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Original Article

Evaluation of frequency of irritable bowel syndrome in patients with chronic urticaria

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Abstract

Aim: Irritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder. Urticaria is a disease with papules and plaques accompanied by pruritus and edema. In this study, the relationship between these two diseases, which have many common features, was evaluated.

Material and Methods: Patients with urticaria and volunteers who did not have any dermatologic disease were included in the study. Participants were assessed for diagnosis of IBS according to Rome III diagnostic criteria. In addition, findings supporting IBS diagnosis, and fecal shape and consistency were evaluated.

Results: Fifty urticaria patients (18 males - 36% and 32 females - 64%) and 70 volunteers (38 males - 54.3% and 32 females - 45.7%) were evaluated. The mean age of the urticaria group was 34.8 ± 15.0; the mean age of the control group was 25.8 ± 10.9. IBS was detected in 34 (68%) patients in the urticaria group; and in 22 (31.4%) controls (p <0.001). Diagnosis-supporting findings were more frequently detected in the group of urticaria (p values respectively: 0.037; < 0.001; 0.036; 0.050). It was observed that the higher the serum IgE level, the higher the incidence of IBS in chronic urticaria patients (p: 0.02; eta: 0.206).

Conclusion: IBS was observed more frequently in urticaria patients. Diagnosis-supporting findings for IBS were found more frequently in urticaria patients. Serum IgE values also seem to be associated with IBS. These results indicate an association between chronic urticaria and IBS. For this reason, the presence of IBS in patients with chronic urticaria diagnosis should be questioned.

Keywords: Urticaria; Irritable Bowel Syndrome; Omalizumab.

INTRODUCTION

Irritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder and is thought to affect about 15-20% of the world population. Although the etiology of IBS has not been fully elucidated, pathogenesis has been tried to be explained by various hypotheses such as intestinal dysmotility, visceral hypersensitivity, immunological and psychological mechanisms (1-3).

Urticaria is a disease characterized by papules and plaques accompanied by pruritus and edema. Clinical processes shorter than six weeks are termed acute urticaria, and longer than six weeks are termed chronic urticaria. Studies reveal that 15-25% of the human population has had urticaria at least once in their lives. There are several factors that are blamed on etiology of urticaria. However, no etiologic factor can be detected in about 50% of chronic spontaneous urticaria cases (4). Urticaria is primarily a disease mediated by mast cells, but the stimuli that cause mast cell activation vary. Mediators such as histamine and platelet activating factor released by stimulated mast cells and various cytokines lead to sensory nerve activation, vasodilatation and plasma extravasation and finally urticarial lesions (4,5).

Immunoglobulin E (IgE), an antibody that is responsible for hypersensitivity reactions, also called type 1 anaphylactic reaction. IgE binding to mast cells leads to mast cell degranulation and release of many cytokines. Mediators released after mast cell degranulation lead to urticarial lesions (4-6).

The skin, respiratory tract and gastrointestinal tract are the three systems in which the human body interacts with the external environment. Although the mast cells are present in many tissues, they are especially present in the skin, respiratory and gastrointestinal tract. The role of mast cells in skin and respiratory diseases is well known. However, its role in gastrointestinal tract diseases is not well researched (7). Studies have shown that mast cell count increases in different anatomical regions of the gastrointestinal tract of IBS patients. Serum IgE levels and IgE-positive stained duedonal cells were also increased in

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IBS patients compared to the control group. It has also been known for a long time that the prevalence of atopic conditions or atopic diseases in IBS patients has increased (8,9). Mast cells and IgE play a role in both urticaria and IBS, suggesting that there may be a link between IBS and urticaria.

There are quite limited publications in the literature evaluating the relationship between urticaria and IBS. In this study, patients with urticaria were evaluated for IBS frequency and its relationship with some disease parameters.

