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Psychological distress is not associated with treatment failure in patients with gastroesophageal reflux disease

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ABSTRACT

Objective: Symptoms of anxiety and depression are common in patients with gastroesophageal reflux disease (GERD). We aim to examine the relationship between psychological distress and response to proton pump inhibitors (PPI).
Methods: In this prospective study, GERD patients receiving PPI once or twice daily were divided into 3 groups: responders to PPI once daily (group A, N = 111), non-responders to PPI once daily (group B, N = 78) and non-responders to PPI twice daily (group C, N = 56). All patients completed demographic and clinical questionnaires, Rome III Diagnostic Questionnaire for irritable bowel syndrome, Hospital Anxiety and Depression Scale (HADS), Satisfaction with Life Scale (SWLS) and the Gastroparesis Cardinal Symptom Index (GCSI) questionnaires.
Results: A total of 245 patients (59.3% females, 52 ± 17.2 years) participated in this study. No differences were observed between groups with respect to age, sex, psychiatric medications or pre-existing major depression. Anxiety (HADS—anxiety > 7) was seen in 32%, 31% and 34% of groups A, B and C, respectively (p = ns). Depression (HADS—depression > 7) was present in 30%, 31% and 21% of groups A, B and C, respectively (p = ns). Global satisfaction with life (SWLS > 20) was present in 63% of group C patients, compared to 78% of group A and 78% of group B ($p = 0.04$, $p = 0.05$, respectively). GCSI scores (mean ± SD) were 11.1 ± 9.2, 14.07 ± 8.5 and 16.3 ± 10.4, for groups A, B and C, respectively ($p = 0.002$). GCSI correlated significantly with HADS—anxiety ($r = 0.20$, $p = 0.002$) and SWLS ($r = -0.2$, $p = 0.01$).
Conclusion: Lack of response to PPI was associated with lower life satisfaction but not anxiety or depression. Symptoms suggestive of gastroparesis were associated with anxiety and low satisfaction with life in patients with GERD.

Introduction

Up to 40% of the patients receiving proton pump inhibitors (PPIs) for gastroesophageal reflux disease (GERD) have an inadequate response to standard dose PPI [1–3]. Traditionally, definitions of PPI failure have been based on symptom frequency and severity thresholds, and vary between studies. A pragmatic approach is to define partial or non-response as a less than satisfactory response to standard dose PPI [4]. This is consistent with the approach of the Montreal Classification which rejects restricting a GERD diagnosis to a defined symptom frequency and intensity, and instead embraces any "troublesome" reflux symptom as GERD [5]. When managing patients who failed standard dose PPI, the most common therapeutic strategy is doubling the PPI dose. This approach is recommended by the 2008 American Gastroenterological Association guidelines for GERD [6]. However, this therapeutic strategy frequently results in less than satisfactory symptomatic response and the majority of patients continue to experience symptoms despite increased PPI dosage [4]. Failure to respond to PPI may be related to residual acid reflux, weakly acid or weakly alkaline reflux, esophageal hypersensitivity, inadequate dosing, poor compliance and psychological comorbidity [2].

The relationship between psychological distress and GERD is complex and poorly defined. GERD may contribute to psychological distress, and in fact, psychological distress may contribute more significantly to poor quality of life than do symptoms [7]. On the other hand, psychological distress may manifest as GERD-like symptoms. This is highlighted by studies which demonstrate the benefit of treating functional gastrointestinal (GI) disorders with psychodynamic therapy and psychoactive medications [8,9].

We have previously shown that lack of response to PPI can be predicted by atypical symptoms, long symptom duration and symptoms suggestive of gastroparesis (such as nausea/vomiting, post-prandial fullness/early satiety and bloating) as measured by the Gastroparesis

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Cardinal Symptom Index (GCSI) [10]. However, the relationship between lack of response to PPI and psychological distress remains unclear. We attempted to examine the relationship between psychological co-morbidity and PPI response in GERD by stratifying patients according to their treatment response to standard or double dose PPI.

Methods

Patient selection

This prospective follow-up-study was conducted from December 2010 to December 2011 in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice (GCP) and was approved by the Human Subjects Protection Program of Rabin Medical Center. All patients provided written informed consent prior to recruitment.

Data on patients' groups were obtained from our previous study (2009–2010) that compared demographic and clinical characteristics of PPI responders vs. non-responders [10]. In our previous study, consecutive patients receiving PPI (omeprazole 20 mg, Dexxon, Israel) once or twice daily for at least 3 months were prospectively recruited from a dedicated heartburn clinic at our institution. Prior to the commencement of PPI all patients reported at least 3 episodes of typical GERD symptoms of heartburn or acid regurgitation per week for the last 3 months. Patients reporting atypical GERD symptoms were included, provided that typical symptoms were also present. Based on their response to PPIs, patients were divided into 3 groups: patients who fully responded to PPI once daily (group A), patients who failed PPI once daily (but responded to PPI twice daily) (group B) and patients who failed PPI twice daily (group C). PPI responders (group A) included patients with a history of classic GERD symptoms (heartburn and acid regurgitation) who reported complete symptom resolution on PPI once daily treated for at least 3 months. The PPI failure groups were defined as patients who continued to report troublesome GERD symptoms (heartburn and acid regurgitation) at least 3 times a week, despite PPI once daily (group B) or twice daily (group C) for at least 3 months. Data from our previous study included patients' age, gender, ethnicity, education, occupation, marital status, current smoking, alcohol and drug use. The GCSI and Rome III criteria for IBS were recorded. Compliance was assessed during the initial personal interview. Patients were asked if they took their PPI at the prescribed dose, half an hour before meals, over the last 3 months [10].

