Characteristics and treatment outcomes of transition in patients with inflammatory bowel disease

Eun Jin Yoo

Department of Medicine

The Graduate School, Yonsei University

Characteristics and treatment outcomes of transition in patients with inflammatory bowel disease

Directed by Professor Jae Hee Cheon

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Eun Jin Yoo

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This certifies that the Master's Thesis of
Eun Jin Yoo is approved.

Thesis Supervisor : Jae Hee Cheon

Thesis Committee Member#1 : Jihye Park

Thesis Committee Member#2 : Hyun Ki Kim

The Graduate School
Yonsei University

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ABSTRACT

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The Graduate School, Yonsei University

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Backgrounds/Aims: This study aimed to assess disease characteristics and outcomes of transition in patients with inflammatory bowel disease (IBD).

Methods: Data from patients younger than 18 years who were diagnosed with IBD (Crohn's disease [CD], ulcerative colitis [UC], or intestinal Behçet's disease [BD]) were investigated. We categorized the patients into two groups, transition IBD group (Group A, diagnosed in pediatric care followed by transfer to/attendance in the adult IBD care) and non-transition group (Group B, diagnosed and followed up in pediatric care or adult IBD care without transfer).

Results: Data from a total of 242 patients (Group A [N=29, 12.0%], Group B [N=213, 88.0%]) were analyzed. A significantly higher number patients was diagnosed at an earlier age in Group A than in Group B ($P < 0.01$). Group A patients had more severe disease in terms of number of disease flare ups ($P < 0.01$), frequency of bowel-related complications ($P < 0.01$), number of IBD-related admission ($P = 0.03$), and number of emergency admissions ($P = 0.01$). Multiple regression analysis showed that group A patients had less medical non-compliance than group B patients ($\beta = 0.01$, $P = 0.04$). After transition, IBD-related admission frequency, emergency admission frequency, disease flare frequency, and medical non-compliance were significantly

improved.

Conclusions: The transition IBD group had more severe disease. Medical non-compliance were lower in the transition IBD group. Clinical outcomes were improved after transition.

Key words : transition, inflammatory bowel disease, adherence, compliance, outcome

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I. INTRODUCTION

Inflammatory bowel diseases (IBD) including ulcerative colitis (UC), Crohn's disease (CD), and intestinal Behçet's disease (BD) are chronic relapsing and remitting immune-mediated inflammatory disorders of the gastrointestinal tract. Approximately 25% of the cases are diagnosed in childhood or adolescence. Moreover, evidence has shown that the incidence of IBD diagnosed in pediatric years is increasing[1, 2]. In addition, more extensive and severe presentations were seen in young people[3]. Young patients usually experience more surgeries or hospitalizations and receive intensive treatments such as immune-modulatory or biological therapies more often than adult patients. Therefore, multiple problems with growth and psychosocial and sexual development are frequent[4]. Schooling and employment are negatively affected.

Usually, IBD patient transfer from a pediatric to an adult care unit is initiated at the age of 16-18 in Western countries[5]. Transfer from a pediatric to an adult IBD care unit usually occurs while the patient is in disease remission. Successful transition involves gradual changes in disease-specific knowledge, attitude toward treatment, clinic attendance behavior, and medical compliance. Thus, careful systemic and constructed transitional care is related with better

disease-specific treatment outcomes[6]. The optimal goal of the transition process is to provide sustainable, comprehensive, and medically appropriate health care to IBD patients.

There is lack of standard guidelines and insufficient data related to the transition process. In particular, there is a lack of studies addressing disease characteristics and treatment outcomes in unselected cohorts of IBD transition groups. Adolescent IBD patients are affected by genetic and environmental differences, and differences in parental influences on the treatment process. These differences are associated with differences in disease characteristics, treatment processes and outcomes. Furthermore, determination of IBD-related transition group outcomes is of extreme importance because this group comprises a growing segment of the IBD population. These transition group patients might need different approaches to therapy from those with solely pediatric or solely adult care. However, few data regarding IBD-related outcomes after transition are available.

This study aimed to assess disease characteristics, treatment processes, and outcomes in an IBD transition group. Specifically, we sought to determine which patients undergo transition care to investigate the major clinical outcomes after transition.

II. MATERIALS AND METHODS

1. Study population

This study was a retrospective review of medical records of patients under 18 years of age who were diagnosed as having IBD in Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, between November 2005 and December 2015. A total of 385 patients was included. Twelve patients were lost to follow up or were being followed up in other institutions (four patients) before the age of 18. These patients were excluded from the study. Patients

without a definite diagnosis of IBD and those who had not been prescribed IBD medications were excluded. Also, patients taking enteral nutrition exclusively were excluded.

