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Brief Communication

Outcomes of Proton Pump Inhibitor Trial for Treatment Naïve Patients with Typical Reflux Symptoms

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Gastroesophageal reflux disease (GERD) is defined as reflux of gastric contents into the esophagus, resulting in symptoms and/or complications[1,2]. The proton pump inhibitor (PPI) test is a short course of high-dose PPI, used to diagnose GERD. This is an easy, simple test with high sensitivity to diagnose GERD[3,4,5]. An Indian study has reported that 72 % of patients with non-cardiac chest pain have relief with 2 weeks of PPI; thereby highlighting the role of PPI test in non-cardiac chest pain[6]. The present study was done to determine the utility of PPI trial in treatment naïve Indian patients with typical symptoms of GERD. Further, an attempt was made to determine the factors predicting a good response to PPI trial.

Methods

The present study is a retrospective analysis from a prospectively maintained dataset of patients with GERD. Treatment naïve patients in the age group of 18-45 years with typical GERD symptoms (heartburn, regurgitation and /or chest pain) of >2 weeks duration formed the study cohort. Few patients have chest pain associated with heartburn and regurgitation. Non cardiac chest pain is also a presentation of GERD[6] and hence was included in the study in presence of one of the two typical symptoms of GERD.

For this study, patients with history of on-going treatment for GERD, age <18 years or >45 years, post foregut surgery cases, atypical symptoms only and those with red flags were excluded.

Baseline frequency scale for symptoms of GERD (FSSG) score was noted for all cases (**Figure 1**). Those with FSSG score <8 were excluded from further analysis. Two week PPI trial (rabeprazole 20 mg twice a day/ pantoprazole 40 mg twice a day/ esomeprazole 20 mg twice a day) was given. Drug dosage, timing and adherence was emphasised to the patients. Life style changes like small, frequent meals, regular exercise, avoiding oily/spicy foods, quitting alcohol/ tobacco use and avoiding late night meals were explained. Follow up was done at 2 weeks and FSSG score was recorded.

Definitions Used In The Study

GERD-reflux of gastric contents into the esophagus, resulting in symptoms and/or complications.[1,2]

FSSG (frequency scale for symptoms of GERD)[7]-FSSG is the standard questionnaire containing

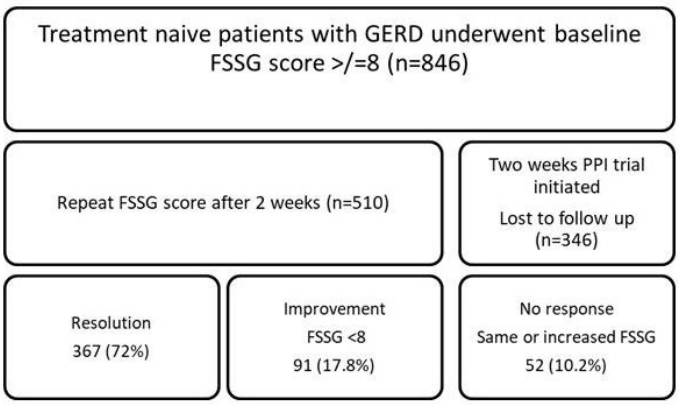

Figure 1: Study flow chart.

12 symptoms most commonly experienced by GERD patients. The score is divided into two subscales acid reflux-related symptoms, including 7 of 12 items (Nos. 1, 4, 6, 7, 9, 10, and 12), and dysmotility, including 5 of 12 items (Nos. 2, 3, 5, 8, and 11). When the cut-off score is set at 8 points, the FSSG shows a sensitivity of 62%, a specificity of 59%, and an accuracy of 60%. For this reason, the cut-off score for GERD has been recognized as 8 points.

Resolution- chest burn score of 0 (score based on questions 1,4,6, 12 of FSSG)[8]

Improvement- FSSG score <8[8]

No response- FSSG score same or increased at 2 weeks compared to baseline score.

Patients with resolution of symptoms or improvement (group 1) were compared with patients showing no response (group 2) and compared for demography, comorbid diseases, smoking, alcohol intake, body mass index and type of drugs used.

