Original Article

Comparative Study of the Quality of Life and Cost-Effectiveness Between Patients Treated with Helicobactor Pylori Eradication and Acid Suppression Therapy in Duodenal Ulcer Disease

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Abstract

This prospective open randomized study was done among 70 duodenal ulcer disease patients of 16 to 60 years age attending the gastroenterology out patient department of Bangabandhu Sheikh Mujib Medical University (BSMMU). Patients were randomized into two groups ; one group (category A) was given H. pylori eradication therapy consisting of Rabeprazole, amoxicillin and levofloxacillin for 14 days then rabeprazole alone for 4 weeks and another group (category B) was given omeprazole for 6 weeks. Both groups were followed up for one year. Objective was to estimate the quality of life of the patients and to see the cost-effectiveness of treatment of the two groups. Quality of life of patients was assessed using a previously used validated questionnaire with high score indicating a better quality of life.

Cost estimation was recorded by the patients themselves using a cost dairy. Cost effectiveness was calculated by using a formula - the cost incurred by the patient / change in health status as estimated by change in QOL.QOL of patient in category A before start was 98.98, at six month was 111.75, at 1 year was 117and the improvement in QOL was statistically significant (P <0.001). QOL of patient in category B before start was 98.98, at six month was 111.56, at 1 year was 116.2and the improvement in QOL was statistically significant (P <0.001).

The cost effectiveness ratio of patient in category A and that in B was respectively 210 per QOL score and 214.6 per QOL score. There was significant improvement in QOL score in both groups but cost effectiveness ratio between the groups showed no significant difference.

In conclusion, quality of life of duodenal ulcer disease patient improves with either H. pylori eradication therapy or by intermittent acid suppression therapy but Cost effectiveness ratio of the two approaches to treatment is same.

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Introduction

For more than a century peptic ulcer disease has been a major cause of morbidity and mortality. Duodenal ulcer is common in Bangladesh. In Bangladesh, the prevalence of duodenal ulcer and gastric ulcer was estimated to be 11.98% and 3.58% respectively.[1] The point prevalence of duodenal ulcer varies from country to country. Approximately 10% of individuals in western countries develop peptic ulcer at some point in their lifetime.[2]

Helicobacter pylori is a ubiquitous gram-negative bacterium infecting half of the world's population[3,4]. Warren and Marshall's first discovered the link between Campylobacter pylori and peptic ulcer disease.[5] Campylobacter pylori causes chronic gastritis[6] and peptic ulcer disease[7,8]. The prevalence of Helicobacter pylori infection is very high in Bangladesh. A study conducted on Bangladeshi children by ICDDR, B scientists has shown that 60% are infected by the age of 3 months and 80% are infected by the 3 years of age.[9] In adults, about 92% have been found to be seropositive for Helicobacter pylori antibody.[10] The prevalence among the middle-aged adults is over 80% in many developing countries and 20 to 50 % in the developed countries.[11]

Majority of duodenal ulcers are caused by Helicobacter pylori[12]. Duodenal ulcer disease, which was once considered to be an incurable, chronic relapsing and remitting condition, is now thought to be the manifestation of a completely curable chronic bacterial infection. Accordingly, treatment approaches have changed from symptom control and maintenance of ulcer healing to one of cure through eradication of underlying Helicobacter pylori infection.

International consensus conferences have recommended that H. pylori eradication should be the treatment of peptic ulcer associated with H. pylori[13,14]. Successful eradication of H. pylori markedly reduces the risk of ulcer recurrence. The risk of re-infection with H. pylori after successful treatment is very low in western countries and ranges between 0.5% and 2% per year in adults and in children older than 5 years of age[15,16,17,18].

All the trials on H. Pylori related peptic ulcer diseases are based on endoscopy and less attention has been paid to the possible effects of eradication therapy on the quality of life. Patients with functional dyspepsia often have dyspeptic symptoms that are indistinguishable from those in ulcer disease and clinical trials in these patients have not been able to show a clinically relevant symptomatic benefit of eradication over placebo[19,20]. The primary focus in most reports on the effects of eradication therapy in

duodenal ulcer disease has been on the frequency of ulcer relapse and on eradication rates. This may be too narrow a perspective. Despite successful eradication of Helicobacter

pylori, many patients remain symptomatic and dependent on acid suppression therapy. Therefore, the assessment of the value of treatment strategy for a chronic relapsing disease like duodenal ulcer should go beyond the value in terms of frequency of relapse, and include impact on symptoms and quality of life. Data from developing countries regarding H.Pylori eradication and subsequent recurrences is small. Most studies indicate that eradication rate is much lower than those obtained in western countries and the recurrence rate is higher[20,21,22,23]. Studies in Bangladesh have largely shown results similar to that of developing countries with a low eradication rate using different H.Pylori eradication regimens and a higher rate of re-infection[24,25,26]. All these factors have led to a confusing picture in the treatment of duodenal Ulcer disease. Some patients are being treated with Helicobacter eradication regimen while others are being treated with ulcer healing drugs alone. Further more; the cost of treatment has not been evaluated in patients with duodenal ulcer.