We categorized patients into three groups, transition IBD group (diagnosed in pediatric care followed by transfer to/attendance in adult IBD care), pediatric IBD care group (diagnosed and followed in pediatric care without transfer to adult IBD care), and adult IBD care group (diagnosed and followed in adult IBD care). Pediatric IBD care and adult IBD care groups were grouped together into a non-transition group (Group B) and compared as the control group of the transition group (Group A).

2. Disease characteristics and treatment outcome variables

We collected written and electronic patient demographic data including age at registration in a pediatric or adult clinic, transition care, previous smoking history, IBD family history, biological and non-biological treatments, intestinal complications (fistula, abscess, stenosis, or colorectal dysplasia or cancer), Montreal classification at presentation, and number of surgeries or hospital admissions. Reasons for admission were categorized as: (1) acute flare such as medical or surgical emergency situations and (2) elective admission for surgery (e.g., seton insertion) and elective procedures and investigations (i.e., disease-reassessment, infusion, or planned colonoscopy). Extra-intestinal manifestations of IBD and drug side effects or complications were assessed. Data on laboratory findings included the level of hemoglobin (Hb), platelet count (PLT), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) level.

For evaluating disease activity, survey modifications of the Crohn's Disease Activity Index and the Colitis Activity Index (S-CDAI, S-CAI) were calculated. Remission was defined as S-CDAI $\leq$ 150 for CD and S-CAI $\leq$ 4 for UC[7]. For pediatric patients, Pediatric Crohn's Disease Activity Index

(PCDAI) or Pediatric Ulcerative Colitis Activity Index (PUCAI) was calculated[8]. Disease Activity Index for Intestinal Behçet's Disease (DAIBD) score was calculated for intestinal BD patients[9].

Finally, we reviewed the recorded electronic medical charts to assess the frequency of not taking prescribed drugs and non-attendance at clinics.

3. Transition process and period

At our institution, during the transition period, medical/surgical histories and past/current disease status of all patients are reviewed by pediatric and adult IBD specialists and nurses. A "transition passport" is provided from the pediatric IBD clinic to fully prepare for transition. Furthermore, both pediatric and adult IBD specialists discuss each patient's case in detail during multidisciplinary meetings prior to transition to establish a comprehensive therapeutic plan. Patients are educated on the disease characteristics and potential complications, importance of IBD medications, side effects of IBD medications, and the need for regular follow up for disease monitoring. Last, pediatricians accompany patients to the adult IBD clinic.

The start of transition was defined as the first registration to the transition clinic. Age at completing transition was defined as the age at which the patient left pediatric care and started visiting adult clinics.

4. Medical non-compliance

Medical non-compliance was defined as adding the number of non-attendance at clinics to the frequency of not taking prescribed drugs in this study.

5. Primary and secondary end points

The primary end point of this study was disease characteristics and outcomes of the transition group that were different from those of the non-transition

group. In addition, major clinical outcome differences before and after transition were assessed. The secondary end point was differences in medical non-compliance between transition and non-transition patients.

6. Data analysis

All data were analyzed using SPSS statistical package 25.0 (SPSS Inc. Chicago, IL, USA). Continuous variables are presented as mean and standard deviation (SD) or median and interquartile range (IQR) or range. Categorical variables are presented as frequency (%). Comparisons between the two groups were conducted using two-sample t-test and Chi-square test for continuous and categorical variables, respectively. The Mann–Whitney U test was used for comparisons of non-parametric continuous variables. Moreover, multiple regression analyses were used to determine the factors associated with medical non-compliance in the study group. Last, the Wilcoxon signed-rank test was used to compare major clinical outcomes before and after transition. All P values resulted from two-sided statistical tests, and values of $P < 0.05$ were considered statistically significant.

7. Ethical considerations

The study received full institutional ethics approval by our institutional review board.

III. RESULTS

1. Baseline characteristics of the study population

Initially, 385 subjects who were diagnosed as having UC, CD, or intestinal BD under the age of 18 were included. Of these, 177 were initially diagnosed in the pediatric IBD clinic and 208 were initially diagnosed in the adult IBD clinic. After excluding patients with non-specific diagnosis or inflammation

associated with other secondary causes (infection or ischemia), those who were under 18 on the last day of the study period or those with a follow-up duration less than 18 months, data from a total of 242 patients (Group A [n = 29, 12.0%], Group B [n = 213, 88.0%] were included in the final analysis (Figure 1).