Statistical Analysis

The collected data were entered in Microsoft excel sheet. Age and BMI were represented as median and interquartile range. Comparison of proportions was done using Chi-square test and Mann–Whitney U-test was used for continuous variables. Analysis was performed using IBM Statistical Package for the Social Sciences (SPSS) version 20 [IBM, Armonk, NY, USA]. $P < 0.05$ was considered as statistically significant.The study was approved by the Institutional Ethics board.

Results

A total of 510 patients formed the study cohort (median age 34 years, males 54.1%). After 2 weeks of PPI trial, resolution of symptoms was noted in 72% of cases (**Figure 1**). In addition, improvement (FSSG <8) was present in 17.8% cases. Thus, 89.8% patients showed good response to PPI trial (Group1).

On comparing group 1 with patients who did not show any response to PPI trial (group 2), it was noted that patients in group 2 had significantly lower BMI compared to patients in group 1 (**Table 1**). Age, sex, smoking, alcohol intake and type of PPI used did not affect the results of PPI trial.

Discussion

In treatment naïve patients with typical GERD symptoms, PPI trial results in resolution and improvement in symptoms in 72% and 17.8% patients respectively. PPI trial is ineffective in 10.2% of cases. Lower BMI is a predictor of poor response to PPI trial.

Earlier studies too have reported that 10%-40% of patients with GERD have incomplete or no response to standard dose of PPI[9,10]. PPI therapy only suppresses gastric acid secretion and does not target the primary

Table 1: Comparison of demographic trends, comorbid diseases, anthropometry and drugs used between responders (group 1) and non-responders (group 2).

Parameter	Group 1 (n=458)	Group 2 (n=52)	P value
Age in years (median, range)	34 (19-45)	35 (19-45)	0.13
Sex (male)	247 (53.9%)	29 (55.8%)	0.79
Comorbid diseases (number, %) Diabetes mellitus Hypertension	 113 (24.7%) 98 (21.4%)	 19 (36.5%) 12 (23.1%)	 0.07 0.78
Smoking (number, %)	192 (41.9%)	25 (48.1%)	0.39
Alcohol (number, %)	178 (38.9%)	22 (42.3%)	0.63
Body mass index in kg per sq.m (median, range)	26 (18-39)	24 (18-34)	0.04
Drugs (number, %) Rabeprazole Pantoprazole Esomeprazole	 192 (41.9%) 168 (36.7%) 98 (21.4%)	 26 (50%) 18 (34.6%) 8 (15.4%)	 0.45

pathophysiology of GERD like excessive or abnormal reflux events, prolonged acid clearance, or altered mucosal sensitivity[11]. Patients may have impaired acid clearance secondary to hiatal hernia, dysmotility and weak lower esophageal sphincter. Epithelial injury may lead to central and/or peripheral hypersensitivity. Moreover, the refluxate may be weakly acidic or non-acidic.These factors are not targeted by PPI therapy, thereby resulting in poor response[12].

PPI efficacy is highest in patients with esophagitis and then diminishes progressively moving from symptomatic heartburn, regurgitation, chest pain, cough and laryngitis in descending order[12]. In the present study, FSSG was used and thus, these symptoms were not studied separately. Moreover, patients with atypical symptoms other than chest pain were excluded. This may have resulted in higher response rates.

It was noted that patients showing non-response had a lower BMI. A Korean study has similarly highlighted that psychological factors, BMI<23 kg/sq.m, sleep dysfunction and non-erosive reflux disease are the major factors leading to a poor response to PPI[13].

Effectiveness of PPI trial has rarely been studied in Indian setting. These drugs are commonly available as over the counter drugs and are frequently misused. The present study has tried to address this lacuna in Indian data with a large sample size of treatment naïve patients. However, it is limited by retrospective design, single study centre, variety of PPI drugs used and lack of objective measurements for drug adherence. Multicentre, prospective studies with single PPI would be more useful to determine effectiveness of PPI trial in Indian setting.

To conclude, PPI trial is effective in resolving typical symptoms of GERD in nearly three fourths of patients. Patients with higher BMI are more likely to respond to PPI trial.

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