

ORIGINAL ARTICLE

Relationship Between Asthma and Irritable Bowel Syndrome: Role of Food Allergy

DUYGU OZOL,^{1,*} EBRU UZ,² RIFAT BOZALAN,² CANSEL TÜRKAY,³ AND ZEKI YILDIRIM¹

¹Fatih University Faculty of Medicine, Department of Pulmonology, Ankara, Turkey

²Fatih University Faculty of Medicine, Department of Internal Medicine, Ankara, Turkey

³Fatih University Faculty of Medicine, Department of Gastroenterology, Ankara, Turkey

The increasing prevalence of both asthma and irritable bowel syndrome (IBS) are major health problems. One hundred twenty-five patients with asthma and 95 healthy subjects were included in this study. The rate of IBS was 29.6% and 12.7% ($p < 0.005$), and the incidence of food allergy was 7.2% and 2.1% ($p > 0.05$) respectively for asthma and control group. There was no significant association between asthma related parameters, IBS, and food allergy. There is not a single clear reason as to what causes IBS, so further studies are needed to clarify the potential pathogenic mechanisms underlying the association between IBS and asthma.

Keywords asthma, irritable bowel syndrome, food allergy

INTRODUCTION

Irritable bowel syndrome (IBS) is characterized by a group of persistent symptoms in which abdominal pain or discomfort is associated with a change in bowel pattern, such as loose or more frequent bowel movements, diarrhea, and/or constipation in the absence of any detectable organic pathological process (1). IBS is a multi-factorial gastrointestinal disorder affecting 5.2 to 22% of the population with a higher prevalence in women, and it is the most common disease diagnosed by gastroenterologists (2).

Asthma is a chronic inflammatory disorder of the airways with recurring episodes of wheezing, breathlessness, and cough. This chronic inflammation causes bronchial hyper-responsiveness (3). In recent studies, excess prevalence of bronchial hyperresponsiveness has been shown among patients with IBS (4). Association between asthma and IBS is not clear. The existence of a generalized abnormality involving smooth muscle and autonomic nervous system has been suggested to explain this association. Motor dysfunction in emptying of gallbladder compared to healthy subjects (5) and recurrent urinary symptoms due to motor abnormalities of the bladder have been observed in IBS patients (6). IBS has also been associated with primary fibromyalgia and chronic fatigue syndrome (7). There are overlaps among these illnesses. Chronic fatigue syndrome patients also had a higher incidence of allergic rhinitis or asthma (8). A general health factor may be involved in the pathogenesis of some cases with these illnesses.

For IBS, it is also known that dietary modification improves symptoms and exclusion diets are beneficial to many IBS patients (9). Patients with IBS often report specific foods aggravate their symptoms. Locke (10) found that there was an

independent association between IBS and self-reported food sensitivities, and this association was stronger in patients with true food allergy.

The aim of this prospective study was to evaluate the presence of IBS in asthma patients, to compare this with healthy subjects, and to investigate the relationship between demographic findings, asthma severity, asthma duration, and IBS; and secondly; to explain the possible causal relationship between asthma and IBS, the role of food allergy was searched.

MATERIALS AND METHODS

Subjects

A total of 144 consecutive asthmatic patients who had been followed up in the outpatient clinics of the Pulmonology Department of Fatih University hospital, defined as having asthma according to GINA (Global Initiative for Asthma) (3) criteria for a three month period, were prospectively evaluated for the study. Exclusion criteria for the study were treatment with antihistamines or oral corticosteroids, presence of skin diseases that may affect the results of skin prick tests like chronic urticaria with dermographism, presence of organic diseases of the gastrointestinal tract, previous abdominal surgery, and pregnancy or lactation.

Excluded from the study were 13 patients who were using systemic steroids or antihistamines, 5 patients who underwent previous abdominal surgery, and 1 patient who was pregnant. A total of 125 asthmatic patients and 95 healthy subjects were enrolled in this study. Respiratory symptoms were examined and pulmonary function tests were performed in a standard fashion using an electronic spirometer (MIR) for every subject. Subjects with a known history of any respiratory disease, gastrointestinal tract pathology, and who had previous abdominal surgery were not included in the control group. All patients completed at least three forced vital capacity

*Corresponding author: Assist. Prof. Dr. Duygu Ozol, Uskup cad. 40A/20 Cankaya, Ankara, Turkey; E-mail: dozol@hotmail.com; ozolduygu@yahoo.com

maneuvers, and the best one was chosen. According to the results of spirometer and medical history, asthma patients were classified into four groups for their asthma severity according to GINA.

