Clinical trial

Duodenal ulcer healing after presentation with haemorrhage

W R MURRAY, G LAFERLA, G COOPER, AND M ARCHIBALD
From the University Department of Surgery, Western Infirmary, Glasgow

SUMMARY Forty patients who were managed conservatively after haemorrhage from an endoscopically verified duodenal ulcer were randomised at discharge from hospital to enter a blind study of ranitidine therapy (150 mg bd) versus a placebo tablet. The patients were re-endoscoped after four weeks, ulcer status defined and the trial code broken revealing that five of 20 placebo patients had healed their duodenal ulcer compared with 16 of 20 ranitidine patients (p=0.001). Lifestyle parameters of both groups improved during the study period but no directly related benefit in duodenal ulcer healing could be shown. We conclude that effective anti-ulcer therapy, such as ranitidine, is required to heal a duodenal ulcer which presents with haemorrhage.

During the years 1983 and 1984 the Haematemesis Management Team at the Western Infirmary, Glasgow, treated 279 patients who had bled from a duodenal ulcer with an overall mortality of 2.2%. Twenty eight patients (10%) underwent surgery to control haemorrhage while 245 patients (88% of the total number) were discharged with an active duodenal ulcer which had stopped bleeding after conservative management during a mean hospital stay of five days. Forty nine of these patients (20%) had no dyspepsia on admission and by the time of discharge from hospital 208 (85%) of the patients managed conservatively without the use of H2 antagonists denied the presence of upper gastrointestinal symptoms.

Haematemesis Management Team members have observed a ready willingness on the part of the patients under their care to change, in the short term at least, personal habits such as smoking and drinking alcohol which may have a detrimental effect on duodenal ulcer healing.1-3 If patients who leave hospital without dyspepsia after conservative management of a duodenal ulcer which has bled do in fact alter their lifestyle in a potentially beneficial way, then a satisfactory short term ulcer healing rate might be achieved without the use of an H2 receptor antagonist drug. We have tested this hypothesis using a prospective randomised blind clinical study of patients who had bled from an endoscopically verified duodenal ulcer.

Patients

METHODS

The patients included in this study were admitted to the Western Infirmary, Glasgow, during 1984 with a diagnosis of acute upper gastrointestinal haemorrhage. All patients with this clinical diagnosis were endoscoped within 24 hours of admission and potential study patients defined as those having blood in the upper gastrointestinal tract with a duodenal ulcer as the only lesion present. Patients receiving H2 receptor antagonist therapy at the time of admission were excluded from the study. Final selection for this study was made at the time of discharge from hospital when patients who had stopped bleeding from their duodenal ulcer on conservative management without specific anti-ulcer therapy and had no upper abdominal pain were offered entry into the clinical trial. Study patients were discharged with trial tablets containing either ranitidine (150 mg) to be taken twice a day or a placebo preparation to be taken at the same frequency. All patients were given a supply of antacid tablets (Rennie's, Glaxo Pharmaceuticals) to be taken as required and were counselled by the members of the Haematemesis Management Team responsible for their care.

Before discharge from hospital 32 data items were recorded for each study patient giving pre-admission

Address for correspondence: Mr W R Murray, MD, FRCS, Department of Surgery, Western Infirmary, Glasgow G11 6NT.

Received for publication 21 February 1986.

1387
and inpatient details. These data included social factors, dyspeptic history, drug history, gastrointestinal symptoms in hospital, haematology, endoscopic findings and an evaluation of lifestyle parameters. This evaluation included dietary history, smoking habits, alcohol consumption and the frequency with which patients went out in the evenings for what were termed ‘pleasurable pursuits’.

During the study patients were given open access to the study team via our research staff nurse (MA) and were encouraged to inform the team of any problems encountered. The patients were recalled four weeks after discharge to undergo an outpatient endoscopy at which time the presence or absence of duodenal ulceration was recorded. Lifestyle parameters were reassessed and data collected concerning postdischarge upper gastrointestinal symptoms, tablet compliance and haematology. The study code was then broken.