MATERIALS AND METHODS

Patients visited to our polyclinic, clinically diagnosed with chronic urticaria, and volunteers who did not have urticaria or any other dermatologic disease were included in this study. Those with a systemic disease in the urticaria and the control group were not included in the study. Also, patients with any gastrointestinal disease (except of IBS) were not included. IBS diagnosis was made according to the Rome-III diagnostic criteria (2). Findings that are not in the diagnostic criteria of Roma-II but which are accepted as diagnosis supporting findings have been removed in the Rome-III diagnostic criteria. Despite the fact that they were not in the Rome-III diagnostic criteria, in this study, this diagnosis supporting findings were asked to the patient and control group. Patients were also asked to indicate fecal shape and consistency according to the Bristol stool form scale (2). Participants with alarm findings were not included in the study. The patient was also asked for defecation frequency, disease duration of urticaria, disease duration of IBS and family history of urticaria or IBS. The patient was also asked "Did you also notice an increase in IBS findings during episodes of urticaria", or "Did you also notice an increase in your urticaria findings during IBS episodes". The patients were asked to answer these questions "yes" or "no". IgE levels of patients with urticaria were recorded with other routine laboratory tests.

Statistical Analysis

For the analysis of the data, the package program SPSS 24.0 (Statistical Package for the Social Sciences Inc.; Chicago, IL, USA) was used. Normal distribution fitness analyzes were performed with the Kolmogorov Smirnov test. Chi-square (x2) test was used to compare categorical data. For comparing continuous data, Student's t test was used for variables with normal distribution and Mann Whitney U test was used for non-normal distribution. The 'eta' coefficient was determined for the correlation between categorical data and continuous data. A p value <0.05 was considered significant in all analyzes.

RESULTS

Fifty patients (18 males - 36% and 32 females - 64%) with chronic urticaria and 70 controls (38 males - 54.3% and 32 females - 45.7%) without any other dermatological disease were included in this study. The mean age of the urticaria group was 34.8 ± 15.0; and of the control group was 25.8 ± 10.9 (Table 1).

Table 1. Demographic and clinical results

		Urticaria group	Controls	p values
Male		18 (%36)	38 (%54.3)	
Female		32 (%64)	32 (%45.7)	
Age (mean±SD)		34.8±15.0	25.8±10.9	
IBS (-)		16 (%32)	48 (%68.6)	x^2: 15.673
IBS (+)		34 (%68)	22 (%31.4)	p < 0.001
Abnormal stool frequency (-)		43 (%86)	58 (%82.9)	p : 0.642
Abnormal stool frequency (+)		7 (%14)	12 (%17.1)	
Abnormal stool form (-)		35 (%70)	60 (%85.7)	x^2: 4.367
Abnormal stool form (+)		15 (%30)	10 (%14.3)	p: 0.037
Passage of mucus (-)		46 (%92)	64 (%91.4)	p: 0.911
Passage of mucus (+)		4 (%8)	6 (%8.6)	
Abdominal distension (-)		18 (%36)	52 (%74.3)	x^2: 17.590
Aabdominal distension (+)		32 (%64)	18 (%25.7)	p < 0.001
Feeling of incomplete evacuation (-)		28 (%56)	52 (%74.3)	x^2: 4.389
Feeling of incomplete evacuation (+)		22 (%44)	18 (%25.7)	p: 0.036
Straining (-)		27 (%54)	50 (%71.4)	x^2: 3.853
Straining (+)		23 (%46)	20 (%28.6)	p: 0.050
Stool frequency (mean±SD)		7.34±4.5	7.80±3.5	p > 0.05
Family history of IBS(-)		43 (%86)	57 (%81.4)	p: 0.508
Family history of IBS (+)		7 (%14)	13 (%18.6)	
Bristol stool form scale	1	6 (%12)	1 (%1.4)	
	2	6 (%12)	3 (%4.3)	
	3	16 (%32)	20 (%28.6)	
	4	21 (%42)	35 (%50.0)	
	5	0	3 (%4.3)	
	6	0	4 (%5.7)	
	7	1 (%2)	4 (%5.7)	
	Mean±SD	3.14±1.16	3.91±1.17	p:0,001

