The effect of long-term omeprazole on the glucose–hydrogen breath test in elderly patients

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Abstract

Objective: to test whether omeprazole taken for longer than 1 month causes an increase in the rate of small bowel bacterial overgrowth in elderly subjects.

Subjects: 44 elderly people, 22 taking omeprazole, 22 not taking omeprazole or H2 receptor antagonists.

Main outcome measures: rate of positive glucose–hydrogen breath tests; anthropometric measures and blood tests reflecting malabsorption.

Results: there was no difference in the rate of positive tests between those taking omeprazole (45%) and those not taking it (59%). The omeprazole group had significantly lower serum albumin concentrations. There was no difference in body mass index, mid-arm circumference, arm fold thickness, adjusted calcium concentration or haemoglobin levels.

Conclusions: omeprazole does not cause increased bacterial small bowel overgrowth in elderly subjects.

Keywords: small bowel bacterial overgrowth, glucose–hydrogen breath test, omeprazole

Introduction

Bacterial overgrowth of the small bowel (BOSB) is a cause of malnutrition in old age [1], although it can also occur in large numbers of asymptomatic elderly people [2]. Risk factors for this condition include diabetes, gastric resection, achlorhydria, scleroderma, small bowel diverticula, strictures, fistulae and pseudo-obstruction [3]. Reports of BOSB in patients taking H2 receptor antagonists have been made, but there has been no evidence of any significant difference when large groups of people have been tested, nor any associated metabolic derangement [4]. Studies have shown that as many as 56% of people who are taking omeprazole have BOSB [6], but this has not yet been shown in older people. The aim of the study was to test whether omeprazole has any effect on bacterial overgrowth in elderly patients.

Methods

Patients from the control group were recruited from an elderly medicine day hospital, and those from the omeprazole group from acute admissions and outpatients and from the day hospital and local general practitioners. All patients were aged over 65. Written consent was gained from all those participating and the trial was approved by the local ethical committee. All those in the omeprazole group had been taking the drug for longer than 1 month.

Patients with risk factors for small bowel bacterial overgrowth and those taking H2 antagonists (control group only) were excluded, as were patients with unexplained diarrhoea. The glucose–hydrogen breath test was used. This is a non-invasive, well-tolerated, safe procedure, which does not involve the use of isotopes and is probably the most sensitive and specific test available [5]. Patients fasted for 14 h before the start of the test and avoided carbohydrate for a further 4 h prior to this.

Breath samples were collected after breath-holding for 15 s and end-expiratory samples were collected. Two baseline samples were obtained and the mean of these was used as a reference point. Glucose (75 g) was administered in the form of ‘Hi-Cal’, which was drunk in the shortest possible time. Chlorhexidine mouth wash was used as a mouth rinse to avoid false positives due to oral fermentation. Further breath samples were collected at 5, 10, 15, 20, 30, 40, 50 and 60 min and thereafter at 15 min intervals to 180 min. A positive result was taken as a rise of 20 ppm over the baseline. If
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Table 1. Age, functional status and nutritional data in the control and omeprazole groups

<table>
<thead>
<tr>
<th></th>
<th>Mean (95% confidence interval)</th>
<th>Omeprazole</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>78.1 (65-91.2)</td>
<td>79 (66.8-81.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Barthel index</td>
<td>16.7 (11.1-22.36)</td>
<td>18.1 (14.9-21.3)</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>26.1 (16.6-35.5)</td>
<td>24.3 (16.9-31.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Mid-arm circumference</td>
<td>26.3 (19.2-33.45)</td>
<td>26.3 (21.9-30.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Arm fold thickness</td>
<td>17.2 (2.9-31.4)</td>
<td>17.2 (7.6-26.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Adjusted serum calcium</td>
<td>2.35 (2.33-2.37)</td>
<td>2.31 (2.07-2.55)</td>
<td>NS</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>40.8 (32.3-49.2)</td>
<td>37.1 (25.8-48.4)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>13.0 (10.2-15.7)</td>
<td>12.1 (7.9-16.3)</td>
<td>NS</td>
</tr>
</tbody>
</table>

BMI, body mass index; NS, not significant.

no such rise was obtained, 30 g of lactulose was given. Breath samples were taken at hourly intervals for 3 h. If no rise was seen in this time, the subject was declared to be a hydrogen non-producer.

Blood samples were taken for haemoglobin, serum albumin and calcium. Height and weight were measured to calculate body mass index. Mid-arm circumference and triceps skin fold thickness were also measured. The Barthel index was taken as an indicator of functional status.

The study was calculated as having a 70% power of detecting a 30% difference, assuming that the normal elderly population have a 20% chance of having a positive breath test [6] and that 50% of patients on omeprazole have bacterial overgrowth.

Results

Fifty patients were recruited into the trial. Of these, six (12%) were non-hydrogen producers (two in the control group, four in the omeprazole group). Of the 44 remaining patients, 22 were in the control group (eight male, 14 female) and 22 in the omeprazole group (six male, 16 female). In the control group 13 patients (59%) had a positive breath test and nine (41%) a negative result. In the omeprazole group 10 patients (45%) had a positive result and 12 (55%) patients a negative one ($\chi^2 = 0.76$; not significant). All patients in the omeprazole were taking 20 mg of the drug daily. They had been taking the drug for a median of 9.5 months (range 1-36 months), with only one patient taking it for a single month.

The results for the nutritional and functional studies are shown in Table 1. The Mann-Whitney $U$ test was employed for the Barthel index. Student's $t$-test was used for all other parameters.

Discussion

This study reinforces the finding that large numbers of elderly people have positive breath tests in the absence of overt symptoms of BOSB. This is the first time that this has been investigated with elderly patients by means of a glucose-hydrogen breath test. Omeprazole was not associated with a significant increase in the number of positive tests, although the small numbers in the study mean that a type 2 error cannot be excluded. Changes of the magnitude suggested by previous studies are unlikely [6]. Other studies have also found that while omeprazole increases the number of bacteria detected by aspiration, the concentration of potentially carcinogenic $N$-nitroso compounds is unchanged [7]. This is in keeping with our finding that although many elderly people both on and off omeprazole have bacteria detectable in their small bowel they seem to suffer no ill effects.

Anthropometric data are not affected by omeprazole, although there is a decrease in serum albumin concentration. We are unable to account for this; perhaps sub-clinical mucosal damage is caused by bacterial overgrowth. Previous studies have shown small decreases in the levels of calcium and folate, similarly with no explanation [2, 4]. Unfortunately, we were unable to get full details of all patients’ underlying diagnoses and how these were made.

Another weakness of this study is that no attempt was made to exclude the previous use of antibiotics, which could convert a positive result to a negative one. However, it seems unlikely that there was any difference between the two groups in this matter.

We conclude that it is unlikely that the use of long-term omeprazole in elderly patients is associated with the development of symptomatic BOSB.

Key points

- Omeprazole causes no significant increase in the rate of positive glucose-hydrogen breath tests in elderly patients.
Long-term omeprazole and the glucose–hydrogen breath test

- Elderly patients who are not taking omeprazole have a high rate of glucose–hydrogen breath tests.
- Patients taking omeprazole have lower concentrations of serum albumin than those not taking the drug, but there is no difference in other measures of nutrition and absorption.

References


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Photograph: Sam Tanner.