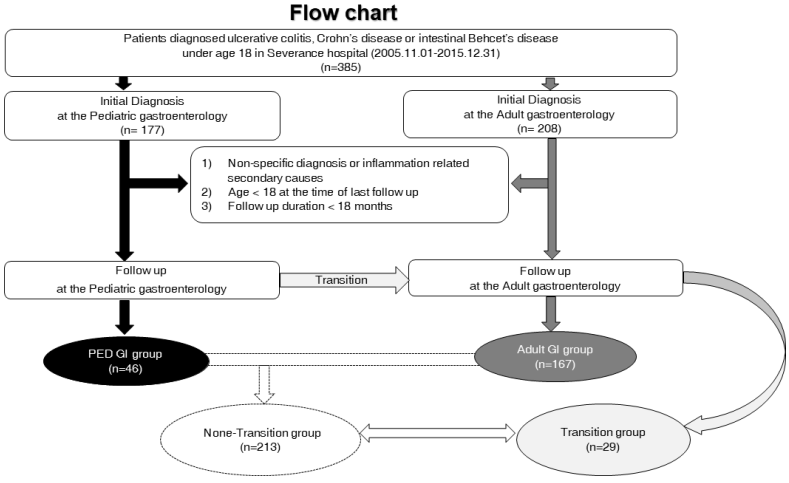

Figure 1. Flow chart of the study.

PED, pediatric; GI, Gastroenterology; UC, Ulcerative colitis; CD, Crohn's disease; BD, Behçet's disease

The mean age at transition was 19 (range, 12-21) years, and median pre- and post-transfer follow-up durations were 53.9 (range, 6.2-112.5) and 23.6 (range, 5.9-125.5) months, respectively. A significantly higher number of patients was diagnosed at an earlier age in Group A than Group B (median age 14 vs. Group B, 16, $P < 0.01$). The baseline data between the two groups are listed in Table 1.

Table 1. Baseline characteristics of the study population (N=242)

Variables	Transition group (N=29)	Non-transition group (N=213)	*P* value
Demographic data			
Current Age (years)	21 (20-22)	21 (20-24)	NS
Age at diagnosis (years)	14 (13-15)	16 (15-17)	<0.001
Male gender	20 (69.0)	147 (69.0)	NS
Smoking history	1 (3.5)	3 (1.4)	NS
IBD family history	0 (0.0)	1 (0.5)	NS
Type of IBD			NS
Crohn's disease	15 (51.3)	124 (58.2)	
Ulcerative colitis	9 (31.0)	63 (29.6)	
Intestinal Behçet's disease	5 (17.2)	26 (12.2)	
Laboratory data at transition			
Hemoglobin (mg/L)	12.51 ± 2.43	12.72 ± 1.89	NS
Leukocyte count ($x10^9$/L)	6.75 ± 3.42	7.78 ± 2.19	NS
Platelet count ($x10^9$/L)	375.05 ± 174.62	325.86 ± 207.73	NS
Erythrocyte sedimentation rate (mm/h)	15.04 ± 6.78	21.94 ± 20.21	NS
C-reactive protein (mg/L)	5.78 ± 9.82	4.67 ± 8.32	NS

Variables are expressed as mean ± SD, median (Interquartile range) or n (%).
IBD, Inflammatory bowel disease; NS, Non-significant

2. Disease characteristics and treatments

Group A patients were followed up for a significantly longer duration (median duration [months], 80 vs. Group B, 65 months, $P = 0.01$). In addition, patients in Group A were shown to experience a significantly higher number of

disease flare-ups than those in Group B (median number 3 vs. Group B, 2, P = 0.01). IBD-related bowel complications were more frequent in Group A patients (n [%], 8 [27.6] vs. Group B, 17 [8.0], $P < 0.01$).

The numbers of total admissions (median number 2 vs. Group B, 1, $P = 0.03$) and emergency admissions (median number 1 vs. Group B, 0, $P = 0.01$) were significantly higher in Group A patients. However, there was no significant difference in terms of the number of surgeries during the study period between the two groups (Table 2).

Table 2. Disease characteristics and clinical outcomes (N=242)

Outcomes	Transition group (N=29)	Non-transition group (N=213)	*P* value
Follow-up period (months)	80 (64-96)	65 (41-94)	0.013
Deaths with all causes	0 (0.0)	0 (0.0)	NS
Number of disease flares	3 (2-5)	2 (1-3)	0.002
Number of needing admissions	2 (1-5)	1 (0-3)	0.027
Number of needing emergency admissions	1 (0-2)	0 (0-1)	0.007
Number of surgeries	0 (0-1)	0 (0-0)	NS
Use of total parenteral nutrition	8 (27.6)	49 (23.0)	NS
Extraintestinal manifestation of IBD	6 (13.8)	24 (11.3)	NS
Complications of IBD (perforation, bowel obstruction, or stricture)	8 (27.6)	17 (8.0)	<0.001
Number of medical-noncompliance	4 (3-6)	6 (3-11)	NS

Variables are expressed as median (Interquartile range) or n (%).
IBD, Inflammatory bowel disease; NS, Non-significant

As for medications, a significantly lower number of Group A patients was treated with aminosalicylates (20 [69.0%] *vs.* Group B, 195 [91.5%], $P < 0.01$).

