

ORIGINAL ARTICLE

## 젊은 염증성 장질환 환자들의 증상 재발과 관련된 원인에 대한 환자와 부모의 의견 불일치

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### Discordance between Patients and Parents Regarding the Perceived Causes of Clinical Relapse in Young Inflammatory Bowel Disease Patients

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**Background/Aims:** Relapse in inflammatory bowel disease (IBD) is not predictable, although several factors have been suggested. The aims of the current study were to assess and compare the possible causes of clinical relapse as perceived by patients and parents.

**Methods:** Of 107 young (<35 years old) IBD patients, 26 patients who experienced recent (<3 month) relapse and their parents completed a questionnaire at the same time. Baseline characteristics and clinical manifestations were reviewed and the most common causes of relapse as perceived by patients and parents were compared.

**Results:** Median patient age was 22.5 years and the male to female ratio was 17 : 9. Crohn's disease was diagnosed in 23 patients and ulcerative colitis in the other three patients. Mean disease duration was 39.8±30.3 months. Eighteen (69.2%) patients experienced stress before relapse. Fifteen (57.7%) parents thought that their children experienced stress before relapse. Agreement between patients and parents for non-adherence to medication and stress was 100% and 73.1%, respectively. Stress was considered the most likely cause of relapse in both groups. Discordance rate between parents and patients with respect to main causes of relapse was 40.4%.

**Conclusions:** Stress was perceived to be the most common condition noted before clinical relapse in young IBD patients and their parents. However, the discordance rate between patients and parents with respect to the main causes of relapse was 40.4%. This result suggests a considerable difference in terms of disease understanding between young IBD patients and parents. (Korean J Gastroenterol 2015;65:99-104)

**Key Words:** Inflammatory bowel diseases; Recurrence; Cause; Parents

## INTRODUCTION

Inflammatory bowel disease (IBD) is an idiopathic, chronic, and relapsing immune-mediated disease that causes inflammation of the gastrointestinal tract characterized by episodes of remission and relapse. Crohn's disease (CD) and ul-

cerative colitis (UC) are the two major components of IBD, and, according to previous reports, cumulative relapse rate of IBD within 10 years of diagnosis has been reported as 90% in CD and 83% in UC.<sup>1,2</sup> Although relapse after entering remission is unpredictable, several factors have been suggested to be associated with relapse. The previously reported

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factors associated with relapse in CD are age at initial diagnosis of < 40 years, the presence of perianal or rectal disease and initial steroid requirement for treatment. In UC, the previously reported factors are disease presentation after the age of 50 years, disease flare within 2 years of diagnosis, fever or weight loss at diagnosis, and active disease during the preceding year.<sup>3,4</sup>

In addition to the factors mentioned above, relapse of IBD has been reported to be associated with environmental factors, including psychosocial stress, non-adherence to medication, smoking, dietary factors, use of antibiotics or NSAIDs, and high physical activity.<sup>5,6</sup> No previous study to compare the perceptions of IBD patients and parents with respect to environmental factors perceived to be related to clinical relapse has been reported. However, an appreciation of these perceived factors by patients and parents might prolong the duration of remission.

Accordingly, the aims of the current study were to assess and compare perceived factors related to clinical relapse in IBD patients and their parents.

## SUBJECTS AND METHODS

IBD patients in remission state and under the age of 35 years who experienced clinical relapse between July 2012 and March 2013 were enrolled. Patients and parents who agreed to participate in this study and complete a questionnaire were included. If parents did not visit the outpatient clinic with their IBD patients, patients were instructed to give the parent's questionnaire to their parents and ask them to complete the questionnaire. For CD, clinical remission was defined as a Crohn's disease activity index (CDAI) of < 150,<sup>7</sup> and for UC, it was defined as a Mayo stool frequency subscore of 0 or 1 (0 point for normal number of stool passes and 1 point for 1-2 stools more than normal) without rectal bleeding (Mayo rectal bleeding subscore of 0).<sup>8</sup> When a CD patient had a CDAI score of > 150 or a UC experienced stool frequency with three stools more than normal or rectal bleeding, clinical relapse was suspected. Recent clinical relapse in IBD patients was defined as clinical relapse within 3 months of completing the questionnaire.

