Evaluation of omeprazole as a cost-effective diagnostic test for gastro-oesophageal reflux disease

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Omeprazole 40mg compared to endoscopy in the initial management of patients with symptoms suggestive of the presence of gastro-oesophageal reflux disease (GERD) based on symptom assessment alone.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients between the ages of 18 and 80 years who presented with symptoms (moderate or severe on at least 1 of the previous 7 days or mild on 2 or more of the previous 7 days) suggestive of GERD, including but not limited to heartburn, dysphagia and regurgitation. The excluded patients were those with symptoms of underlying complications such as malignancy as well as those who were lactating or pregnant, those with alcohol, drug or substance abuse problems or any condition associated with poor compliance.

Setting
A hospital setting. The economic analysis was carried out in the UK.

Dates to which data relate
The dates for effectiveness and resource use data collection were not reported. The price year appears to have been 1998.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

Link between effectiveness and cost data
Costing was prospectively performed on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size since no data were available to aid the calculation of sample size. It was planned to recruit 160 patients. A total of 90 patients entered the study, of whom 69, with a mean (SD) age of 47 (14) years, were included in the effectiveness analysis.
Study design
This was a prospective cohort study, carried out in 12 centres. The duration of the follow-up was 2 weeks. A total of 21 patients were excluded from the final effectiveness analysis, with 10 withdrawing because they could not tolerate the pH monitoring procedure. Endoscopic examination of the oesophagus, stomach and duodenum was performed and patients underwent ambulatory oesophageal pH monitoring for 18-24 hours. These procedures had to be completed within 5 days of informed consent being obtained. On completion of these procedures, patients received "open" (unblinded) omeprazole 40mg for a period of 14 days (range: 13 - 16 days). For ambulatory pH monitoring, the pH probe was positioned 5cm above the lower oesophageal sphincter and was left in place for 18-24 hours. Patients were categorised as GERD positive if the pH was below 4.0 for at least 4% of the monitoring time. Patients completed a diary card each day while taking omeprazole in which they graded their overall acid-related symptoms on a scale of 0 (none) to 3 (severe) and recorded whether they had taken their omeprazole (yes/no).

Analysis of effectiveness
The principle used in the analysis of effectiveness was treatment completers only. The health outcome measures were sensitivity, specificity, predictive values, percentage of patients with a correct diagnosis when pH monitoring was used as the standard test, percentage of patients experiencing an improvement in overall symptoms by at least one grade, time to complete symptom relief, and the percentage of patients who accomplished complete symptom relief. Survival analysis techniques were used to determine the median time to symptom relief using daily diary-card data.

Effectiveness results
Response to 2 weeks of omeprazole therapy, when defined as an improvement in overall symptoms by at least two grades (or from mild to none), was found to be significantly associated with the diagnosis from pH monitoring (p< 0.05). Sensitivity was 0.69 (SD, 0.08), specificity was 0.58 (0.10), predictive value of a positive test was 0.67 (0.08), and predictive value of a negative test was 0.60 (0.10). A total of 63.8% (95% CI: 51.4% - 76.2%) had a correct diagnosis.

Omeprazole response, when defined as an improvement by at least one grade, was found to be significantly associated with the results from pH monitoring (p< 0.05). In this case sensitivity was 0.91 (0.05) and specificity was 0.31 (0.09). Positive and negative predictive values were 0.62 (0.07) and 0.73 (0.13), respectively.

When omeprazole response was defined as an improvement in heartburn symptoms by at least two grades (or from mild to none) and compared to the diagnosis from pH monitoring, sensitivity was 0.89 (0.06) and specificity was 0.35 (0.12). Positive and negative predictive values were 0.68 (0.08) and 0.67 (0.16), respectively. There was no significant correlation between the diagnoses obtained from endoscopy and those obtained from pH monitoring. Endoscopy had a sensitivity of 0.66 (0.08), specificity of 0.47 (0.09), and positive and negative predictive values of 0.59 (0.08) and 0.54 (0.10), respectively. A total of 56.9% (95% CI: 44.9% - 69%) had a correct diagnosis. 82% of patients had experienced an improvement in overall symptoms by at least one grade. Daily diary card data showed that the median time to complete symptom relief was 3 days, which was accomplished in 59% of patients.