In contrast, the numbers treated with steroids (28 [96.6%] *vs*. Group B, 151 [70.9%], $P < 0.01$), immunomodulators (25 [86.2%] *vs*. Group B, 139 [65.3%], $P < 0.01$), methotrexate (3 [10.3%] *vs*. Group B, 11 [5.2%], $P < 0.01$), or infliximab (17 [58.6%] *vs*. Group B, 43 [20.2%], $P < 0.01$) were significantly higher in Group A patients than Group B patients (Table 3). There was no remarkable difference in drug complications between the two groups ($P = 0.23$).

Table 3. Medical treatments (N=242)

Type of medication	Transition group (N=29)	Non-transition group (N=213)	*P* value
Aminosalicylate	20 (69.0)	195 (91.5)	<0.001
Immunomodulator (AZA/6-MP)	25 (86.2)	139 (65.3)	<0.001
Methotrexate	3 (10.3)	11 (5.2)	<0.001
Corticosteroid	28 (96.6)	151 (70.9)	<0.001
Biologic agents			
Infliximab	17 (58.6)	43 (20.2)	<0.001
Adalimumab	0 (0.0)	22 (10.3)	NS
Colchin	2 (6.9)	12 (5.6)	NS
Antibiotics (Metronidazole/Ciprofloxacin)	21 (72.4)	116 (54.5)	NS
Drug intolerance/complication	3 (10.3)	13 (6.1)	NS

Variables are expressed as n (%).

AZA, Azathioprine; 6-MP, 6-mercaptopurine; NS, Non-significant

3. Medical non-compliance

There was no remarkable difference in medical non-compliance between the two groups in univariate analysis (median number, Group A, 4 *vs*. Group B, 6,

P = 0.26) (Table 2). However, multiple regression analysis showed that group B patients had a higher frequency of medical non-compliance than did group A patients (β = 0.008, *P* = 0.04) (Table 4). Medical non-compliance were demonstrated to be associated with longer follow-up duration (β = 0.001, *P* < 0.01), higher number of disease flares (β = 0.673, *P* < 0.01), higher aminosalicylate usage (β = 0.001, *P* = 0.02) and higher steroid usage (β = 0.004, *P* = 0.01).

Table 4. Independent predictors of medical non-compliance (N=242)

Variables	β	95% CI	*P* value
Follow up duration (months)	0.001	0.000-0.001	<0.001
Number of disease flares	0.673	0.350-0.995	<0.001
Aminosalicylate use	0.001	0.000-0.001	0.018
Steroid use	0.004	0.001-0.007	0.009
Transition group	0.008	0.000-0.017	0.043

CI, confidence interval

4. Changes in clinical outcomes before and after transition

Total admission number (pre-transition, median number, 2 *vs*. post-transition, 0, *P* < 0.01), emergency admission frequency (pre-transition, median number, 1 *vs*. post-transition, 0, *P* < 0.01), disease flares (pre-transition, median number, 2 *vs*. post-transition, 0, *P* < 0.01), and medical non-compliance (pre-transition, median number, 3 *vs*. post-transition, 1, *P* = 0.01) were significantly improved after transition in Group A patients. Otherwise, total number of surgeries was not different before and after transition (pre-transition, median number, 0 *vs*. post-transition, 0, *P* = 0.06) (Table 5 and Figure 2).

Table 5. Differences in Clinical Outcomes before and after transition (N=29)

Variables	Pre-transition	Post-transition	*P* value
Follow up duration (months)	**54 (6-113)**	**24 (6-105)**	**0.005**
Number of needing admissions	**2 (0-16)**	**0 (0-4)**	**0.001**
Number of needing emergency admissions	**1 (0-3)**	**0 (0-3)**	**0.003**
Number of surgeries	0 (0-2)	0 (0-1)	0.058
Number of disease flares	**2 (1-16)**	**0 (0-4)**	**<0.001**
Medical non-compliance	**3 (0-32)**	**1 (0-15)**	**0.006**

Variables are expressed as median (range).