Aims And Objectives: 1. To see and compare the "quality of life" of patients with duodenal ulcer treated with Helicobacter eradication vs. conventional therapy.

2. To see the cost-effectiveness of treatment with H..Pylori eradication therapy vs. conventional therapy.

Materials And Methods

Study design

This is a prospective open randomized study. Patients suffering from duodenal ulcer disease of 16 to 60 years of both sexes were recruited from the out patient department of Gastroenterology, Bangabandhu Sheik Mujib Medical University.

The patients were divided into two groups using random table. One group was given H.pylori eradication therapy with proton pump inhibitor for 6 weeks and the other group was given only proton pump inhibitor for 6 weeks. Informed consent was obtained from all patients.

Patients

Inclusion criteria

a) Symptomatic patients with endoscopically proven duodenal ulcer.
b) Presence of H. pylori, proven by rapid urease test.
c) Patients aged between 16 to 60 years.
d) Ambulatory patients of both genders.

Exclusion criteria

a) Pre-treatment with proton pump inhibitor, H2-receptor antagonist, bismuth preparation or antibiotics with in 4 weeks prior to study.
b) History of being treated with H. pylori eradication regimen in the past.
c) Complicated duodenal ulcer patients (narrowing of duodenal bulb, active bleeding and perforation).
d) Patients with regular intake of NSAIDs or steroids.
e) Female patients who are pregnant, breast-feeding or intended to become pregnant within the duration of the study.
f) Patients with gastric ulcer.
g) Erosive gastro esophageal reflux disease.
h) Patients with concomitant other disease which requires drug therapy.
i) Patients who previously have undergone gastric surgery.
j) Patients who have a history of substance abuse.
k) Concurrent disease or therapy that could complicate the drug evaluation.
l) Patients not giving informed consent.

Treatment

Patients were randomized to receive either, 1) Omeprazole 20mg twice daily for six weeks, or 2) eradication therapy (Tab Rabiprazole 20mg daily, cap Amoxicillin 1gm twice daily and Tab Laevofloxacin 500mg daily for 2 weeks) followed by Tab Rabiprazole 20mg daily for another 4 weeks.Randomization was done with the help of a random table.Patients allocated eradication therapy was evaluated for H.Pylori status three months after eradication therapy. Those patients who were put on omeprazole alone were evaluated for ulcer healing at six weeks of therapy.Both groups of patients were followed up for a total of one year.Any patient of either group developing dyspeptic symptoms they were given six weeks of Omeprazole 20mg twice daily.Compliance were checked by counting the medicine foils at each visit and by evaluating the daily drug intake diary.

Assessments

Quality of life: Quality of life of duodenal ulcer patients was assessed using a previously used validated questionnaire - The SF 3628.Scoring was done by a doctor or by the patient before the start of therapy, at six months and at twelve months after the start of therapy. QOL instrument was previously translated into Bengali by using forward backward translation system. In this system a high score indicates a better quality of life.

Cost-estimation: Both groups of patients were given a cost diary. They were instructed to fill up the diary and show it at each visit. The diary recorded expenses incurred by the patient or others. It included a) cost of consultation with doctors, b) cost of medication, c) cost of any lost income due to morbidity, d) cost of investigations, e) cost of patients time spent during consultation or investigation, f) cost of care givers, if required, g) other expenses e.g.: travel, accommodation etc. Cost was estimated at the end of the study.

This was estimated by using the following formula-

$$\text{Cost effectiveness} = \frac{\text{The cost incurred by the patient}}{\text{Change in the health status as estimated by change in QOL.}}$$

Statistical analysis

Paired 't' test was used to compare the quality of life score before and after treatment. Unpaired 't' test was used to compare QOL score between the two groups at different intervals.

Results

A total of 70 patients were enrolled in the study, fulfilling the inclusion criteria. With the help of random table-I 35 patients were given H.pylori eradication regimen (category A), while the rest were given conventional acid suppression therapy (category B).

Table I : No of patients in different study groups

Cat A	Cat B
32	30

Of the patients receiving category A regimen 03 patients were lost to follow-up (8.57%). Of the patients receiving category B regimen 05 patients were lost to follow-up (14.28%).

The age range of patients receiving category A regimen was 18 to 65 years. The mean age of this group was 34.34 9.98 years. The age range of patients receiving category B regimen was 38.86 13.38 years (Table-II).

Table II: Age of participants

Cat A	Cat B
34.34±9.98 years	38.86±13.38 years

The QOL score (Table-III) of patients receiving category A regimen before the start of treatment was 98.78, at six months was 111.75 and at twelve months after the start of treatment was 117. This improvement in QOL score is statistically significant (P=<0.001). A sub-group analysis did not find any significant difference in improvement of QOL score between patients eradicated of H.Pylori vs. those not eradicated.

