

Reflux symptoms are associated with psychiatric disease

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SUMMARY

Aims: To evaluate the frequency of reflux symptoms in patients with a diagnosed psychiatric disorder and to assess potential risk factors for symptom occurrence.

Methods: The presence of reflux symptoms was compared between a case population of 94 psychiatric patients and a control population of 198 non-psychiatric patients.

Results: Heartburn, exercise-induced heartburn, cough and dysphagia were all reported significantly more frequently by subjects with psychiatric disorders than by control subjects. The presence of any psychiatric

diagnosis exerted an increased risk for both heartburn (odds ratio, 2.71; 95% confidence interval, 1.01–7.30) and exercise-induced heartburn (3.34; 1.12–9.96). The type of psychiatric disorder, the type of psychotropic medication and the lifestyle did not influence the presence of reflux symptoms.

Conclusions: Reflux symptoms occur more frequently in patients with than without a diagnosed psychiatric disorder. The reflux symptoms are not associated with any specific type of medication and may reflect a generally reduced threshold for or distorted perception of symptoms.

INTRODUCTION

Studies using psychological inventories or diagnostic tools of psychiatry have revealed common psychopathology among patients with various oesophageal disorders.^{1, 2} Anxiety and depression have been reported to be associated with oesophageal dysmotility disorders.^{3, 4} Psychiatric diagnoses are frequently established in patients with chest pain and negative coronary arteriography, as well as in patients with oesophageal motor disorders.^{5–8} The relationship between psychiatric disorders and reflux disease, however, has remained largely uninvestigated. Gastro-oesophageal reflux disease (GERD) affects one-third of the adult population,⁹ and daily or monthly heartburn occurred in 7% and 36%, respectively, of subjects in a reflux survey.¹⁰ The mechanisms by which psychiatric

disease may influence the oesophagus are numerous. Psychiatric diseases may affect the enteric nervous system and compromise oesophageal motor function. Benzodiazepines and anticholinergic antidepressants may precipitate gastro-oesophageal reflux by changing oesophageal motor function.¹¹ They could also cause a prolongation of oesophageal acid clearance by decreasing salivary secretion of bicarbonate. Lastly, psychiatric disorders might indirectly affect oesophageal physiology through increased consumption of alcohol and nicotine.^{12, 13} The aims of this study were to evaluate the frequency of gastro-oesophageal reflux symptoms among patients with various psychiatric disorders and to determine the potential risk factors for symptom occurrence in this patient population.

METHODS

Study population

The presence of reflux symptoms was compared between a case population of patients with well-

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documented psychiatric disorders, without previously diagnosed reflux disease, and a control population of patients without diagnosed psychiatric disorders or previously diagnosed reflux disease. The case population comprised the entire population of psychiatric patients who were domiciled in the psychiatric unit at Hines VA for a 30-day psychiatric treatment programme. The psychiatric diagnoses were classified according to the *Diagnostic and Statistical Manual of Mental Disorders* of the American Psychiatric Association.¹⁴ All patients were on active medical treatment at the time of the interview. The control population comprised subjects followed by the General Medicine Out-patient Clinic at the Hines Veterans Affairs Hospital during the same time period. Control patients were being seen for a variety of medical problems other than gastrointestinal disease. We excluded from the control population subjects who were enrolled in the psychiatric clinic, who had a psychiatric diagnosis or who were taking benzodiazepines, tricyclic antidepressants or phenothiazines at any time before or during the interview. In addition, subjects who were taking antacids or other antisecretory medications before or during the interview were excluded.

Case and control subjects alike underwent 45–60-min oral interviews conducted by a designated study coordinator (H.G.). The coordinator gathered information about demographic characteristics, social habits and a large variety of symptoms suggestive of reflux disease or other gastrointestinal conditions. Information regarding the medical history and the use of medications was not known to the study coordinator until after the interview was completed. All subjects were interviewed before the initiation of any specific therapy for GERD. The study protocol was approved by the Human Studies Committee of the Hines Veterans Affairs Hospital.

Definition of symptoms

It has been reported that patients frequently have difficulty understanding medical terms used by physicians and other medical personnel to describe reflux symptoms, such as heartburn.^{15, 16} During the interview, therefore, all symptoms were described in words as follows: (i) heartburn: a burning sensation behind the chest bone that radiates towards the throat or the mouth; (ii) regurgitation: an effortless return of stomach contents into the feeding tube and mouth as evidenced

by an acid taste; (iii) dysphagia: a difficulty experienced while swallowing food or drinking liquids. Case and control subjects were questioned about different food products and exercise manoeuvres that potentially aggravated gastro-oesophageal reflux symptoms, and about their ability to swallow meat, bread and vegetables. In addition, patients were asked whether, during eating, they had to make an effort to swallow, such as prolonged chewing, concentrating on swallowing or cutting food products into small pieces. Other upper gastrointestinal symptoms, such as nausea, dyspepsia, bloating, belching or indigestion, were not included in the present analysis.