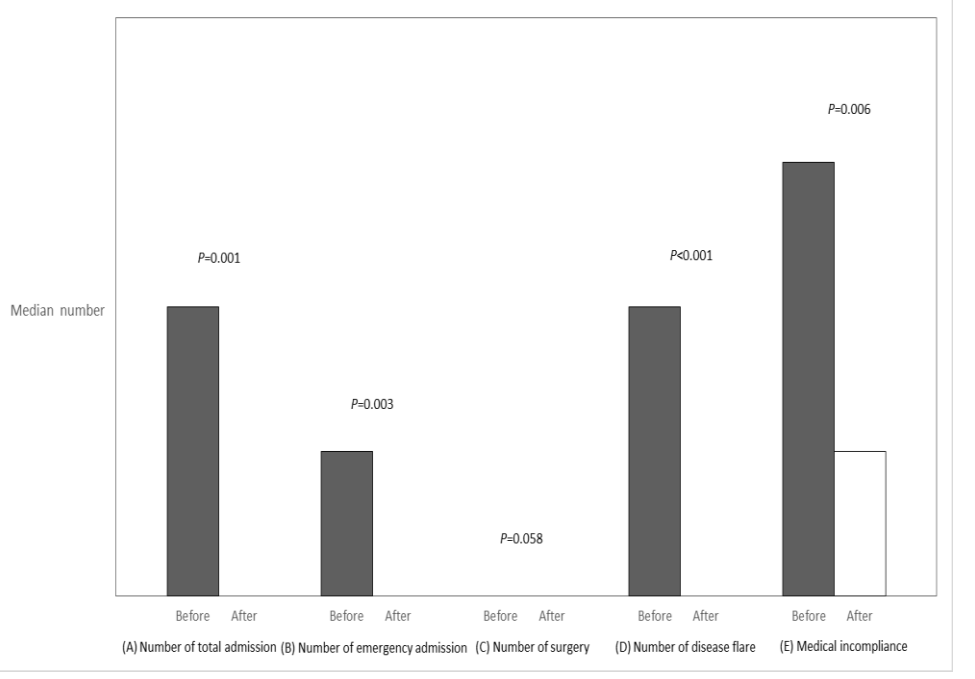

Figure 2. Differences in Clinical Outcomes before and after transition (N=29).

Total admission number (A) (pre-transition, median number, 2 *vs*. post

transition, 0, $P<0.01$), emergent admission number (B) (pre-transition, median number, 1 *vs*. post transition, 0, $P<0.01$), disease flares (D) (pre-transition, median number, 2 *vs*. post transition, 0, $P<0.01$) and medical non-compliance (E) (pre-transition, median number, 3 *vs*. post transition, 1, $P=0.01$) were significantly improved after transition in Group A patients. Otherwise, total number of surgeries (C) was not remarkably different before and after transition (pre-transition, median number, 0 *vs*. post transition, 0, $P=0.06$).

IV. DISCUSSION

In previous studies, adherence to medical treatment regimens has varied. The transition period was associated with poorer medical adherence in pediatric liver transplant recipients and type I diabetes mellitus patients[10]. However, a study on congestive heart disease patients reported better medical adherence with higher clinical attendance rates during and after the transition process[11]. Similarly, coordinated transition brought beneficial effects on medical adherence to adolescents with juvenile rheumatoid arthritis[12]. However, there have been few studies documenting that an effective transition process can improve clinical outcomes while promoting medical adherence in adolescent patients with IBD. Jeganathan et al. prospectively compared medical non-adherence among a transition group (initially managed by pediatric gastroenterologists and transferred to adult gastroenterologists), young adult group (always managed by adult gastroenterologists), and pediatric group (always managed by pediatric gastroenterologists) of IBD patients. These researchers reported that transition patients did not have worse adherence than the young adult group patients[6]. However, a survey by Fu N et al. showed that adolescents with IBD had low overall medical adherence despite adequate disease-specific knowledge[13]. In addition, a survey by Bennett et al. revealed no significant differences in medical compliance, disease complications,

surgeries, admission rate, or number of disease flares up between transition patients and age- and sex-matched patients who received treatment only in an adult IBD clinic[14].

However, to our knowledge, there have been no previous studies concerning disease characteristics, clinical outcomes, and medical adherence of IBD patients during transition periods, particularly in Asia. IBD patients in Asia have several differences compared with IBD patients in Western countries. The incidence and prevalence of CD and UC appear to be lower in Asia and the Middle East[15]. As a result, the social awareness of IBD is low, patients attempt to hide the disease more frequently, and the interest in and knowledge of treatment are low. Also, in the East, there is a greater disease stigma, and patients tend to endure the disease alone[16].

