Sulphoxidation status in rheumatoid arthritis

Str: In a recent issue of this journal Emery et al found an increased prevalence of poor sulphoxidation in patients with rheumatoid arthritis (RA). Using the same methods as Emery's group, we have found similar results. Sulphoxidation status was assessed in 116 of 200 patients enrolled in a comparative study of sulphalazine and penicillamine as second line drugs in RA (table). Follow up data are available on these patients for between 5 to 7 years from entry into the trial. Surprisingly, no increase in toxicity from either drug was observed in the poor sulphoxidisers group (figure).

Previous studies have suggested that toxicity from intramuscular gold and penicillamine is related to sulphoxidation status. In contrast with gold and penicillamine, however, sulphalazine is metabolised predominantly by acetylation rather than sulphoxidation, and one would therefore have predicted that toxicity from sulphalazine would not be influenced by sulphoxidation status. In this study we failed to find any association between toxicity from penicillamine and sulphoxidation status. Although the period of follow up in this study was longer than in previous studies, this finding cannot be explained by an excess of late toxicity in the good sulphoxidisers group.

A second possible explanation is that the group in whom sulphoxidation status was measured was not representative of the group as a whole. To consider this point we noted toxicity in those patients in whom sulphoxidation status was not assessed. Of the patients receiving sulphalazine in whom sulphoxidation status was known, 35% developed toxicity compared with 30% of those in whom sulphoxidation status was not known. In those receiving penicillamine the figures were 34% and 38% respectively. Thus although there was a small excess in toxicity in those receiving penicillamine who did not have sulphoxidation status assayed, this was not statistically significant ($\chi^2$). We cannot rule out the possibility that the ratio of good and poor sulphoxidisers might have been different in those who were not assayed. There were 12 deaths (five sulphalazine, seven penicillamine) in the group where sulphoxidation status could not be evaluated compared with two in the group where sulphoxidation status was assayed (one sulphalazine, one penicillamine). None of these deaths was directly attributable to drug toxicity.

The consistent finding that poor sulphoxidisers are overrepresented in RA compared with the normal population is of great interest, and the effect of sulphoxidation status on susceptibility to RA or disease expression, or both, merits further study.

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1 McNeil P H, Simpson R J, Chesterton C N, Krils S A. Anti-phospholipid antibodies are directed against a complex antigen that includes a lipid-binding inhibitor of coagulation: glycoprotein I (apolipoprotein H). Proc Natl Acad Sci USA 1990; 87: 4120-4.


9 Numbers (percentages) of patients receiving sulphalazine or $\alpha$-penicillamine who were good or poor sulphoxidisers

<table>
<thead>
<tr>
<th>Poor</th>
<th>Good</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulphalazine (n=63)</td>
<td>49 (78)</td>
</tr>
<tr>
<td>$\alpha$-penicillamine (n=53)</td>
<td>36 (68)</td>
</tr>
</tbody>
</table>

Expected

26 (22) 90 (78)

<table>
<thead>
<tr>
<th>Sulphalazine</th>
<th>$\alpha$-penicillamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>64%</td>
<td>36%</td>
</tr>
<tr>
<td>36%</td>
<td>59%</td>
</tr>
<tr>
<td>6%</td>
<td>59%</td>
</tr>
<tr>
<td>35%</td>
<td>70%</td>
</tr>
<tr>
<td>20%</td>
<td>30%</td>
</tr>
</tbody>
</table>

Toxicity due to sulphalazine or $\alpha$-penicillamine in the good and poor sulphoxidisers groups.

Toxicity: 0 No toxicity: 1

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