Increased prevalence of irritable bowel syndrome in patients with bronchial asthma

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Abstract Irritable bowel syndrome (IBS) is one of the most common diseases of the gastrointestinal tract. IBS may represent a primary disorder of gastrointestinal motility, accompanied with motor dysfunction in various extraintestinal sites. Recent studies suggest that IBS is associated with bronchial hyper-responsiveness and bronchial asthma might be more prevalent in IBS patients than in control subjects. The aim of our study was to assess the prevalence of IBS in a cohort of asthmatic patients. We evaluated 150 patients with bronchial asthma (71 males and 79 females, aged 45.1 ±14.9 years) and two control groups including 130 patients with other pulmonary disorder and 120 healthy subjects. All subjects enrolled (asthmatic and controls) completed the Greek version of the Bowel Disease Questionnaire (BDQ). BDQ is a, previously validated, self-report instrument to measure gastrointestinal symptoms. Diagnosis of IBS was based on Rome II criteria. The IBS prevalence was significantly higher in asthmatics (62/150, 41.3%) than in subjects with other pulmonary disorders (29/130, 22.3%, $P < 0.001$) and healthy ones (25/120, 20.8%, $P < 0.001$). For all subjects studied, the prevalence of IBS was significantly higher in females (78/214, 36.4%) than in males (38/186, 20.4%, $P < 0.001$). The IBS prevalence in asthmatic males was 29.5% *vs.* 15.2% in male patients with other pulmonary disorders ($P=0.002$) and 14.2% in male healthy subjects ($P=0.002$). The IBS prevalence in asthmatic females was 51.8% *vs.* 28.1% in females patients with other pulmonary disorders ($P < 0.001$) and 26.5% in females healthy subjects ($P < 0.001$). None of the asthma medications were associated with increased or decreased likelihood of IBS. We conclude that patients with bronchial asthma have an increased prevalence of IBS. Further studies are needed to clarify the potential pathogenetic mechanisms underlying the association between IBS and asthma.

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Keywords bronchial asthma; irritable bowel syndrome; autonomic nervous system.

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional disorder consisting of altered bowel habits, abdominal pain and the absence of any detectable organic pathologic process. It is recognized widely as one of the most common gastrointestinal disorders. Symptoms consistent with IBS are reported by 15–20% of the general population (1) and IBS accounts for 50% of all referrals to gastroenterologists (2). Because of absenteeism from work and hospitalization this syndrome imposes a substantial economic burden on society (3).

Despite the clinical and socioeconomic importance, the etiology and pathophysiology of IBS remain unclear. The current concept is that IBS represents a primary disorder of gastrointestinal motility (4). It is well known that any part of gastrointestinal system may be involved, as gastroesophageal reflux disease (5) and motor disorders of the esophagus (6) and small intestine (7) are common findings in patients with IBS. In IBS patients motor dysfunction has also been observed in extraintestinal sites including genitourinary and vascular system. It has been suggested that 33–50% of patients with IBS experience recurrent urinary symptoms due to motor abnormalities of the bladder (8). Moreover, sexual dysfunction, including dyspareunia and inhibited sexual desire, has been shown to be 5–15 times more common in IBS subjects, compared with patients suffering from organic bowel disease (9). Recently, IBS has also been associated with primary fibromyalgia (10). The existence of a generalized abnormality involving smooth muscle and/or autonomic nervous system has been suggested to explain all these associations. This abnormality might be responsible for both gastrointestinal and extragastrointestinal symptoms in patients with IBS.

Association of IBS with bronchopulmonary disease was initially suspected in 1991, when White *et al*. showed that IBS patients had an increased prevalence of bronchial hyper-responsiveness (11). Seven years later, a study in a randomly selected community sample showed that

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IBS symptoms might be associated with symptoms of bronchial hyper-responsiveness (12). More recently, it has been reported that bronchial asthma might be more prevalent in IBS patients than in control subjects (13). As far as we know, there are no studies focused on the prevalence of IBS symptoms in patients with bronchial asthma.

In order to investigate the relation between IBS and bronchial asthma, we assessed the prevalence of IBS symptoms in a cohort of asthmatic patients and control subjects.

METHODS

Patients selection

The present study was conducted at the 9th Department of Pulmonary Medicine, in "Sotiria" Chest Diseases Hospital (Athens, Greece). The local ethics committee approved the study and written informed consent was obtained from each participant. Following a predefined protocol, between September 1, 1998 and September 30, 2001, 198 consecutive patients with bronchial asthma, both newly referred and follow-up, were recruited from the outpatient clinics. In all cases, diagnosis of bronchial asthma was based on the American Thoracic Society criteria (14). Briefly, bronchial asthma was diagnosed as "the presence of symptoms of episodic wheezing, cough and shortness of breath responding to bronchodilators and reversible airflow obstruction documented in at least one previous pulmonary function study". Exclusion criteria were: (i) an acute asthma exacerbation the month prior to study, (ii) a known organic bowel disease and (iii) a previous abdominal surgery. A total of 48 patients were excluded from the study. Twenty-three of them had undergone a previous abdominal surgery (appendectomy: 18 cases, cholecystectomy: four and hysterectomy: one), and 20 had an acute asthma exacerbation the month prior to study. Moreover, five patients suffered from known organic bowel diseases (inflammatory bowel disease: two cases, diverticular disease of the colon: two and celiac sprue: one). Therefore, 150 patients were eligible for analysis.

