances

the elimination rate of SDZ, but reduced AcSDZ formation. The remained clearance was increased from 0.0015 ± 0.0003 L/min/kg to 0.0026 ± 0.0006 L/min/kg ($P < 0.005$). The probability reason was sod. PA increased the renal clearance of SDZ in slow acetylation rabbits.