Patients and parents who agreed to participate were asked to complete a questionnaire. Questionnaires addressed symptoms at relapse, including abdominal pain, diarrhea, fever,

and rectal bleeding, factors perceived to be related to clinical relapse of IBD, and factors perceived to be related to relapse. On the questionnaire, factors mentioned as being associated with recent clinical relapse of disease were psychosocial stress, non-adherence to medication, specific food intake, high physical activity, smoking status, history of alcohol intake and use of medications, such as antibiotics and NSAIDs. Among these factors, patients and parents were asked to indicate one or two main factors perceived to be related to relapse and if they perceived main factors related to relapse besides those written on the questionnaire, such as recent illness including upper respiratory tract infection, febrile sensation, or chilling, they were asked to check "others". Definitions of each factor were provided on the questionnaire. Smoking status was defined as follows: non-smokers as patients who never smoked; ex-smokers as patients who stopped smoking for more than one year before study enrollment; current smokers as patients who are currently smoking or stopped smoking within one year of study enrollment.<sup>9</sup> Recent alcohol intake was defined as any alcohol intake within one month of clinical relapse. High physical activity was defined as having vigorous activities for at least three days during the week before clinical relapse and vigorous activity was defined as activities requiring hard physical efforts making breathing much more difficult than usual. Baseline patient characteristics, including age, sex, height, weight, extent of disease involvement, and dates of diagnosis and relapse were reviewed.

Regarding main factor perceived to be related to clinical relapse, agreement between IBD patients and their parents was defined if each IBD patient and their parent had proposed the same main factor among seven factors included in the questionnaire. Agreement rate was calculated by dividing the number of patients who were in agreement with their parents on the main factor perceived to be related to clinical relapse by total number of patients.

Statistical analysis was performed using PASW Statistics software version 18.0 (IBM Co., Armonk, NY, USA), and p-values of < 0.05 were considered statistically significant.

This study has been approved by institutional review board of Yeungnam University Hospital (PCR-11-187).

## RESULTS

During the study period, 107 IBD patients aged below 35

and in remission were treated at our hospital. Of these patients, 26 patients who had experienced recent clinical relapse were enrolled in the current study. Median age of these 26 patients was 22.5 (range, 15-34) years and the male to female ratio was 17 : 9. Of the 75 CD patients treated, 23 patients experienced clinical relapse and of the 32 UC patients, three patients experienced clinical relapse. Mean disease duration from diagnosis to recent relapse was  $39.8 \pm 30.3$  months. Of the 23 CD patients, 16 (69.6%) had disease of the ileum and colon and 7 (30.4%) had isolated colonic disease. All three of the UC patients had extensive colitis. Sixteen (69.6%) of the 23 CD patients exhibited inflammatory type disease behavior. Of the remaining patients, 6 (26.1%) were of the stricture type and 1 (4.3%) was of the penetrating type. Perianal disease was noted in 12 (52.2%) of the 23 CD patients. All of the 26 study subjects were taking 5-aminosalicylic acid, 16 (61.5%) were taking azathioprine or 6-mercaptopurine and 6 (23.1%) were taking biologic agents (Table 1).

One CD patient was a current smoker and the other 25 were either non-smokers or ex-smokers. Three patients (11.5%) reported alcohol consumption before relapse.

Regarding factors perceived by patients to be associated with clinical relapse, 18 (69.2%) mentioned stress; 15 (57.7%),

non-adherence to medication; 10 (38.5%), a food problem; 4 (15.4%), high physical activity; and 4 (15.4%), antibiotic or NSAID medication.

Parents thought clinical relapse was associated with stress in 15 (57.7%), non-adherence to medication in 15 (57.7%), a food problem in 8 (30.8%), medication with antibiotics or NSAIDs in 8 (30.8%), and high physical activity in 2 (7.7%) (Table 2).

Thirteen (50.0%) of the 26 patients answered that stress was the main factor perceived to be associated with clinical relapse: 7 (26.9%), high physical activity; 6 (23.1%), a food problem; 5 (19.2%), non-adherence to medication; and 2 (7.7%), medication with antibiotics or NSAIDs. Of the 26 parents of IBD patients, stress was the main factor perceived to be associated with clinical relapse in 11 (42.3%) parents, high physical activity in 7 (26.9%), non-adherence to medication in 5 (19.2%), a food problem in 5 (19.2%), and medication with antibiotics or NSAIDs in 1 (3.8%).

