up as a double blind, controlled endoscopy study comparing an ulcer healing agent with placebo. As can be seen from our paper\(^1\) the study described was in two parts, the first being a survey of patients routinely attending a rheumatology outpatient clinic and the second phase of the study consisting of a report of the effects of an ulcer healing agent on non-steroidal anti-inflammatory drug (NSAID) induced peptic ulceration with the NSAID continued throughout treatment. The discrepancy between the prevalence of peptic ulceration in our patient population compared with that described by Dr Roth could possibly be due to patient selection and the type of population studied. In our own study we showed that smoking was an important risk factor in the development of the peptic ulceration in the rheumatoid population and yet this is a variable which is not always taken into account in previously reported studies of the prevalence of peptic ulceration in rheumatic disease. We would entirely agree with Dr Roth’s comments that separate terminology should be used for NSAID gastropathy as one of the problems of multicentre studies is the standardisation of the criteria for gastric ulceration and the grading of mucosal lesions in this group of patients. Whether rheumatoid arthritis itself may predispose to peptic ulceration is an open question, and further studies with large numbers of patients whose demographic characteristics are carefully standardised will be required to answer this.

Centre for Rheumatic Diseases, R D STURROCK
Royal Infirmary, Glasgow G4 0SF

Reference


Hepatitis induced by non-steroidal anti-inflammatory drugs

Sir, We read with interest the letter by Llorca et al entitled ‘Changing the class of NSAID in cases of hepatotoxicity’.\(^1\) We would like to draw attention to the incidence and clinical features of this side effect. In 1985 the French drug surveillance centres collected 56 cases (37 women and 19 men) of hepatitis associated with non-steroidal anti-inflammatory drug (NSAID) administration.\(^2\) They consisted of acute cytolytic (24), acute cholestatic, (nine) or mixed (15) hepatitis. The remainder included subclinical biochemical abnormalities such as an increase of serum aminotransferase (four) or serum alkaline phosphatase (four). Most patients recovered after the drug was stopped. Three patients died, however, of fulminant hepatitis due to pirprofen (two cases) and niflumic acid (one case).

Moreover, this study allowed the classification of NSAIDs according to the incidence of hepatitis, expressed as the number of cases by months of treatment (Table 1).

<table>
<thead>
<tr>
<th>Group</th>
<th>Incidence of hepatitis</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;1/ 50 000</td>
<td>Oxyphenbutazone</td>
</tr>
<tr>
<td>2</td>
<td>1/ 50 000 to 1/100 000</td>
<td>Isoxicam, pirprofen, sulindac</td>
</tr>
<tr>
<td>3</td>
<td>1/100 000 to 1/300 000</td>
<td>Fenbufen, Ibuprofen, indomethacin, ketoprofen</td>
</tr>
<tr>
<td>4</td>
<td>1/300 000 to 1/500 000</td>
<td>Didlofenac, piroxicam</td>
</tr>
<tr>
<td>5</td>
<td>&lt;1/500 000</td>
<td>Flurbiprofen, sodium naproxen, niflumic acid, tiaprofenic acid</td>
</tr>
</tbody>
</table>

Finally, hepatitis is a relatively rare side effect, but it has been reported to occur with almost all the NSAIDs commonly in use.\(^3\) Although NSAID hepatotoxicity cannot be predicted, the following measures may limit its seriousness: (a) If clinical signs appear, even non-specific ones such as asthenia, fever, abdominal pain, or vomiting, the administration of NSAIDs should be interrupted and a serum liver test should be carefully carried out, especially if these signs are unusual for the patient; (b) In a patient with a history of NSAID induced hepatitis the readministration of the same drug must be strictly avoided. As cross hepatotoxicity between different NSAIDs of the same chemical class has been reported\(^4\) an NSAID of a different chemical structure should be used.

Centres de Pharmacovigilance de Nancy et Paris, Fernand Widal et INSERM U 24, Paris, France

Patrick Netter
Anne Castot
Dominique Larrey
Patrick Carlier
Bernard Bannwarth
Philippe Trechot

References

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P Netter, A Castot, D Larrey, P Carlier, B Bannwarth and P Trechot

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