IBS Evaluation

Diagnosis of IBS was based on Rome 2 (1) criteria. Rome 2 criteria require 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 not be explained on the basis of structural or biochemical abnormalities and that has at least two of the following three features: (1) pain is relieved with defecation, (2) its onset is associated with a change in the frequency of bowel movements, and (3) its onset is associated with changes in the stool consistency. Subjects who fulfilled the Rome 2 criteria for IBS were seen by a gastroenterologist or specialized internists, and additional diagnostic tests such as stool sample testing, blood tests, sigmoidoscopy, or colonoscopy were performed to rule out organic diseases in necessary cases.

Allergy Tests

A medical history with the emphasis on food-related complaints was taken detailly. A battery of eight food antigens (fresh water fish, strawberry, peanut, cow's milk, onion, cocoa, whole egg, and wheat flour) (Stallergens S.A., Pasteur, France) were searched by skin prick tests (SPT). Skin prick tests were performed in each subject using above antigens on the volar side of the forearm, according to the guidelines of the subcommittee on skin tests of the European Academy of Allergology and Clinical Immunology (EAACI). Histamine hydrochloride (1 mg/mL) and normal saline solutions were used as positive and negative controls, respectively. The skin prick tests were read after 15 minutes and, a wheal of at least 3 mm greater than the negative control was considered positive. Serum total IgE levels (IU/mL) was measured by nephelometric method (Dade Behring Marburg GmbH). The diagnosis of food allergy was accepted only on the basis of a medical history (such as worsening in urticaria or asthma symptoms or developing bronchospasm and anaphylactoid reactions after eating certain foods) with a positive skin test.

Statistics

All results were expressed as means $\pm$ (SD) values. Significance of difference between groups was assessed by unpaired Student's *t* test or Mann Whitney U tests for continuous variables. The chi-square test or Fischer's Exact test was used for testing prevalence between groups. The statistical analysis was performed using SPSS-11 programme and *p* values <0.05 are considered significant.

RESULTS

There were 102 female and 23 male patients with a mean age of 52.4 ± 13.9 years in the asthma group, and there were 77 women and 18 men with a mean age of 52.2 ± 14.3 years in the control group. Forty-seven patients with asthma also have allergic rhinitis. The average duration of asthma was 7.8 ± 7.8 years. Based on the asthma classification, 17.6% of the patients belonged to intermittent group, 27.2% to the mild, 32% to the moderate, and 23.2% to the severe persistent group.

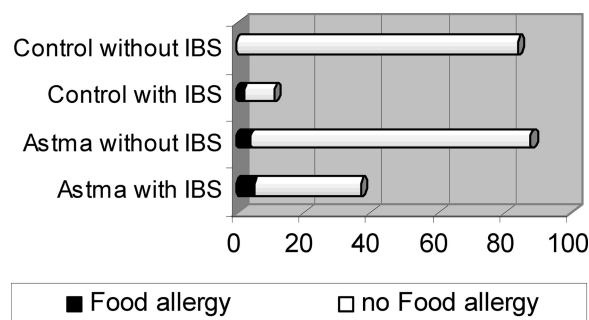


FIGURE 1.—Relationship between asthma, IBS, and food allergy.

The mean immunoglobulin E (IgE) level in the asthma and control group was 147.9 ± 229.7 IU/mL and 43.8 ± 32.6 IU/mL, respectively. Sixty-eight asthma patients and 8 control patients were determined as atopic. The incidence of food allergy was 7.2% (9/125) in the asthma group and 2.1% (2/95) in the control group. In the asthma groups, 4 patients were allergic to strawberry, and onion, 3 were allergic to fresh water fish and peanuts, 3 of them were allergic to whole egg and wheat flour, 1 was allergic to cocoa, and 1 was allergic to whole egg. In the control group, 2 subjects were allergic to strawberry and fresh water fish.

IBS was found in 37 (29.6%) patients in the asthma group and in 11 (12.7%) patients in the control group, and this was statistically significant. Five patients in the asthma group and 2 subjects in the control group had food allergy with IBS (Figure 1). According to asthma severity classification, although the rate of IBS was higher in moderate and severe asthmatics than mild asthmatics, this was not significant. There was no significant association between IBS and all other investigated parameters (Table 1).