The agreement rate between patients and parents was highest for non-adherence to medication (100%), followed by use of antibiotics or NSAIDs (88.5%) (Table 3). Stress was considered the most common cause of clinical relapse by patients and parents (Table 3). Of the 26 patients and parents, 10 (40.4%) showed discordance regarding perceived main

**Table 1.** Clinical Characteristics of IBD Patients

Characteristic	Value
Patient (n)	26
Age (yr)	22.5 (15-34)
Male	17 (65.4)
Current smoker	1 (3.8)
Recent alcohol intake	3 (11.5)
Crohn's disease	23 (88.5)
Ulcerative colitis	3 (11.5)
Mean disease duration (mo)	39.8 $\pm$ 30.3
Location of disease in CD	
Ileum and colon	16 (69.6)
Colon	7 (30.4)
Location of disease in UC	
Extensive disease	3 (100)
Disease behavior in CD	
Luminal type	16 (69.6)
Stricture type	6 (26.1)
Penetrating type	1 (4.3)
Treatment	
5-ASA	26 (100)
Azathioprine/6-MP	16 (61.5)
Biologic agents	6 (23.1)

Values are presented as n only, median (range), n (%), or mean $\pm$ SD. IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; ASA, aminosalicylic acid; MP, mercaptopurine.

**Table 2.** Perceived Possible Factors of Clinical Relapse by IBD Patients and Parents

Factor	Patient	Parent
Psychosocial stress	18 (69.2)	15 (57.7)
Non-adherence to medication	15 (57.7)	15 (57.7)
Dietary problem	10 (38.5)	8 (30.8)
High physical activity	4 (15.4)	2 (7.7)
Use of antibiotics/NSAIDs	4 (15.4)	8 (30.8)

Values are presented as n (%).

IBD, inflammatory bowel disease.

**Table 3.** Concordance of Main Perceived Causes of Clinical Relapse between IBD Patients and Parents

Cause	Patient	Parent	Concordance rate
Non-adherence to medication	5 (19.2)	5 (19.2)	100
Psychosocial stress	13 (50.0)	11 (42.3)	73.1
Dietary problem	6 (23.1)	5 (19.2)	73.1
High physical activity	7 (26.9)	7 (26.9)	76.9
Use of antibiotics/NSAIDs	2 (7.7)	1 (3.8)	88.5

Values are presented as n (%) or percent only.

IBD, inflammatory bowel disease.

**Table 4.** Perceived Main Factors Associated with Clinical Relapse and Their Concordances

Number	Patient	Parent	Concordance
1	PA NA	PA OM	Yes
2	S	D	No
3	AI	NA OM	No
4	NA OM	O	No
5	PA	PA D	Yes
6	S PA	S	Yes
7	D	S PA	No
8	S	S PA	Yes
9	S	Sm AI	No
10	S PA	NA	No
11	NA S	NA	Yes
12	S PA	S	Yes
13	D	PA	No
14	S PA	PA	Yes
15	D	D PA	Yes
16	NA PA	NA	Yes
17	S PA	S	Yes
18	D S	S	Yes
19	D	S	No
20	S	S PA	Yes
21	NA OM	OM	Yes
22	S	NA S	Yes
23	O	S	No
24	O	O	Yes
25	O	D	No
26	D S	S PA	Yes

PA, high physical activity; NA, non-adherence to medication; S, stress; D, dietary problem; AI, alcohol intake; OM, use of antibiotics or NSAIDs; Sm, smoking; O, others (including recent illness such as upper respiratory infection and febrile sensation and chilling).

factors related to IBD clinical relapse. Of the 13 IBD patients who perceived stress as the main causative factor, five were discordant with parents, and these parents perceived non-adherence to medication, dietary problem, smoking, alcohol intake, or high physical activity as the main factor (Table 4).

According to responses to a question on causes of psychosocial stress, the two most common perceived causes by patients and parents were examinations and occupational problems. Of the 26 patients, six considered examinations and five occupational problems as causes of relapse, and among parents, six considered examinations and six occupational problems as causes.

