Bioavailability of paracetamol and ibuprofen in single and combination dosage in rabbits

Sir,

Paracetamol (PA) is an analgesic and antipyretic drug with no antiinflammatory properties. But ibuprofen (IB) is an analgesic with antiinflammatory properties. A combination of PA with IB is used for treatment of pain with fever. Although the reports on the individual kinetics of either IB or PA are available, the effects of the combination on the kinetics of each in experimental animals are largely unknown. In the present study we have investigated the effect of IB on the absorption and distribution kinetics of PA and vice-versa in rabbits, following the method of Glynn and Kendall (1975). Healthy New Zealand white rabbits of either sex weighing (2.1 ± 0.12) kg were divided into different groups of six each and housed under standard animal room conditions. After overnight fasting, a single dose of 46 mg/kg, b.w. of IB, and 56 mg/kg, b.w. of PA in propylene glycol (Pg) was given orally to each animal of Group I and Group II respectively. Animals of Group III received a single mixture of the above doses of IB + PA each while those of Group IV were given a similar volume of Pg each. All experimental protocols were approved by the departmental animal ethics committee.

Two ml of blood was collected from the ear vein of each animal at 15, 30, 45, 60, 90 and 120 min in centrifuge tubes, allowed to clot and centrifuged. 0.5 ml of supernatant was mixed with 1 ml of trichloro acetic acid (15% w/v), shaken for 2 min and centrifuged at 4000 rpm for 15 minutes. One ml supernatant was taken and diluted to 25 ml with glass distilled water and absorbance of the solutions was recorded at 267 nm for IB (Group I) and 242 nm for PA (Group II). The treated serum solution of Group IV was used as blank (Hitachi U-2000 spectrophotometer). The serum concentration of the drugs was calculated from standard graphs of the drugs in methanol. The serum concentration of IB and PA of Group III was calculated following the simultaneous equation method.

The mean values (SEM) of the serum concentrations (µg/ml) of the drugs were plotted against time (min), and the pharmacokinetic parameters were calculated and are shown in Table 1. The data were analyzed using Student’s ‘t’ test and P<0.05 was considered statistically significant.

A combination of IB with PA did not alter the peak times of 45 min of either of the drugs. However, the absorption phase of IB was lowered in the presence of PA (Figure 1). For PA there was a significant rise of peak concentration (P<0.05) and a fall of absorption phase while the rate of distribution was enhanced in the presence of IB (Figure 1). The higher peak concentration of PA with a combination dose might be because of less distribution and hence an increase in concentration in the central compartment which led to lower AUC value. The significant increase of Vd and decrease of AUC of both the drugs in combination may lead to sub-therapeutic or ineffective drug concentration.
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