DISCUSSION

In this study, the prevalence of IBS was found to be significantly higher in asthmatic patients than age-matched control subjects. The reason why asthma is associated with IBS is unknown and unfortunately we could not prove our hypothesis which was considering food allergy as a reason for this association.

Roussos et al. (11) found the prevalence of IBS significantly higher (41.3%) in asthmatics than in patients with other pulmonary disease (22.3%) and in healthy patients (20.8%). White et al. (12) showed that 27% of patients with IBS were in the asthmatic range and 18% were in the borderline range

TABLE 1.—Relationship between asthma-related parameters and IBS.

	With IBS	Without IBS
Gender (F/M)	29/8	73/15
Age (years)	50.9 ± 13.8	53.01 ± 14
Duration of asthma (years)	8.6 ± 8.6	7.4 ± 7.5
Total IgE level (IU/mL)	143.9 ± 167.7	93.2 ± 132.6
Food allergy (n)	5	4
Severity of Asthma (n)		
Mild intermittent	5	17
Mild persistent	6	28
Moderate persistent	13	27
Severe persistent	13	16

for asthma by methacholine challenge test. Similarly Yazar et al. (13) showed that symptoms of asthma and airway limitation are more common in asthmatics than control subjects. Kennedy et al. (4) reported an interdependent association with IBS, gastroesophageal reflux, and symptomatic bronchial hyperresponsiveness. Recently Amra et al. (14) showed that symptoms of IBS and asthma related symptoms occur more frequently together than expected and independent association exists between them in a large (4,762 subjects), population based sample. In our study, we found the same association between IBS and asthma.

Huerta et al. (15) found that the risk of developing IBS is reduced among oral corticosteroids users in asthma patients. We had 29 patients with severe persistent asthma who were using high doses of inhaled steroids, and we did not have any patients who were using oral corticosteroids continuously. We could not find any significant association between severity of asthma and IBS. Ekici et al. (16) reported the prevalence of IBS especially high in young asthmatics but not in elderly asthmatics. Although in earlier studies IBS seemed more common in younger age groups, other surveys have not confirmed this trend (2). In our study, 41 patients were older than 60 years old; most of our patients ranged between 40 to 65 years of age, so possibly because of this narrow range, we could not find a relationship between age and IBS.

A number of possible mechanisms were considered for IBS and extracolonic symptoms such as inflammatory etiology that affects both the lungs and gastrointestinal tract (17), diffuse disorders of smooth muscles (18), a more complex neuromuscular disorder with altered visceral sensitivity (19), and imbalance in neurotransmitters (20). One theory is that people who have IBS have a colon that is particularly sensitive and reactive to certain foods and stress. A person's colon may respond strongly to stimuli such as certain foods or stress that would not bother most people. Food sensitivities are frequently present in IBS but role of IgE-mediated food hypersensitivity still remains controversial. We could not find a relationship between food allergy, IBS, and asthma. Both Dainese (21) and Zar (22), found that there was no correlation between skin prick test results for foods and IBS. In contrast, Soares (23) found the rate of positivity to foods in skin tests significantly higher in IBS patients (19.4%) than control subjects (4%) and functional dyspepsia (2.3%). Other mechanisms including IgG antibodies against food may play a role in IBS symptoms. Zar (22) also reported significantly higher IgG4 titers to wheat, beef, and lamb in IBS patients, and then in controls. One of the limitations of our study is that, we could not look at IgG antibodies for foods, but according to our knowledge, this is the first study evaluating the relationship between food allergy, asthma, and IBS.

There is not a single clear reason as to what causes IBS, and further studies are needed to clarify the potential pathogenic mechanisms underlying the association between IBS and asthma.