Results

Forty patients entered the study and were equally randomised between the ranitidine and placebo groups. Analysis of the data collected revealed that the two groups of patients were well matched, the only statistically significant difference being that smokers in the ranitidine group smoked more cigarettes per day than smokers in the placebo group (Table 1).

At the four week postdischarge endoscopy it was found that five of the 20 patients receiving placebo tablets had healed their duodenal ulcer while 16 of the 20 patients receiving ranitidine had healed their duodenal ulcer. This difference is statistically highly significant (p=0.001; Fisher’s exact test) and led to the study being terminated after only 40 patients had entered. A secondary analysis was carried out to compare the 21 patients who had a healed duodenal ulcer four weeks postdischarge with the 19 patients whose duodenal ulcer was still present. The only statistical significant difference between these two groups was found to be the use of ranitidine by patients with a healed duodenal ulcer (p<0.001).

No patient in the study was admitted to hospital during the study period and we are unaware of any significant complication arising from duodenal ulceration or its therapy in this group of patients in the four weeks after haemorrhage. No patients receiving placebo tablets required H2 receptor antagonist therapy during the study. Despite the significant difference in duodenal ulcer healing rates, dyspepsia was reported as frequently from patients receiving ranitidine as from those receiving the placebo (11 in each group). Antacid consumption was found to be similar for the placebo and ranitidine groups and for patients with healed or unhealed duodenal ulcers at four weeks. Six of the 15 patients in the placebo group with an unhealed duodenal ulcer at four weeks denied dyspepsia during the study period.

No significant difference was noted in lifestyle parameters or their changes during the four weeks after discharge between ranitidine (n=20) and placebo (n=20) patients, healed (n=21), and unhealed (n=19) duodenal ulcer patients and healed (n=5) and unhealed (n=15) duodenal ulcer patients receiving the placebo preparation. Although lifestyle parameter changes did not correlate with duodenal ulcer healing, potentially beneficial changes were recorded amongst the 40 patients studied during the four week period after discharge from hospital (Table 2).

Discussion

Ulcer healing is generally accepted as a criteria of successful short term conservative management of a duodenal ulcer which has bled but has not led to urgent surgery. This study has shown that in this situation the use of an H2 receptor antagonist such as ranitidine will achieve a significantly greater duodenal ulcer healing rate than placebo therapy. Our four week duodenal ulcer healing rates, as defined by endoscopy, were strikingly different for the two groups of patients studied. We are unaware

Table 1 Data analysed according to study group randomisation

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Ranitidine</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>16</td>
<td>19</td>
<td>NS</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>56±6±4±5</td>
<td>55±3±4±6</td>
<td>NS</td>
</tr>
<tr>
<td>Cigarette smokers</td>
<td>9</td>
<td>14</td>
<td>NS</td>
</tr>
<tr>
<td>Cigarettes per day</td>
<td>11±2±3±6</td>
<td>22±3±2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Alcohol drinkers</td>
<td>12</td>
<td>14</td>
<td>NS</td>
</tr>
<tr>
<td>Units alcohol per week</td>
<td>15±3±3±4</td>
<td>15±4±4±3</td>
<td>NS</td>
</tr>
<tr>
<td>Duodenal ulcer history</td>
<td>15</td>
<td>15</td>
<td>NS</td>
</tr>
<tr>
<td>Admission Hb (g/dl)</td>
<td>10±9±6±5</td>
<td>11±3±0±7</td>
<td>NS</td>
</tr>
<tr>
<td>Four week Hb (g/dl)</td>
<td>13±7±0±3</td>
<td>14±0±3</td>
<td>NS</td>
</tr>
</tbody>
</table>

(Student's non-paired t test: mean±standard error).

