Correspondence

Non-steroidal anti-inflammatory drugs and peptic ulcer perforation

Sir,—We read with great interest the recent article by D St J Collier and J A Pain.1 We have recently completed a retrospective study of 304 emergency admissions for peptic ulcer disease and found an incidence of NSAID ingestion of 29% in perforated gastric ulcer and 16% in perforated duodenal ulcer. While it may simply reflect the differences in the populations studied we are surprised by the high percentage of perforated duodenal ulcers taking NSAID’s in their survey, 32% in comparison with 44% in perforated gastric ulcer. Our figures are in agreement with recently published data, Glarborg Jørgensen2 who quote 13% for perforated duodenal ulcer and 31% for perforated gastric ulcer. In both these studies1,2 in agreement with our own work the incidence of NSAID intake in perforated gastric ulcer is higher than in perforated duodenal ulcer. In view of this we feel it is wrong to consider perforated peptic ulcer over the age of 65 as a single group and we would be interested to know if removal of the gastric ulcers from their study influences the statistical significance of their results.

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References


Reply

Sir,—We are pleased to be given the opportunity to reply to the letter by Smedley and Hickish. The removal of patients with a perforated gastric ulcer does not influence the statistical significance of our results (Table).

Whilst the disparity in the percentages of patients taking NSAID between our study1 and those of Smedley and Hickish may be because of studying different population groups, another explanation may be the methodology of data collection. In Glarborg Jørgensen’s2 prospective study >80% of patients with a perforated peptic ulcer were taking NSAID. Furthermore in a study of patients with upper gastrointestinal bleeding Haglund et al3 found that on retrospective note review 38% of patients were taking NSAID before admission. When the same group of patients were later interviewed, however, it was revealed that 71% had taken NSAID.

Table Ingestion of NSAID in patients with perforated duodenal ulcers (DU) compared with age/sex matched controls for specified age groups

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Taking NSAID</th>
<th>No NSAID</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 65*</td>
<td>Controls</td>
<td>5</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td>Patients</td>
<td>11</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>16</td>
<td>162</td>
</tr>
<tr>
<td>Over 65†</td>
<td>Controls</td>
<td>10</td>
<td>118</td>
</tr>
<tr>
<td></td>
<td>Patients</td>
<td>58</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>68</td>
<td>188</td>
</tr>
</tbody>
</table>

* X²=2.47; DF=1; p<0.05 NS with Yates’s correction.
† X²=46.13; DF=1; p<0.001.

The diligence with which note review is done must influence the results, and all retrospective studies will to varying degrees underestimate the true incidence of NSAID ingestion.

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References


Appropriate statistical test in comparative ulcer healing studies

Sir,—Boyd and Marks’ in their letter state that the statistical method used by Lam et al,2 namely, a X²-test (without Yates’ correction), is inappropriate for the analysis of their data.

For many years there has been some controversy in the statistical literature as to whether Yates’
correction should be applied in $\chi^2$ tests. Although some authors advocate the use of this continuity correction others, for example Grizzle, Conover and Camilli and Hopkins have argued against it, especially in the case of random marginal totals which Lam obtained in his study.

Boyd and Marks further state that it would be preferable to use Fisher’s test for sample sizes up to 60, irrespective of the values of the individual cells. They compute the one tailed probability correctly as $p=0.0286$ but then, after arguing that a two tailed test should be carried out, simply double the one tailed probability to obtain the two tailed $p$ value of $0.057$ (which would indicate a statistically non-significant difference). The procedure of doubling the one tailed probability, however, is appropriate only in cases of equal sample sizes. As in Lam’s results these were 12 and 13 respectively, a different method of obtaining the two tailed probability should be used, namely the summation of all probabilities, under the marginal totals, which are equal to or less than the probability of the observed configuration of frequencies. This method reveals one tailed probabilities of $0.0286$ and $0.0127$ respectively, which produce a two tailed value of $p=0.041$, statistically significant at conventional levels. In this context it may be useful to realise that the choice of significance levels, in this case $\alpha=0.05$, is quite arbitrary. In practice one should further consider probabilities just below and just above the level of statistical significance as equivalent in result and avoid raising the ‘magic’ limit of 0.05 to the boundary between true and false.

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References


Effect of morphine on the human oesophagus

six,—How bitter the memory, but how sweet the vindication.

Dowlatshahi et al (Gut 1985; 26: 802–6) have described it and, more importantly, got it published. Five years ago my colleagues and I tried, but failed. In their study of the effect of morphine on the human oesophagus they found that morphine decreased lower oesophageal sphincter relaxation in response to swallowing and that, contrary to accepted medical dogma, it caused a small, albeit non-significant, increase in lower oesophageal sphincter pressure and in the amplitude of distal oesophageal peristaltic contraction.

Some years ago, in a very similar study (which was never accepted for publication) we carried out oesophageal manometry in six healthy volunteers on three separate occasions. After steady state basal recordings were obtained intravenous injections of saline, naloxone 0.8 mg or morphine 7.5 mg were given in random order to each subject on different days. Five minutes after the injection of the test drug, contraction of the body and sphincter of the oesophagus was stimulated by a subcutaneous injection of 12.5 mg of methacholine. Fifteen minutes later, after the effect of methacholine had worn off, maximal sphincteric contraction was stimulated by an intramuscular injection of 500 $\mu$g of pentagastrin.

Basal LOS pressure and oesophageal peristaltic pressure were not significantly different in the three study periods and neither saline nor naloxone affected the basal motility of the oesophageal body and sphincter or their response to methacholine or pentagastrin. Morphine significantly increased LOS pressure, (18±3 to 23±3 mmHg, mean±1 SD, $p<0.05$) and as in Dowlatshahi’s study there was a significant decrease in LOS relaxation (50±15%, mean±1 SD) in response to swallowing. In addition, morphine caused a non-significant increase in peristaltic pressure 10 cm above the sphincter (67±40 to 75±50 mmHg, mean±SD). When peristalsis was stimulated by methacholine, however, morphine premedication markedly augmented the peristaltic pressure immediately above the LOS (128±88 mmHg for morphine, 76±38 mmHg for saline and 63±16 mmHg for naloxone; mean±SD, $p<0.025$). Peristaltic pressures in the striated muscle portion of the oesophagus were not affected by morphine premedication and morphine did not affect the sphincter’s response to either methacholine or pentagastrin.

As the authors of the recent study aptly point out, the divergent results of their study when compared with others is not entirely unexpected, for if the oesophagus does indeed contain five different types of opioid receptors, why should they all behave in