Effects of etoricoxib on the pharmacokinetics of phenytoin

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Abstract:
Etoricoxib is presently the most commonly prescribed cyclooxygenase-2 (Cox-2) inhibitor for chronic pain and inflammatory conditions. In clinical practice, phenytoin and etoricoxib are used in chronic conditions of generalized seizure with concomitant chronic pain. Hence, there are chances of drug-drug interaction because modulations of isoenzymes involved in metabolism CYP2C9/10 and CYP2C19 which partially inhibited by etoricoxib. It is important to maintain the therapeutic level of phenytoin in plasma for effective control of seizure. So, the aim of the study was to determine the effect of etoricoxib on the pharmacokinetics of phenytoin in rabbits. In a parallel design study, phenytoin (30 mg/kg/day) was given daily for seven days. On day 7, blood samples were taken at various time intervals between 0–24 h. In etoricoxib group, phenytoin was administered for seven days as above. On day 8, etoricoxib (5.6 mg/kg) along with phenytoin (30 mg/kg/day) was administered and blood samples were drawn as above. Plasma phenytoin levels were assayed by HPLC and pharmacokinetic parameters were calculated. In etoricoxib group, there was a decrease in $t_{1/2}$ of phenytoin and $t_{1/e}$ decreased significantly as compared to phenytoin group. Significant changes were observed in the pharmacokinetic parameters in etoricoxib-treated group. These results suggest that etoricoxib alters the pharmacokinetics of phenytoin. Confirmation of these results in human studies will warrant changes in phenytoin dose or frequency when etoricoxib is co-administered with it.

Key words:
etoricoxib, phenytoin, pharmacokinetics