Table III: Quality of life score of the participants

	Cat A	Cat B
Before treatment	98.78	98.78
At 6 months	111.75	111.56
At 12 months	117	116.2

The QOL score patients receiving category B regimen before the start of treatment was 98.78, at six months was 111.56 and at twelve months after the start of treatment was 116.2. This improvement in QOL score is statistically significant (P=<0.001).

However, there was no significant difference in the QOL score between the two groups at various intervals.

The cost effectiveness ratio (Table IV) for patients receiving category A regimen was Tk 210 per QOL score. The cost effectiveness ratio for patients receiving category B regimen was Tk 214.6 per QOL score.

Table IV: The cost effectiveness ratio.(In taka)

Cat A	Cat B
Tk 210 per QOL score	Tk 214.6 per QOL score

Discussion

For more than a century peptic ulcer disease has been a major cause of morbidity and mortality. There is an important association of H. pylori infection and duodenal ulcer disease[12]. Numerous trials using a variety of treatment regimens have provided convincing evidence that successful treatment aiming at the cure of H. pylori infection results in the healing of duodenal ulcer disease and a very low recurrence rate[15, 16,17,18].

Several international consensus conference[13,14] recommended that all patients with duodenal or gastric ulcer who have H. pylori infection should receive anti H. pylori therapy to cure the infection.

Prevalence of H. pylori infection is high in Bangladesh[10]. Several trials for H. pylori eradication were under taken in Bangladesh which have largely shown a low eradication rate with different H. pylori eradication regimens and a higher rate of re-infection[28,29,30,31]. In most of the studies, the eradication rate was between 30-64%[29,30,31].

The re-infection rate was found to be 13% after one year and recrudescence rate was found to be 14% within first three months[28]. Most studies in other developing countries indicate that eradication rate is much lower than those obtained in western countries and the recurrence rate is also higher[23,24,25,26]. Recurrence rates of 11-40% have been reported from India 166,167,168 and 23.5% in Vietnam[26].

So, conventionally duodenal ulcer disease has been treated with intermittent acid suppression therapy in these countries.

Although there have been many studies looking into the ulcer recurrence rates of duodenal ulcers there are very few studies who have compared in a randomized way, quality of life in groups of patients before and after eradication therapy[33-34]. Phull[33] found that 80.9% of duodenal ulcer patients were still symptomatic while receiving acid-suppressing maintenance therapy. However, selection bias may have skewed the figures, since only a few eligible patients managed with long-term acid inhibition participated in the study. Furthermore, most of the patients received H2 blockers as maintenance therapy, and the more powerful acid suppression offered by proton pump inhibitors might have lowered the proportion of symptomatic patients.

This study focused on the QOL of Duodenal ulcer disease patients treated with H.Pylori eradication regimen vs. intermittent acid suppression therapy. This study showed that although both the treatment groups showed significant improvements in QOL score, there was no significant difference in the score of the two groups. The QOL was estimated by using a validated questionnaire, 'The SF-36'. The instrument was translated in to Bangla by forward -backward translation method. The study population included illiterate, semi-literate and some literate people. The interpretation of various questions was confusing to some. There is scope for improvement in this aspect.

Acid-peptic disorders are very common in the U.S. with 4 million individuals (new cases and recurrences) affected each year. Lifetime prevalence of PUD in the United States is 12% for men and 10% for women. Moreover, an estimated 15,000 deaths per year occur as a consequence of complicated PUD. The financial burden of these common disorders has been substantial, with an estimated burden on direct and indirect healthcare costs of $10 billion per year in the United States.

This study tries to evaluate the economic burden of duodenal ulcer on an individual basis in a third world country like Bangladesh. We tried to evaluate the cost of the disease the individual incurred. We calculated both direct and indirect costs of treatment, which included the cost of medication, professional advice, investigation, work loss, transport, etc. We calculated the cost per improvement in QOL parameters. The study showed that whatever approach is taken for treatment of duodenal ulcer disease; the C/E ratio does not show significant difference.

The patients taken for the study were from the out patient department of the university. They predominantly belong to the middle and lower income groups. The cost of medications, consultations and investigations are dominant over expenditures due to work loss and patients time loss. The cost of patient's time in higher income group is expected to be significantly higher.

From this study it can be concluded that the quality of life of duodenal ulcer disease patients improves significantly whether they are treated by H.Pylori eradication regimen or by intermittent acid suppression therapy. Again the quality of life of duodenal ulcer disease patients is not significantly different whether they are treated by H.Pylori eradication regimen or not.

The C/E ratio of the two approaches to treatment of duodenal ulcer disease patients is not that different.

It appears from this study whether to treat duodenal ulcer disease patients with H.Pylori eradication therapy is to be individualized and the patient can be brought into the decision making process.

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