Table 2 Short term (4 weeks) lifestyle parameter changes after successful conservative management of haemorrhage from a duodenal ulcer in 40 patients

<table>
<thead>
<tr>
<th></th>
<th>Took more rest 60%</th>
<th>Alcohol drinkers reduced their intake significantly 55%</th>
<th>Socialised less frequently 48%</th>
<th>Slept longer 45%</th>
<th>Improved their diet 38%</th>
<th>Smokers smoked significantly less 31%</th>
</tr>
</thead>
</table>
Duodenal ulcer healing after presentation with haemorrhage

of a comparable study of patients who have recently bled from a duodenal ulcer but the observed four
week ranitidine healing rate of 80% can be regarded
as satisfactory and in keeping with the literature on
ranitidine treatment of a symptomatic duodenal
ulcer without haemorrhage.4–8 The four week
placebo healing rate of 25% is in the lower range
reported for placebo treatment from any country
and gives no indication of satisfactory spontaneous
duodenal ulcer healing after presentation with haemorrhage.9–11 Paoluzi et al have recently shown
that complete healing of a duodenal ulcer using full
dose cimetidine therapy is associated with a signifi-
cantly lower recurrent ulcer rate than if full dose
therapy is reduced or stopped before complete
duodenal ulcer healing.11

The relationship between complete duodenal
ulcer healing and the success of further medical
management of the ulcer diathesis may well be
important. The results of this study support the
general view that the absence of dyspepsia does not
correlate well with duodenal ulcer healing. Patients
who leave hospital with an active duodenal ulcer
which has bled should therefore undergo a further
endoscopy to ensure that H2 receptor antagonist
therapy has completely healed the duodenal ulcer
before the dose is reduced to maintenance level or
therapy stopped.

The hypothesis that potentially beneficial changes
in lifestyle parameters will encourage spontaneous
duodenal ulcer healing after presentation with
haemorrhage cannot be supported by this study.
Our observations suggest that the majority of the
study patients did alter at least one aspect of their
lifestyle in an apparently beneficial way during the
four weeks after discharge from hospital. Despite
these observations we were unable to correlate short
term postdischarge lifestyle changes with duodenal
ulcer healing and conclude that beneficial lifestyle
changes, even if they do occur, cannot be relied
upon to induce satisfactory spontaneous duodenal
ulcer healing in patients who have presented with
haemorrhage.

The authors gratefully acknowledge the cooperation
of the Haematemesis Management Team at the
Western Infirmary, Glasgow. We thank Glaxo
Pharmaceuticals Ltd who supported this study.

References

1 Sonnenberg A, Muller-Lissner SA, Vogel E et al. Predictors of duodenal ulcer healing and relapse.
2 Wormsley KG. Smoking and duodenal ulcer. Gastro-
3 Kurata JH, Haile BM. Epidemiology of peptic ulcer
4 Dobrilla G, Barbara L, Bianchi Porro G, Mazzacca G,
Verme G. Placebo controlled studies with ranitidine in
5 Korman MG, Hansky J, Merrett AC, Schmidt GT. Ranitidine in duodenal ulcer: healing rate and effect of
smoking. [Abstract]. Gastroenterology 1981; 80:
A1197.
6 Gibinski K, Nowak A, Gabryelewicz A et al. Multi-
centre double-blind trial on ranitidine for duodenal
7 Mackay C, Mohammed R, Lee FI, Fielding JD,
Holmes JKT, Hine K. The effect of ranitidine, a new
histamine H2-receptor antagonist, on healing rate of
duodenal ulceration. [Abstract]. Gastroenterology
1981; 80: A1219.
8 Marks IN, Wright JP, Denyer M, Hatfield A, Gird-
wood AH, Lucke W. Ranitidine heals duodenal ulcers.
9 Jones DB, Rose JDR, Smith PM, Calcraft BJ. Treat-
ment of peptic ulcer with ranitidine – a clinical trial. In:
Misiewicz JJ, Wormsley KG, eds. The clinical use of
ranitidine. Proceedings of the Second International
Symposium on Ranitidine. Oxford: Medicine Pub-
lishing Foundation, 1982; 185–8.
10 Chatterji AN. A double-blind and randomised
placebo-controlled study of ranitidine in duodenal ulcer
and completely healed duodenal ulcers’ outcome in main-
tenance treatment: a double-blind control study. Gut
Duodenal ulcer healing after presentation with haemorrhage.

W R Murray, G Laferla, G Cooper and M Archibald

Gut 1986 27: 1387-1389
doi: 10.1136/gut.27.11.1387

Updated information and services can be found at:
http://gut.bmj.com/content/27/11/1387

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections
Stomach and duodenum (1689)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/