SD: standart deviation
IBS: Irritable Bowel Disease

Thirty four patients (68%) in urticaria group and 22 patients (31.4%) in control group were diagnosed with IBS according to Roma III diagnostic criteria and this difference was statistically significant (p <0.001). Diagnosis supporting findings including abnormal stool form, abdominal distension, feeling of incomplete evacuation and straining were more frequent in the urticaria group (p values respectively: 0.037, <0.001, 0.036, 0.050), but abnormal stool frequency and passage of mucus were similar between two groups (p> 0.05). There was no difference between the two groups (urticaria group: 7.34 ± 4.5; control group: 7.80 ± 3.5 and p> 0.05) in mean stool frequency per week (Table 1). Distribution of stool patterns according to Bristol stool form scale of participants is shown in Table 1. In the urticaria group, while the mean

Bristol stool form scale was 3.14 ± 1.16, this value was 3.91 ± 1.17 in the control group (p: 0.001) (Table 1). This result indicates that patients with urticaria in this study tend to have harder stool shape and consistency.

In urticaria group, 18 (%36) of the patients had family history for urticaria. In terms of family history of IBS, there were no significant differences between urticaria and control groups (7 patients - 14% and 13 controls - 18.6%, respectively) (p: 0.508). Thirty (88.2%) of the 34 patients with IBS in urticaria group answered "no"; and 4 (11.8%) answered "yes" to questions of "Did you also notice an increase in IBS findings during episodes of urticaria", or "Did you also notice an increase in your urticaria findings during IBS episodes". In addition, there was no significant difference in the frequency of IBS between patients who used omalizumab treatment (relatively severe patients, resistant to conventional treatments) and who did not use omalizumab treatment for chronic urticaria (respectively: 44.1% and 55.9%, p: 0.697) (Table 2). When the relationship between serum IgE levels and IBS was evaluated, it was observed that as the serum IgE level increased, the frequency of IBS also increased in chronic urticaria patients (p: 0.02, eta: 0.206).

Table 2. IBS frequency in patients treated with omalizumab and non-omalizumab group

	OMA(-)	OMA(+)	p value
Number of patients	27 (%54)	23 (%46)	
IBS (+)	19 (%55.9)	15 (%44.1)	p: 0.697

SD: standart deviation
IBS: Irritable Bowel Disease
OMA: omalizumab

DISCUSSION

The results of this study revealed several important data: 1- IBS is more common in urticaria group than controls. 2- Findings that are not diagnostic criteria of IBS, but supporting the diagnosis of IBS including abnormal stool form, abdominal distension, and feeling of incomplete evacuation and straining are more common in urticaria patients. 3- When serum IgE levels increase, IBS frequency also increases. 4- Urticaria patients tend to have stiffer stool.