Control subjects selection

Two control groups were surveyed. The first included 130 patients with other pulmonary disorders, attending the outpatient clinics during the period of the study (chronic obstructive pulmonary disease: 62 patients, respiratory infections: 45, pulmonary tuberculosis: 10, sarcoidosis: 13). The second group included 120 healthy subjects who attended courses designed for public health education, during the same period. Subjects with a known history of gastrointestinal tract pathology were not included in the control groups. Control subjects were matched with the asthmatics for sex and age (within 2 years).

Asthma medication use—lung function

In all asthmatic patients current asthma medication use was recorded. Patients were specifically asked about the use of theophylline preparations, β-agonists, ipratropium bromide, inhaled or oral corticosteroids, cromolyn and ketotifen. Moreover, in all cases spirometric values (FEV_1, FVC and FEV_1/FVC) were measured using a dry spirometer (Vica-test, Mijhardt, Holland). The best value of three maneuvers was expressed as a percentage of the predicted value.

IBS evaluation

IBS symptom was evaluated using the Bowel Disease Questionnaire (BDQ). The BDQ was developed as a self-report instrument to measure gastrointestinal symptoms experienced over the prior 1 year and to facilitate the diagnosis of functional gastrointestinal illness, including IBS. This questionnaire has been validated (15) and extensively applied in epidemiological studies in the United States and Europe (16–18). Previous testing has shown this instrument to be reliable, with a median k-statistic for symptom items of 0.78 (interquartile range 0.52–1.0), as well as having adequate content, predictive and construct validity in the outpatient setting. The BDQ was translated into Greek and an authorized translator trained in gastrointestinal terminology checked the translation. All subjects (patients and controls) completed the Greek version of the BDQ. To confirm the reliability of the Greek version of the BDQ, 50 subjects from the study population were also asked to complete this version on two separate occasions. The median time between completion of the surveys was 50 days (range 15–85). Of the symptom items, all were significantly reliable and most questions produced well to excellent agreement in the tested subjects. The median kappa statistic for the symptom items was 0.70 (interquartile range 0.47–1.00).

Diagnosis of IBS was based on Rome II criteria (19). The Rome II criteria required the existence of abdominal discomfort or pain for at least 12 weeks, which need not to be consecutive, in the preceding 12 months. The discomfort or pain should be characterized by at least two of the following three features: (i) relief with defecation, (ii) onset associated with a change in frequency of stool and (iii) onset associated with a change in form (appearance) of stool.

Statistical analysis

Results are expressed as mean $\pm$ one standard deviation ($\pm$SD). Significance of difference between groups was

assessed by unpaired Student's *t*-test for continuous variables and χ^2-test for proportions. Associations between binary variables were tested using Fisher' s Exact Test. The statistical analysis was performed using the SPSS program (SPSS Inc, IL, U.S.A.) and *P*-values were two-tailed analyzed. *P* values of less than 0.05 were considered statistically significant.

RESULTS

The demographic data of both asthmatic patients and controls are shown in Table 1. The mean age and gender ratios of the asthmatics did not differ significantly from those of the control groups. Table 1 shows also the spirometric values of patients with bronchial asthma.

The prevalence of IBS in asthmatic patients and controls is shown in Table 2. The IBS prevalence was significantly higher in asthmatics (41.3%) than in subjects with other pulmonary disorders (22.3%, $P < 0.001$) and healthy ones (20.8%, $P < 0.001$). Most of the asthma patients used β-agonists (142 patients, 94,6 %) and inhaled corticosteroids (122 patients, 81%). Only 48 (32%) and 46 patients (30.6%) used oral corticosteroids and theophylline preparations respectively. Neither corticosteroids (inhaled and oral), nor theophylline preparations were associated with increased or decreased likelihood of IBS. Moreover, no statistically significant difference, as regards the spirometric values, was detected between asthmatic patients with IBS (FEV_1/FVC: 64.9 ± 11.6) and those without IBS (FEV_1/FVC: 65.7 ± 12.2, $P > 0.05$).

For all subjects studied, irrespective of whether they were asthmatics or controls, the prevalence of IBS was significantly higher in females (78/214, 36.4%) than in males (38/186, 20.4%, $P < 0.001$) (Table 2). The IBS prevalence in asthmatic males was 29.5% *vs*. 15.2% in males patients with other pulmonary disorders (P=0.002) and 14.2% in males healthy subjects (P=0.002). The IBS prevalence in females with asthma was 51.8% *vs*. 28.1% in females patients with other pulmonary disorders ($P < 0.001$) and 26.5% in females healthy subjects ($P < 0.001$).