Clinical conclusions
This study has demonstrated that a therapeutic trial of omeprazole is a useful clinical tool in the initial management of patients presenting with typical symptoms of GERD, not suggestive of underlying complications such as malignancy. In this study, omeprazole provided rapid symptoms relief in patients with and without endoscopic findings.

Measure of benefits used in the economic analysis
The measure of benefit was the percentage of patients with a correct diagnosis when pH monitoring was used as the standard test.

Direct costs
Costs were not discounted because of the short time frame of the cost analysis. Quantities were reported separately.
from the costs. Cost items were reported separately. Cost analysis covered the cost of 14 days of treatment with omeprazole 40mg o.m. and the mean cost per endoscopy. The perspective adopted in the cost analysis was that of the UK National Health Service (NHS). The price year appears to have been 1998. It was reported that the cost of misdiagnosis was beyond the scope of this study.

**Indirect Costs**
Indirect costs were not considered.

**Currency**
UK pounds sterling (€).

**Sensitivity analysis**
A sensitivity analysis was not conducted.

**Estimated benefits used in the economic analysis**
With omeprazole, a total of 63.8% patients (95% CI: 51.4% - 76.2%) had a correct diagnosis when pH monitoring was used as the standard test. The corresponding value for the endoscopy was 56.9% (95% CI: 44.9% - 69%).

**Cost results**
The cost of treating 100 patients with omeprazole 40mg for 2 weeks was 3,012 versus 27,319 for the cost of endoscopy for 100 patients.

**Synthesis of costs and benefits**
The cost per correct diagnosis was calculated as the cost-effectiveness ratio, resulting in a value of 47 (95% CI: 40 - 59) for omeprazole compared to 480 (95% CI: 396 - 608) for endoscopy.

**Authors’ conclusions**
The authors concluded that omeprazole can be used as a clinically effective tool in the initial management of GERD and that it is of diagnostic value in patients who present with typical symptoms, such as heartburn, when the diagnosis is based on symptom assessment alone.

**CRD COMMENTARY - Selection of comparators**
The strategy of using pH monitoring, as the gold standard procedure in the context in question, was regarded as the comparator. You, as a database user, should consider whether this is a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness results are likely to be internally valid given the prospective nature of the study design. However, the internal validity may be weakened by the fact that no power analysis was performed and that the effectiveness analysis was based on treatment completers only. The study sample appears to have been representative of the study population.

**Validity of estimate of measure of benefit**
The estimate of benefits was obtained directly from the effectiveness analysis. This choice of estimate was justified.
Validity of estimate of costs
The authors reported some quantities separately from the costs. The perspective adopted in the cost analysis was not explicitly stated. More details of methods of cost estimation would have been useful. The price year was not clearly reported, the costs of misdiagnosis was not included in the cost analysis, the effects of alternative procedures on indirect costs were not addressed and statistical analyses were not performed on cost data. Cost results may not be generalisable outside the study setting.

Other issues
The authors’ conclusions appear to be justified given uncertainties in the data. The issue of generalisability to other settings was not addressed, although, appropriate comparisons were made with other studies. The degree to which the study sample was representative of the study population was addressed in the authors' comments.

Implications of the study
In practice, endoscopy could be reserved for selected patients (i.e. those with alarm symptoms or signs) with others being considered for a therapeutic trial as the initial management step. Any patients failing to respond to empirical treatment would warrant further investigation, e.g. pH monitoring, as the presumptive diagnosis of GERD may also be incorrect. A trial of omeprazole is a simple, non-invasive method and so should be more acceptable to the patient as a first line of investigation than endoscopy or pH monitoring.

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