According to the results of this study, prevalence of IBD-related bowel complications and incidence of disease flares were significantly higher in the transition group compared to the non-transition group with IBD. In a previous study, intestinal complications tended to be more frequent in IBD patients with pediatric period onset[17]. According to another previous study, surgery and admission rates were significantly higher in the transition group compared with adult controls[18]. Similarly, numbers of elective and emergency hospitalizations were significantly higher in transition group IBD patients in our study. This can be interpreted as indicating that more clinically active or symptomatic patients are more likely to undergo transition. Also, in South Korea, IBD is considered an adult disease, and there are many drugs that have been recognized for insurance benefits only in adults. Therefore, adult IBD patient cases can appear more complicated[19]. Therefore, to ensure successful transition processes, multidisciplinary care should be performed through precise understanding of individual patient disease status, obstacles for transition, and possible outcomes. In addition, efforts are needed to share and improve information on treatment plans with patients, their families, and both

pediatric and adult IBD care providers.

In medical treatments, frequency of steroids, immunomodulators, methotrexate, and infliximab administration were significantly higher in the transition group in our study, while aminosalicylate was administered infrequently. These findings could be related with higher incidence of IBD-related bowel complications and disease flares in transition group patients. Systemic steroids, immunosuppressants, and biologics are used commonly in severe or refractory diseases[20, 21] and can be associated with severe disease activity and progress in the transition group. In contrast to our findings, previous studies have shown no significant differences in drug administration between transition and non-transition groups[6, 12, 18].

Importantly, we found medical non-compliance to be significantly lower in transition group patients. Non-compliance to medications in IBD is related to a 5-fold increase in relapse risk[6]. Medication compliance rate for adolescents with IBD were reported at about 50%-75% in a previous study[22]. Similarly, medical compliance rates in adolescents with other chronic diseases such as type I DM and bronchial asthma were reported to be 40%-80%[23, 24]. Significant increase in medical non-compliance during transition is well known in type I DM as well as renal transplantation subjects[25, 26]. Contrary to the results of our work, the medical compliance between transition groups and non-transition groups showed no significant difference in several previous studies [6, 13, 14]. Also, some studies have shown that the transition group has higher medical non-compliance rates than the non-transition group[12, 18]. The difference between previous studies and the results of this study is probably related to patients in the transition group having a longer average follow-up period and a higher level of disease activity than non-transition patients. Consequently, patients in the transition group showed greater trust or dependence on the medical staff and a better understanding of the need for drugs than did patients in the non-transition group. Also, patients in the transition group have higher

self-determination and self-confidence in treatment process. In addition, pediatric and adult IBD physicians were involved cooperatively in increasing drug compliance in the transition process by organizing disease progress or treatment plans and understanding disease characteristics and treatment progress, medication or surgical treatment, and future treatment plans. In particular, the process of converting from pediatric- to adult-centered treatment had a significant impact on the study results by changing the focus of treatment from growth, puberty, and nutrition to cancer surveillance and fertility. In doing so, the focus of care can be shifted from family-centered to individuals, and patients have to participate actively and voluntarily in their treatment.

Another intriguing point in our study is that the transition process could have a positive change in major clinical outcomes such as admission rate, disease flares, and medical non-compliance. Both elective and emergency admission numbers, disease flares, and medical non-compliance were significantly improved after transition, similar to the results of Cole et al. in 2015[18]. Also, a retrospective study published by Otto et al. showed improved disease remission rate and planned outpatient attendance rate after transition[12]. Throughout the transition process, education about disease and treatment is provided via communication between patients and IBD medical staff and increases patient drug compliance and willingness to treat, leading to reduced disease flares and hospitalization rates. In a prospective study of 59 patients with transition, adolescents held significantly stronger beliefs that planned disease evaluation and treatment were necessary and had positive attitudes toward their prescribed medicine[13]. Previous studies of type 1 diabetes patients have shown that the transition process reduced diabetes complications and hospitalization rates[27].

Our study, for the first time, revealed the disease characteristics, treatment outcomes, and medical compliance in a transition group with IBD patients in East Asia. Unlike Western countries, major life events including financial

independence and moving away from family and home tend to occur at later ages in East Asia countries. As such, the Asian adolescent is thought to be more dependent on parents when making decisions[28]. Likewise, in the context of IBD care, major decisions tend to be a shared family opinion, especially since there is a financial consideration with regard to the high cost of treatment. Therefore, there is bound to be a difference in the course of treatment and compliance of patients in the East and the West, indicating the importance of individualized transition according to country. Another strength of this study is that the number of samples in the study group is higher than in previous studies. This study also has a difference in that previous papers studied in the West included only CD and UC patients among IBD, while this study included intestinal BD, which is relatively common in Northeast Asia.