The word of "atopy" was first used by Coca and Cooke in 1923. There are evidences that atopic conditions or allergic diseases are more common in functional bowel diseases (9). In a study from United Kingdom with a very large population, it was reported that atopic symptoms were more frequent in all functional bowel diseases and up to 44.8% in IBS patients (10). Urticaria, an allergic disease, is a skin disease usually associated with atopic dermatitis or other atopic findings. As with other atopic or allergic diseases, IBS has many common features with urticaria (9-11). These common features suggest an association between the two diseases. For example, mast cells play an essential role in the pathophysiology of urticaria. Mediators such as histamine and platelet activating factor released by stimulated mast cells and various cytokines lead to sensory nerve activation, vasodilation, and plasma extravasation and finally urticarial lesions (6). Studies have shown that mast cells play an important role in IBS as well as in urticaria. It was shown in studies that mast cell count increases in different anatomical regions of the gastrointestinal tract of IBS patients. It is also known that some mediators released from mast cells affect enteric nerves and enteric smooth muscle function. In addition, mast cells lead to gastrointestinal mucosal changes and increase permeability. On the other hand, it has been shown that mast cells increase visceral hypersensitivity in IBS patients and mast cell stabilizers such as ketotifen reduce this sensitivity (9,11,12). Another finding suggesting that there may be a relationship between urticaria and IBS is that IgE has been shown to have crucial effects in both diseases. It was observed that an increase in serum IgE levels and an increase in IgE-positive duedonal cells in IBS patients (9,13). IgE binding to mast cells leads to mast cell degranulation and release of many cytokines. Mediators released after mast cell degranulation also have critical importance for the formation of urticarial lesions. For this reason, omalizumab, an IgE blocker developed in recent years, emerges as a highly effective agent in the treatment of urticaria (6). Interestingly, there are several reports showing that omalizumab also suppresses IBS symptoms. Pearson et al. administered omalizumab treatment to a 27-year-old female with IBS, allergic rhinitis and asthma and observed nearly complete recovery in allergic rhinitis and asthma as well as IBS symptoms (9). Magen et al. administered a 150 mg subcutaneous omalizumab treatment every 4 weeks to a 42-year-old female patient with both urticaria and IBS, and observed nearly complete improvement in urticaria and IBS symptoms (13). In the literature there is very limited data evaluating the relationship between chronic urticaria and IBS. A study from Israel with 11271 patients (currently in press), is the only study in the literature showing that IBS increases in chronic urticaria patients (1.7% in urticaria and 0.8% in the control group) (7). Tan et al. reported that urticaria was seen more frequently in children with IBS than non-IBS (4.3% vs. 2.8%) (11). The results obtained from our work also support these studies. In our study, IBS was found in 68% of urticaria patients and in 31.4% of the control group (Table 1). This result indicates that IBS is more frequent in chronic urticaria patients. Two cases mentioned above who obtained improvement in IBS symptoms with omalizumab treatment also had severe allergic rhinitis, asthma or urticaria (9,13). This suggests that the incidence of IBS may be increased when allergic disease is severe. In our study group, IBS frequency in patients treated with omalizumab because of resistance to conventional treatments (severe chronic urticaria) was similar to those who did not receive omalizumab (mild chronic urticaria) (55.9% vs 44.1%, p: 0.697). This result indicates that the frequency of IBS in chronic urticaria is not related to disease severity. In addition, our study has revealed one more important result. Findings supporting IBS diagnosis such as abnormal stool form, abdominal

distension, and feeling of incomplete evacuation and straining were more frequent in chronic urticaria patients (Table 1). Mean Bristol stool form scale in the urticaria group was 3.14 ± 1.16 and in the control group was 3.91 ± 1.17 (p: 0.001) (Table 1). This result indicates that patients with urticaria participating in this study are prone to stiffer stool form and consistency. Previous studies have shown that serum IgE levels in IBS patients are higher than normal levels (14). In our study, it was also detected that as the serum IgE levels increased, the incidence of IBS in patients with chronic urticaria was increased (p: 0.02, eta: 0.206). This result suggests that serum IgE levels play a role in the emergence of IBS. Interestingly, despite all these common features between the two diseases, in chronic urticaria group, only 4 (11.8%) of 34 patients with IBS stated that there was a link between the urticaria symptoms and IBS symptoms.

Our study is one of two studies in the literature evaluating the relationship between urticaria and IBS. It is also the only study showing how various characteristics of two diseases (serum IgE levels, severity of urticaria disease, number of defecation, findings supporting IBS diagnosis, etc.) affect these diseases. Our study was conducted with a limited number of patients but revealed important conlusions. For this reason it is clear that there is a need for further studies. Our study revealed a strong association between chronic urticaria and IBS. For this reason, the presence of IBS in patients with chronic urticaria should be questioned and perhaps the treatment should be shaped accordingly.

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