Statistical analyses

The chi-squared test and Fisher's exact test were used to compare the occurrence of demographic characteristics, social habits and symptoms among the case and control subjects. The average values of continuous variables, such as age and lifetime consumption of alcohol or cigarettes, were compared using a two-tailed *t*-test. All variables (with the exception of age) were subsequently treated as categorical variables in the multivariate analysis. In a set of separate multiple logistic regressions, each individual symptom found to be significantly increased in the case population was chosen as an outcome variable. All other parameters, such as demographic characteristics, social habits and case-control status, served as predictor variables. Separate logistic regression models were also calculated using either the case-control status or the specific psychiatric diagnosis as predictor variables. The odds ratios and their corresponding 95% confidence intervals served to describe the strength of influence associated with each individual predictor variable.

RESULTS

The case population comprised 94 patients with documented psychiatric disorders according to the classification of the *Diagnostic and Statistical Manual of Mental Disorders*, and the control population comprised 198 patients without a diagnosed psychiatric disorder. Bipolar disorder, found in 18 patients (19%), was the most common diagnosis, followed by major depression ($n = 17$, 18%), paranoid schizophrenia ($n = 17$, 18%), depression ($n = 16$, 17%), schizophrenia ($n = 15$, 16%), alcohol dependence ($n = 8$, 9%), polysubstance

abuse ($n = 2$, 2%) and borderline personality ($n = 1$, 1%). All psychiatric patients were treated on a regular basis with three types of medication: phenothiazines, tricyclic antidepressants and benzodiazepines, taken by 46 (49%), nine (10%) and 39 (41%) of patients, respectively. Forty-six patients (49%) used their drug as a single treatment and 48 patients (51%) used a combination treatment.

The general characteristics of the case and control populations are displayed in Table 1. Patients with psychiatric disorders were significantly younger than the control subjects. The case and control populations did not differ with respect to gender, ethnicity and alcohol consumption. Cigarette smoking was significantly more common among psychiatric patients. Symptoms suggestive of gastro-oesophageal reflux were common in both populations. However, the prevalence of reflux was higher in psychiatric patients, the most frequently reported symptoms being heartburn, exercise-induced heartburn, coughing and dysphagia (Figure 1). In a set of univariate analyses, symptom frequency was evaluated separately for each psychiatric disorder. Of all the reflux symptoms, only heartburn and exercise-induced heartburn were significantly associated with individual psychiatric disorders (Figure 2). Compared with control subjects, heartburn was more common in patients with alcohol dependence (7/7 vs.

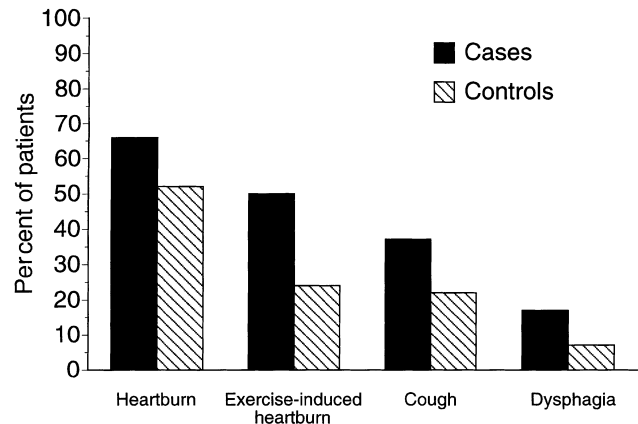


Figure 1. Comparison of symptom frequency between case and control subjects. All comparisons significant by chi-squared test.

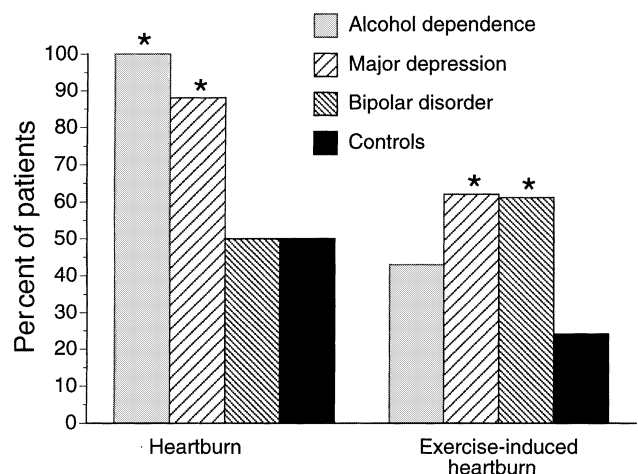


Figure 2. Frequency of heartburn and exercise-induced heartburn among controls and cases with specific psychiatric disorders. *Compared to controls, the symptom frequency is significantly increased by Fisher's exact test.

