

Distribution Kinetics of Ketoprofen into Synovial Fluid After Systemic Administration

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For the pharmacokinetic analysis of ketoprofen transfer into synovial joint fluid, steady-state multiple ketoprofen concentrations of plasma and knee joint fluid were measured at steady-state in twelve subjects. Ketoprofen was assayed by HPLC and pharmacokinetic parameters were estimated with using modified PK/PD model.

Peak plasma levels($4.63 \pm 3.23 \mu\text{g/ml}$) were achieved at 2.23 ± 0.65 hours after multiple ketoprofen dose(100mg b.i.d.). Elimination half-life($t_{1/2}$), plasma clearance (Cl/F) and volume of distribution(Vd/F) were $1.34 \pm 0.28\text{hr}$, $0.20 \pm 0.13\text{L/hr/kg}$ and $0.39 \pm 0.25\text{L/kg}$, respectively.

In the mean concentration-time curve of synovial fluid ketoprofen, peak levels of ketoprofen concentration were achieved at 5hr. The ratio of synovial fluid/plasma drug concentration were 0.28 ± 0.16 at 1hr, 0.35 ± 0.05 at 2hr, 1.24 ± 0.13 at 5hr, 2.82 ± 2.19 at 6hr and 3.65 ± 3.21 at 8hr. AUC ratio of synovial fluid/plasma was estimated to 0.77 and the MRT was 3.17 in plasma and 5.35 in synovial fluid.

Pharmacokinetic parameters for distribution kinetics were estimated from modified PK/PD model, the disposition rate constant(k_{eo}) was estimated to 0.20hr^{-1} and the equilibration partition coefficient(k_{ie}) of synovial fluid/plasma was estimated to 0.71. In simulated ketoprofen concentration-time courses of plasma & synovial fluid, the peak concentration of synovial fluid was simulated to 35.33% of the plasma peak concentration and there was 2.6hr time gap.

Anti-clockwise hysteresis curve was shown in the plasma ketoprofen concentration versus synovial fluid ketoprofen concentration curve.

These results provide the basic data for understanding the ketoprofen concentration-time course in synovial fluid after systemic administration.