REFERENCES

- Longstreth GF. Definition and classification of irritable bowel syndrome: current consensus and controversies. *Gastroenterol Clin North Am* 2005; 34(2):173–187.
- Cremonini F, Talley NJ. Irritable bowel syndrome: epidemiology, natural history, health care seeking and emerging risk factors. *Gastroenterol Clin North Am* 2005; 34:189–204.
- <http://www.ginasthma.org>
- Kennedy TM, Jones RH, Hungin AP, O'flanagan H, Kelly P. Irritable bowel syndrome, gastro-oesophageal reflux, and bronchial hyper-responsiveness in the general population. *Gut* 1998; 43:770–774.
- Guliter S, Yilmaz S, Yakaryilmaz F, Keles H. Evaluation of gallbladder motility in patients with irritable bowel syndrome. *Swiss Med Wkly* 2005; 135:407–411.
- Cukier JM, Cortina-Borja M, Brading AF. A case-control study to examine any association between idiopathic detrusor instability and gastrointestinal tract disorder, and between irritable bowel syndrome and urinary tract disorder. *Br J Urol* 1997; 79:865–878.
- Frissora CL, Koch KL. Symptom overlap and comorbidity of irritable bowel syndrome with other conditions. *Curr Gastroenterol Rep* 2005; 7:264–271.
- Endicott NA. Chronic fatigue syndrome in psychiatric patients: lifetime and premorbid personal history of physical health. *Psychosom Med* 1998; 60:744–751.
- Zar S, Mincher L, Benson MJ, Kumar D. Food-specific IgG4 antibody-guided exclusion diet improves symptoms and rectal compliance in irritable bowel syndrome. *Scand J Gastroenterol* 2005; 40:800–807.
- Locke GR III, Zinsmeister AR, Talley NJ, Fett SL, Melton LJ. Risk factors for irritable bowel syndrome: role of analgesics and food sensitivities. *Am J Gastroenterol* 2000; 95:157–165.
- Roussos A, Koursarakos P, Patsopoulos D, Gerogianni I, Philippou N. Increased prevalence of irritable bowel syndrome in patients with bronchial asthma. *Respir Med* 2003; 97:75–79.
- White AM, Stevens WH, Upton AR, O'Byrne PM, Collins SM. Airway responsiveness to inhaled methacholine in patients with irritable bowel syndrome. *Gastroenterology* 1991; 100:68–74.
- Yazar A, Atis S, Konca K, Pata C, Akbay E, Calikoglu M, Hafta A. Respiratory symptoms and pulmonary functional changes in patients with irritable bowel syndrome. *Am J Gastroenterol* 2001; 96:1511–1516.
- Amra B, Hoseini-Asl MK, Rahmani AR, Golshan M, Mohamad-Zadeh Z. Correlation between asthma and irritable bowel syndrome in a general population in Iran in 2003. *Respir Med* 2006; 100:110–114.
- Huerta C, Garcia Rodriguez LA, Wallander MA, Johansson S. Risk of irritable bowel syndrome among asthma patients. *Pharmacoepidemiol Drug Saf* 2002; 11:31–35.
- Ekici A, Guliter S, Ekici M, Kalpaklioglu F, Kara T, Keles H, Tunckol M, Akin A, Kocyigit P. Irritable bowel syndrome in young and elderly patients with stable asthma. *Dig Liver Dis* 2005; 37:773–778.
- Collins SM. Is the irritable gut an inflamed gut? *Scand J Gastroenterol Suppl* 1992; 192:102–105.
- Vassallo MJ, Camilleri M, Phillips SF, Steadman CJ, Talley NJ, Hanson RB, Haddad AC. Colonic tone and motility in patients with irritable bowel syndrome. *Mayo Clin Proc* 1992; 67:725–731.
- Smart HL, Atkinson M. Abnormal vagal function in irritable bowel syndrome. *Lancet* 1987; 29:2(8557):475–478.
- Collins SM, Vallance B, Barbara G, Borgaonkar M. Putative inflammatory and immunological mechanisms in functional bowel disorders. *Baillieres Best Pract Res Clin Gastroenterol* 1999; 13:429–436.
- Dainese R, Galliani EA, De Lazzari F, Di Leo V, Naccarato R. Discrepancies between reported food intolerance and sensitization test findings in irritable bowel syndrome patients. *Am J Gastroenterol* 1999; 94:1892–1897.
- Zar S, Benson MJ, Kumar D. Food-specific serum IgG4 and IgE titers to common food antigens in irritable bowel syndrome. *Am J Gastroenterol* 2005; 100:1550–1557.
- Soares RL, Figueiredo HN, Maneschy CP, Rocha VR, Santos JM. Correlation between symptoms of the irritable bowel syndrome and the response to the food extract skin prick test. *Braz J Med Biol Res* 2004; 37:659–662.