## DISCUSSION

As suggested by an epidemiologic study conducted in Iceland,<sup>10</sup> environmental factors play an important role in on-

set and relapse of IBD. In addition, acknowledgement and management of causative factors related to IBD relapse is important in prevention of relapse. Typically in Korea, young unmarried adults reside with their parents even after entering a local university. In addition, patients often visit out-patient clinics with their parents. Furthermore, as is observed in child and adolescent IBD patients, the parents of young unmarried adults may have some influence in disease management.

In the current study, IBD patients and parents perceived stress as the main cause of clinical relapse with a patient/parent concordance rate of 73.1%, which was the lowest concordance rate found among the five most frequently answered factors mentioned in the questionnaire. Stress is defined as a process whereby environmental demands exceed adaptation capacity and may result in psychological and biological changes in individuals at risk of disease. Because stress is a subjective parameter, discrepancy between patients' and parents' perceptions of the amount of stress might be expected. Abernethy<sup>11</sup> reported that 74% of IBD patients, a higher percentage than those observed in other disease groups, thought that psychosocial factors affect the course of IBD. However, previous studies on the relationship between psychosocial stress and IBD relapse have reported inconsistent results, although a positive relationship between psychosocial stress and IBD relapse has also been reported.<sup>12,13</sup> In an animal study, Mawdsley and Rampton<sup>14</sup> suggested that stress might affect inflammation in IBD via mechanisms involving hypothalamic-pituitary-adrenal function, alterations in bacterial-mucosal floral interactions, activation of mucosal mast cells, and the peripheral release of corticotrophin releasing factors.

Only five IBD patients and five parents thought that non-adherence to medication was related to clinical relapse; however, the concordance rate for non-adherence to medication was the highest observed at 100%. Adherence to medication is important in management of IBD, and non-adherence can lead to suboptimal symptom management, more severe disease, and increase the risk of relapse.<sup>15,16</sup> This higher concordance rate of adherence to medication was probably due to the objective nature of this parameter. Furthermore, the checking of adherence to medication by parents probably increased adherence. Previous studies reported that 20-72% of IBD patients are non-adherent to medication according to duration of treatment<sup>17,18</sup> and in our

study, only a small portion of patients and parents perceived non-adherence to medication as being related to clinical relapse.

Two patients (7.7%) and one parent (3.8%) perceived that the use of medications, such as antibiotics or NSAIDs, was related to IBD relapse. Changes in microbiota compositions complicated by antibiotic use have been suggested to contribute to development of IBD (particularly CD).<sup>19-21</sup> Disruption of the intestinal barrier by NSAIDs may also increase the risk of IBD.<sup>22</sup> Use of medication is also an objective factor and showed a high concordance rate between patients and parents. Diets containing high levels of sugar or sugar containing foods, high levels of animal protein, and low levels of vegetables have been reported to show association with increased risk of IBD.<sup>23</sup> However, in the current study dietary factors were perceived as factors related to IBD relapse by only six patients (23.1%) and five parents (19.2%) with a low concordance rate (73.1%). Food intake outside home makes it difficult for parents to assess the possible effects of food intake unless they choose to question children on the subject, and this probably contributed to the low concordance rate observed.

Limitations of this study were the small number of IBD patients enrolled from a tertiary medical center and it is difficult to generalize these results to IBD patients. Factors perceived to be related to clinical relapse in IBD used in our study were epidemiologic factors and meaning of such factors may have been perceived differently between patients and parents, making quantification and application of these factors difficult in practice. However, the primary purpose of the current study was to assess the factors that were thought to be related to clinical relapse by IBD patients and their parents and to evaluate the degree of difference in these perceptions between patients and parents. Parents could pay more attention and may have influence in management of the environmental factors which their son or daughter thought were the main cause. Although, unlike in pediatric and adolescent IBD patients, the role of parents in managing IBD may be limited, considering co-residence of unmarried young IBD patients with their parents, parents may have some role in management of their young IBD son or daughter. In the current study, stress was the most common perceived causative factor related to clinical relapse by both young IBD patients and their parents, but the concordance rate of psychosocial stress be-

tween IBD patients and parents was lowest. The total discordance rate between IBD patients and their parents in main factor perceived to be related to clinical relapse in IBD was 40.4%. Our results suggest that a considerable discrepancy exists between young IBD patients and parents. Considering that these environmental factors could be modified in some part, parents' understanding of environmental factors of their children's IBD could be helpful in reducing the risk of clinical relapse in young IBD patients.

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