However, some limitations of this study should be considered. First, this is a retrospective study conducted in a single institution and was not only uncontrolled but not randomized. Hence, although it might indicate trends, firm conclusion and generalization of the results should be validated. Thus, further multi-institution-based, controlled, randomized, prospectively designed study should be performed based on our study. Practically, most institutions in Korea do not have a documented transition protocol and lack the manpower or resources involved for transition care. Structured transition guidelines have been published by major international gastroenterology societies in the West, including North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) (2002) and European Crohn's and Colitis Organization (ECCO) (2017)[29, 30]. In Northeast Asia, the Japanese Society for Pediatric Gastroenterology, Hepatology, and Nutrition (JSPGHAN) recently published guidelines for transition of IBD patients[28]. In Korea, there is no officially documented guideline for transition clinic or care for IBD patients. There have been studies reporting that effective transition care system and protocol can promote medical adherence and disease outcomes[6, 31]. Therefore,

based on our study, more research on transition groups of IBD patients should be conducted, and appropriate guidelines should be established to improve the lifelong clinical results of the transition group. Besides, there have been occasions when records of disease activity have been omitted (27%), and medial compliance surveys were investigated using only the medical chart or the number of outpatient cancellations without questionnaires or telephone interviews as in other studies[6, 13, 14]. In addition, we did not investigate socioeconomic factors and educational background, which can influence clinical outcomes and medical non-compliance. Therefore, systematic data collection and analysis are needed through a prospective study. Finally, in the comparison of major clinical results before and after transition, there may be limitations in interpreting the results because the follow-up period after transition was significantly shorter than the follow-up period before transition (pre-transition, median follow up duration, 54 months *vs*. post transition, 24 months, $P<0.01$).

V. CONCLUSION

IBD is a chronic, lifelong disease that repeats cycles of improvement and deterioration. Also, disease-associated morbidity can be high. Therefore, an efficient and systematic transition from pediatric to adult clinic is indispensable. Our study revealed that a transition group in IBD patients had longer follow up duration and higher number of disease flare up with bowel-related complications than did the non-transition group. Meanwhile, non-attendance at clinic and drug incompliance were significantly lower in transition group patients. Indeed, after transition, medical non-compliance and several clinical outcomes were improved. Multicenter-oriented prospective studies should be carried out in the future to help create efficient transition protocols or guidelines for IBD groups in Korea.

REFERENCES

1. Lehtinen P, Ashorn M, Iltanen S, Jauhola R, Jauhonen P, Kolho K-L, et al. Incidence trends of pediatric inflammatory bowel disease in Finland, 1987–2003, a nationwide study. Inflammatory bowel diseases. 2011; 17:1778-83.

2. Benchimol EI, Guttmann A, To T, Rabeneck L, Griffiths AM. Changes to surgical and hospitalization rates of pediatric inflammatory bowel disease in Ontario, Canada (1994–2007). Inflammatory bowel diseases. 2011; 17:2153-61.

3. Van Limbergen J, Russell RK, Drummond HE, Aldhous MC, Round NK, Nimmo ER, et al. Definition of phenotypic characteristics of childhood-onset inflammatory bowel disease. Gastroenterology. 2008; 135:1114-22.

4. Rosen DS. Pubertal growth and sexual maturation for adolescents with chronic illness or disability. Pediatrician. 1991.

5. Escher JC. Transition from pediatric to adult health care in inflammatory bowel disease. Digestive Diseases. 2009; 27:382-6.

6. Jeganathan J, Lee CH, Rahme A, Tiao DK, Weston C, Dutt S, et al. Pediatric-to-adult transition and medication adherence in patients with inflammatory bowel disease. Inflammatory bowel diseases. 2017; 23:1065-70.

7. Timmer A, Kemptner D, Takses A, Klebl F, Jöckel K-H. A survey-based index was validated for measuring disease activity in inflammatory bowel disease. An evaluation study. Journal of clinical epidemiology. 2009; 62:771-8.

8. Moon JS. Clinical aspects and treatments for pediatric inflammatory bowel diseases. Pediatric gastroenterology, hepatology & nutrition. 2019; 22:50-6.

9. Cheon JH, Han DS, Park JY, Ye BD, Jung SA, Park YS, et al.

Development, validation, and responsiveness of a novel disease activity index for intestinal Behçet's disease. Inflammatory bowel diseases. 2011; 17:605-13.

10. Leung Y, Heyman MB, Mahadevan U. Transitioning the adolescent inflammatory bowel disease patient: guidelines for the adult and pediatric gastroenterologist. Inflammatory bowel diseases. 2011; 17:2169-73.