Table 1. Patient characteristics

Variable	Control subjects ($n = 198$)	Case subjects ($n = 94$)	<i>P</i> value
Demographics			
Male sex	97%	96%	0.437
Age in years (mean \pm s.d.)	56 \pm 13	46 \pm 15	< 0.001
White ethnicity	84%	89%	0.281
Habits			
Ethanol consumption	62%	48%	0.361
Smoking	39%	68%	< 0.001
Symptoms			
Heartburn	52%	66%	0.034
Heartburn at night-time	50%	45%	0.469
Exercise-induced heartburn	24%	50%	< 0.001
Food-induced heartburn	77%	70%	0.289
Retrosternal pain	25%	35%	0.108
Cough	22%	37%	0.010
Dysphagia	7%	17%	0.016

P value based on *t*-test for age and chi-squared test for all other variables.

100/198, $P = 0.01$) and major depression (14/16 vs. 100/198, $P = 0.004$). Compared with control subjects, exercise-induced heartburn was more common in patients with bipolar disorder (11/18 vs. 48/198, $P = 0.002$) and major depression (10/16 vs. 48/198, $P = 0.002$).

Table 2 shows the results of three separate multiple logistic regressions for the three reflux symptoms that were found to occur significantly more often in patients with a psychiatric diagnosis, i.e. heartburn, exercise-induced heartburn and dysphagia. (Coughing was the least frequent of the significant symptoms, and its increased prevalence among psychiatric patients could be attributed solely to the increased prevalence of

Variable	Odds ratio	95% CI	<i>t</i> value	<i>P</i> value
Heartburn				
Age	1.00	0.99–1.02	0.633	0.527
Smoking	0.93	0.55–1.58	0.253	0.801
Use of medications*	0.65	0.22–1.88	0.799	0.425
Case vs. control†	2.71	1.01–7.30	1.899	0.050
Alcohol dependence†	3.73	0.67–21.16	0.857	0.393
Major depression†	4.31	0.88–9.68	1.801	0.075
Exercise-induced heartburn				
Age	0.99	0.96–1.02	0.845	0.399
Smoking	0.68	0.31–1.51	0.943	0.347
Use of medications*	1.04	0.33–3.33	0.069	0.945
Case vs. control†	3.34	1.12–9.96	2.165	0.032
Bipolar disorder†	1.88	0.25–7.44	0.894	0.375
Major depression†	1.42	0.40–5.09	0.224	0.823
Dysphagia				
Age	1.00	0.97–1.03	0.168	0.867
Smoking	1.68	0.69–4.07	1.151	0.251
Use of medications*	1.92	0.39–9.46	0.799	0.425
Case vs. control†	1.27	0.26–6.13	0.299	0.765
Major depression†	0.34	0.04–2.61	1.085	0.281

*Medication = benzodiazepines, antidepressants or phenothiazines. Separate analyses for each type of medication or any combination of treatment did not change the overall result.

†Regression models tested with general case–control status or specific psychiatric diagnoses as predictor variables.

smoking in this population.) The presence of any psychiatric diagnosis, by itself, was associated with a three-fold increased risk for heartburn or exercise-induced heartburn. Age, consumption of cigarettes and type of psychiatric medication (alone or in combination) did not exert a significant influence on the occurrence of reflux symptoms. In a second set of logistic regressions, the general predictor variable of case–control status was replaced by more specific predictor variables associated with individual psychiatric diagnoses. In contrast with the results of the univariate analyses, no specific psychiatric diagnosis was found to exert a significant influence on the occurrence of reflux symptoms. Among the various psychiatric diagnoses, only major depression exerted a marginally increased influence on the occurrence of heartburn.

DISCUSSION

The aims of the present study were to evaluate the frequency of GERD symptoms in patients with well-documented psychiatric disorders and to characterize the risk factors for their occurrence. By comparing case subjects with a variety of psychiatric disorders with a

large control population without psychiatric disorders, we found that both heartburn and exercise-induced heartburn were significantly more common among patients with psychiatric disorders. The mere presence of a psychiatric condition was, by itself, the only factor exerting a significant influence on the occurrence of reflux symptoms. Neither the specific psychiatric diagnosis nor the usage of a particular type of medication was found to be associated with an increased risk for heartburn or other reflux symptoms.

