LETTER TO THE EDITOR

THE EFFECT OF RIFAMPICIN ON PIROXICAM KINETICS

Sir,

(Rceived on June 8, 1988)

Rifampicin is known to influence the metabolic disposition of other drugs because of its 'enzyme inducing' effects in the liver (1, 6). The microsomal enzymes catalyze glucuronide conjugations and most of the oxidation of the drugs. Reduction and hydrolysis of drugs are catalyzed by both microsomal and non-microsomal enzymes (3). Hydroxylation and glucuronide formation are involved in the metabolic pathway of piroxicam, a non-steroidal anti-inflammatory drug (NSAID) (4). The metabolite is less active than piroxicam (5). Hence we report here interaction study between rifampicin and piroxicam.

Six healthy young volunteers (who signed a consent form) aged 25±35 years and weighing between 56 to 62 kg participated in the study. No other drugs were taken for ten days prior to and during the study.

On day 1 all volunteers were given piroxicam 40 mg in a single oral dose on an empty stomach (overnight fasting) with 100 ml of water at 9.00 a.m. Food was withheld for 4 hr. Standard lunch and supper were taken at 1.00 p.m. and 6.00 p.m., respectively. A complete absorption and elimination curve was prepared by frequent blood sampling upto 96 hr after drug. After a washout period of 15 days the volunteers were given rifampicin 600 mg as a single dose for 7 days. On the last day they were also given piroxicam 40 mg again and its elimination curve worked out again.

Piroxicam plasma concentrations were determined by means of a spectrophotometric assay method (2) with little modification. Plasma 2 ml was acidified with 0.5 ml, 1N HCl and extracted thrice with 20, 10 and 10 ml of dichloroethane. The combined organic extract was extracted with 10 ml pH 9 carbonate buffer and the optical density of the latter was determined at 355 nm. Plasma from undosed subjects was fortified with standard piroxicam for the
construction of a standard curve. The minimum concentration detected with the method was approximately 0.5 \( \mu g/ml \).

Piroxicam plasma levels did not decline smoothly during the study both before and after rifampicin treatment. It showed multiple peaks, two in each subject during the first 24 hr and additional one or two in some during subsequent blood sampling with varying concentrations and time. It will be noticed that rifampicin did not significantly alter the pharmacokinetic of piroxicam (Table I).

**TABLE I**: (Mean±SE) pharmacokinetic data for piroxicam (P) obtained after intake of a single dose of 40 mg in six volunteers before and after 7 days treatment of rifampicin (R) 600 mg, po, once daily.

<table>
<thead>
<tr>
<th>Study day</th>
<th>Peak concentration (( \mu g/ml ))</th>
<th>Time to peak concentration (hr)</th>
<th>( t_{1/2} ) (hr)</th>
<th>( AUC(0\rightarrow\infty) ) ( \mu g/ml\cdot hr )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (R)</td>
<td>9.37±1.14</td>
<td>2.17±0.6</td>
<td>41.0±8.20</td>
<td>377.21±56.4</td>
</tr>
<tr>
<td>2 (P+R)</td>
<td>9.98±0.73</td>
<td>1.00±0.0</td>
<td>45.5±6.78</td>
<td>394.66±44.13</td>
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Piroxicam is extensively metabolised in man by the routes of 5'-pyridine ring hydroxylation, glucuronide formation, cyclodehydration and amide hydrolysis leading to decarboxylation, ring contraction and N-dealkylation. The principal metabolite is that produced by hydroxylation of the pyridyl ring and exist either free or conjugated with glucuronic acid and is less active than piroxicam (4, 5). Literature reports suggest interaction between rifampicin and drugs like aminosalicylic acid, corticosteroids, oral contraceptives, antidiabetics, digoxin, isoniazid, dapsone probenecid etc. (1, 6). However our data indicate that rifampicin can be used in conjunction with piroxicam without alteration of the kinetics of piroxicam.

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