All patients were managed at a dedicated heartburn clinic, and reviewed on a quarterly basis to ensure that responders did not become non-responders, and vice versa. In this continuation study, all patients from our previous study completed the Hospital Anxiety and Depression Scale (HADS) and the Satisfaction with Life Scale (SWLS) questionnaires during a single-session face-to-face interview by the study physician (RD).

Patients receiving H2-receptor antagonists, antacids or alginates, and patients with a history of esophageal or gastric surgery, were excluded.

Study questionnaires

Rome III Diagnostic Questionnaire for irritable bowel syndrome

All patients completed a validated Hebrew language Rome III Diagnostic Questionnaire for irritable bowel syndrome (IBS) [11]. The Rome III criteria are widely used for the diagnosis of functional gastrointestinal disorders.

Gastroparesis Cardinal Symptom Index

A validated Hebrew translation of the Gastroparesis Cardinal Symptom Index (GCSI) questionnaire was completed by all patients [12]. The GCSI consists of 3 subscales for patient assessment of upper gastrointestinal symptoms (PAGI-SYM). These include nausea/vomiting, post-prandial fullness/early satiety and bloating [13]. The nausea/vomiting subscale is comprised of 3 items: nausea, retching and vomiting. The post-prandial fullness/early satiety subscale is comprised of four items: stomach fullness, inability to finish a normal-sized meal, feeling excessively full after meals and loss of appetite. The bloating subscale is comprised of 2 items: bloating and stomach or belly becoming visibly larger. Overall the GCSI includes 9 questions and each question is rated by the responder according to severity from 0 to 5 (0 = no symptoms to 5 = severe symptoms). The total GCSI score is categorized as "extreme" (GCSI > 27) or "mild" (GCSI ≤ 27).

Hospital Anxiety and Depression Scale

Subjects' levels of anxiety and depression were assessed by using a non-validated Hebrew version of the Hospital Anxiety and Depression Scale (HADS), originally designed by Zigmond and Snaith [14]. The HADS includes the HADS—anxiety and the HADS—depression subscales (7 items each). Each item is graded on a Likert-type scale with four possible choices (0–3) for situational scoring of anxiety and depression. According to the sum of the scores for each subscale, patients are considered to have normal (0–7), mild (8–10), moderate (11–14) or severe (15–21) levels of anxiety or depression. HADS was designed to detect states of depression, anxiety and emotional distress among patients being treated for a variety of clinical problems, and not as a diagnostic tool. Advantages of HADS include its widespread availability, simplicity and reproducibility [15]. HADS has a high validity and reliability when compared to other scales such as Beck Depression Inventory (BDI-PC), Structured Clinical Interview for DSM-IV (SCID) and General Health Questionnaire (GHQ-28) [16]. Internal consistency ranges between 0.4 and 0.8 for the anxiety scale and 0.3 and 0.6 for the depression subscale. The concurrent criterion validity of HADS was determined by the developers to be acceptable when compared with the BDI-PC and GHQ-28 [14].

Satisfaction with Life Scale

Satisfaction with life was measured with a non-validated Hebrew translation of the Satisfaction with Life Scale (SWLS) [17]. The SWLS is designed to measure global cognitive judgments of satisfaction with one's life, and consists of five items: "In most ways my life is close to my ideal", "The conditions of my life are excellent", "I am satisfied with my life", "So far I have gotten the important things I want in life", and "If I could live my life over, I would change almost nothing". Respondents indicated the extent to which they agreed with each item on a seven-point Likert scale ranging from "strongly agree" to "strongly disagree". The responses to each item are summed to yield an aggregate score. Higher scores reflect greater satisfaction with life.

Statistical methods

Data analysis was carried out using SPSS 11.0 statistical analysis software (SPSS Inc., Chicago, IL, USA). Continuous variables such as age and duration of illness were reported as mean ± SD or median (min–max) where appropriate. Normality of distribution of continuous variables was assessed using the Kolmogorov–Smirnov test (cut off at $p = 0.01$). Categorical variables such as sex and the presence of co-morbidities were described using frequency distributions and were presented as frequency (%). Depending on the distribution, continuous variables were compared across groups using one way analysis of variance (ANOVA) or the Kruskal Wallis test. Pair wise, post hoc comparisons for significance across differences were assessed by Bonferroni's test or the Mann–Whitney U. Categorical variables were compared across groups using the chi square test (exact as necessary). Multinomial logistic regression was used to model group membership. The Pearson's correlation coefficient was used to test correlation between variables. Odds ratios were estimated with 95% confidence intervals. All tests were 2-sided and considered significant at $p < 0.05$.