DISCUSSION

Data in the literature on the relationship between bronchial asthma and IBS are poor. A previous study, in a relatively small sample of IBS patients, has shown an increased prevalence of bronchial hyper-responsiveness (11). Bronchial hyper-responsiveness is defined as excessive airway constriction in response to an inhaled stimulus. It is a ubiquitous finding in asthmatic patients and has been incorporated into recent definition of bronchial asthma (19). Recently, Kennedy *et al*. carried out a questionnaire-based study in a randomly selected community sample of 4432 adults. They showed that: (i) symptomatic bronchial hyper-responsiveness, gastroesophageal reflux disease and IBS occur together more often than expected and (ii) these conditions are independently associated with each other (12). More recently, Yazar *et al*. studied 133 patients with IBS and showed that 15.8% of them had bronchial asthma according to history, clinical findings and values of pulmonary function test (13).

Our study is the first focused on the prevalence of IBS in a population of patients with bronchial asthma. According to our results, the IBS prevalence in asthmatic patients is significantly higher than that of the control subjects. The detected IBS in healthy controls (20.8%) is comparable with reported prevalence in previous studies concerning the general population (1). The preponderance of women, which characterizes both IBS asthmatics and IBS controls, is also a well documented, although unexplained yet, feature of all functional gastrointestinal disorders (20).

We considered consumption of asthma medication as a potential confounding factor in our study. Antiasthmatic agents could produce symptoms indistinguishable from those of IBS (theophylline preparations) (21), or even mask symptoms of an existed IBS (oral corticosteroids) (22). However, we showed that neither corticoster-

Table 1 Demographic data of asthmatics and controls and spirometric values of asthmatic patients

	Asthmatics	Other disorders	Healthy subjects
	(*n*=150)	(*n*=130)	(*n*=120)
Age, y	45.1 ±14.9	48.6 ±13.2	44.1 ±15.1
Male/female	71/79	59/71	56/64
FVC[a]	88.2 ±18.6		
FEV1[a]	71.3 ±21.4		
FEV1/FVC[a]	65.5 ±12.0		

[a]Expressed as percentages of the predicted values.

Table 2 Prevalence of IBS in asthmatic patients and control subjects

	Asthmatics	Other disorders	Healthy subjects
Sample size	150	130	120
Total IBS	62 (41.3%)	29 (22.3%)	25 (20.8%)
Total males	71	59	56
Male IBS	21 (29.5%)	9 (15.2%)	8 (14.2%)
Total females	79	71	64
Female IBS	41 (51.8%)	20 (28.1%)	17 (26.5%)

oids, nor theophylline were associated with increased or decreased likelihood of IBS. Unfortunately, due to the widespread use of β-agonists, we cannot exclude the possibility that these agents might represent such a confounding factor. β-agonists may influence small bowel motility and produce symptoms indistinguishable from those of IBS, as it is well known that motor abnormalities of small bowel represent a common finding in IBS patients (23).

The present study has not focused on the potential pathogenetic mechanisms underlying the association between IBS and bronchial asthma. This association might reflect either a kind of causal relationship between these diseases or susceptibility induced by common factors. As far as we know, there are no data in the literature supporting a causal relationship between asthma and IBS. On the other hand, we cannot rule out the possibility that an, unidentified yet, disorder affecting both gastrointestinal tract and respiratory system may be implicated in the susceptibility to both IBS and asthma. It is well known that these two, seemingly disparate, conditions share several common pathogenetic features. An altered contractility and smooth muscle tone have been observed in both diseases (24). Moreover, recent studies, concerning the altered vagal activity in IBS patients, showed that the expression of IBS might reflect an autonomic imbalance, perhaps stemming from disturbed hypothalamic function (25). Although the role of the autonomic nervous system in the pathogenesis of asthma has not been clarified yet, a generalized autonomic imbalance might also result to inappropriate bronchoconstriction as a response to an inhaled stimulus (26). Therefore, asthma and IBS may represent subsets of the same entity. This entity could be a primary neuromuscular disorder producing respiratory, gastrointestinal symptoms and, in a relatively large proportion of patients, both of them.

This hypothesis is further supported by the, observed in previous studies, high prevalence of gastroesophageal reflux disease in both asthma and IBS. Gastroesophageal reflux disease and IBS often coexist. It has been suggested that a primary autonomic dysfunction might be responsible for the coexistence of these two functional gastrointestinal disorders (5). Recent studies based on clinical symptoms, endoscopic esophagitis and 24-h ambulatory esophageal pH recordings showed gastroesophageal reflux disease to be more prevalent in asthmatic patients than in control subjects (27,28). A large proportion of asthmatic patients with gastroesophageal reflux disease has also evidence of autonomic dysfunction with primarily hypervagal responsiveness (29). However, the existence of a neuromuscular disease affecting both gastrointestinal tract and respiratory system remains only a hypothesis. We can not exclude the possibility that other factors may be responsible for the observed association between IBS and asthma.

In conclusion, the present study suggests that patients with bronchial asthma have an increased prevalence of IBS. Our results must be confirmed in a larger number of patients. Further studies should be undertaken to clarify the pathogenetic mechanisms underlying the possible association between IBS and asthma.

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