Before initiating the present study, careful attention was paid to the arrangement of the interviews and the phrasing of the questions for data collection. Gastro-oesophageal reflux is diagnosed by its typical symptomatology, but patients often fail to understand medical phrases used to describe the presence of reflux symptoms unless those phrases are explained in layman's terms. In a study by Tendler *et al.*, only 70% of subjects who initially complained about heartburn after detailed questioning were considered to actually suffer from true heartburn.¹⁵ In the same study, 23% of subjects who initially denied the presence of heartburn were found on further questioning to have symptoms consistent with heartburn. Carlsson *et al.* also showed that detailed

Table 2. Results of multiple logistic regression (CI, confidence interval)

descriptions of heartburn are needed to identify all symptomatic reflux patients and correctly predict future response to antisecretory treatment.¹⁶ For the present study, therefore, efforts were made to explain the meaning of reflux symptoms, and all information was gathered through personal oral interviews, with multiple opportunities for the patients to obtain further clarification or additional explanation if needed. The present study was focused on the frequency of reflux symptoms among psychiatric patients. Although nausea, bloating, belching and indigestion are common in patients with gastro-oesophageal reflux,¹⁷ we intentionally did not consider these symptoms in the present analysis because of their poor specificity with respect to GERD.¹⁸ We believe that our control population matched, as closely as possible, our case population. Control subjects were recruited from the General Out-patient Medical Clinic, whereas case subjects were enrolled in a 4-week closely supervised program involving group therapy and medication adjustment.

There are three potential mechanisms by which psychiatric disease may exert an influence on the oesophagus: (i) the effect of different psychiatric medications; (ii) an intrinsic psychological effect; and (iii) an indirect effect of an injurious lifestyle. Dysfunctional oesophageal motility contributes to the development of gastro-oesophageal reflux.^{19–21} We initially thought that the increased frequency of reflux symptoms among psychiatric patients might be related to a drug-induced impairment of oesophageal motility, as psychiatric medications have potential adverse effects on oesophageal contractile activity. Although Reveille *et al.* have shown that intravenous benzodiazepines acutely reduce the lower oesophageal sphincter pressure,¹¹ the long-term influence of these medications when taken orally is unknown. We also reasoned that tricyclic antidepressants and phenothiazines, by blocking cholinergic receptors, could compromise oesophageal acid clearance. In the final analysis, however, our study failed to reveal any clear-cut association between reflux symptoms and the usage of a particular type of medication.

In certain psychiatric conditions, concurrent oesophageal dysfunction may promote acid reflux. A high rate of psychiatric diagnoses, such as anxiety and affective disorder, has been reported in patients with vigorous oesophageal contractions and non-cardiac chest pain.^{7, 22} Previous studies have provided indirect evidence for an association between psychiatric disease and the occurrence of reflux symptoms.^{23, 24} Typical

reflux symptoms were described by 42% of psychiatric patients with a somatization disorder compared to only 5% of healthy control subjects.²⁵ Nielzen *et al.* showed that psychopathology segregated best with the occurrence of reflux symptoms without objective evidence of reflux disease.²⁶ In our study, the high frequency of reflux symptoms in the control population was not surprising. A population-based study has already shown that weekly reflux symptoms occur in 20% of the surveyed population and intermittent reflux symptoms in as many as 59%.²⁷ Despite this high prevalence, the frequency of reflux symptoms in the psychiatric population was still significantly higher than that in the control population without psychiatric diagnosis. The specific type of psychiatric condition was not associated with a significant risk for the presence of reflux symptoms. This lack of a relationship may reflect a generally reduced threshold for or distorted perception of symptoms in this patient population.

Alcohol consumption and cigarette smoking may adversely affect the oesophageal mucosa.^{12, 13} Although cigarette smoking was more common in patients with psychiatric disorders than in patients without psychiatric disorders, the final analysis in our study showed that neither alcohol ingestion nor cigarette smoking had a significant influence on the occurrence of gastro-oesophageal reflux symptoms. When all three mechanisms by which psychiatric disorders may influence oesophageal reflux symptoms are considered. It is the psychiatric disease itself, as shown in our study, that adversely influences oesophageal symptoms—not the use of psychiatric medication or a self-abusive lifestyle.

In conclusion, physicians can expect to frequently find symptoms suggestive of gastro-oesophageal reflux in patients with psychiatric conditions. These symptoms occur more frequently in patients with than without psychiatric disorders. No specific psychiatric disorder or medication appears to constitute a particular risk for the occurrence of such symptoms. In some of these patients, the increased frequency of reflux symptoms could therefore reflect a distorted perception of symptoms and a low threshold for bodily sensation.

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