11. Reid GJ, Irvine MJ, McCrindle BW, Sananes R, Ritvo PG, Siu SC, et al. Prevalence and correlates of successful transfer from pediatric to adult health care among a cohort of young adults with complex congenital heart defects. Pediatrics. 2004; 113:e197-e205.

12. Otto C, Tárnok A, Erős A, Szakács Z, Vincze Á, Farkas N, et al. Planned transition of adolescent patients with inflammatory bowel disease results in higher remission rates. Journal of pediatric nursing. 2019; 45:62-6.

13. Fu N, Jacobson K, Round A, Evans K, Qian H, Bressler B. Transition clinic attendance is associated with improved beliefs and attitudes toward medicine in patients with inflammatory bowel disease. World journal of gastroenterology. 2017; 23:5405.

14. Bennett AL, Moore D, Bampton PA, Bryant RV, Andrews JM. Outcomes and patients' perspectives of transition from paediatric to adult care in inflammatory bowel disease. World journal of gastroenterology. 2016; 22:2611.

15. Ng SC, Shi HY, Hamidi N, Underwood FE, Tang W, Benchimol EI, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. The Lancet. 2017; 390:2769-78.

16. Tan B, Ong D. Pediatric to adult inflammatory bowel disease transition: the Asian experience. Intest Res. 2020; 18:11-7.

17. Herzog D, Fournier N, Buehr P, Rueger V, Koller R, Heyland K, et al. Prevalence of intestinal complications in inflammatory bowel disease: a comparison between paediatric-onset and adult-onset patients. European

journal of gastroenterology & hepatology. 2017; 29:926-31.

18. Cole R, Ashok D, Razack A, Azaz A, Sebastian S. Evaluation of outcomes in adolescent inflammatory bowel disease patients following transfer from pediatric to adult health care services: case for transition. Journal of Adolescent Health. 2015; 57:212-7.

19. Kim YS, Jung S-A, Lee K-M, Park SJ, Kim TO, Choi CH, et al. Impact of inflammatory bowel disease on daily life: an online survey by the Korean Association for the Study of Intestinal Diseases. Intestinal research. 2017; 15:338.

20. Oh SJ, Shin GY, Soh H, Lee JG, Im JP, Eun CS, et al. Long-term outcomes of infliximab in a real-world multicenter cohort of patients with acute severe ulcerative colitis. Intest Res. 2021; 19:323-31.

21. Suzuki Y, Hagiwara T, Kobayashi M, Morita K, Shimamoto T, Hibi T. Is adalimumab safe and effective in patients with intestinal Behcet's disease in real-world practice? Intest Res. 2021; 19:301-12.

22. Mackner LM, Crandall WV. Oral medication adherence in pediatric inflammatory bowel disease. Inflammatory Bowel Diseases. 2005; 11:1006-12.

23. McGrady ME, Hommel KA. Medication adherence and health care utilization in pediatric chronic illness: a systematic review. Pediatrics. 2013; 132:730-40.

24. Koster ES, Philbert D, Winters NA, Bouvy ML. Adolescents' inhaled corticosteroid adherence: the importance of treatment perceptions and medication knowledge. Journal of Asthma. 2015; 52:431-6.

25. Kipps S, Bahu T, Ong K, Ackland F, Brown R, Fox C, et al. Current methods of transfer of young people with type 1 diabetes to adult services. Diabetic Medicine. 2002; 19:649-54.

26. Watson AR. Non-compliance and transfer from paediatric to adult transplant unit. Pediatric Nephrology. 2000; 14:469-72.

27. Nakhla M, Daneman D, To T, Paradis G, Guttmann A. Transition to adult care for youths with diabetes mellitus: findings from a Universal Health Care System. Pediatrics. 2009; 124:e1134-e41.

28. Tan B, Ong D. Pediatric to adult inflammatory bowel disease transition: the Asian experience. Intestinal research. 2020; 18:11.

29. Baldassano R, Ferry G, Griffiths A, Mack D, Markowitz J, Winter H. Transition of the patient with inflammatory bowel disease from pediatric to adult care: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Journal of pediatric gastroenterology and nutrition. 2002; 34:245-8.

30. Kumagai H, Suzuki Y, Shimizu T. Transitional care for patients with inflammatory bowel disease: Japanese experience. Digestion. 2021; 102:18-24.

31. Kim J, Ye BD. Successful transition from pediatric to adult care in inflammatory bowel disease: what is the key? Pediatric gastroenterology, hepatology & nutrition. 2019; 22:28.

ABSTRACT(IN KOREAN)

염증성 장질환 이행 집단 환자들의 질병 및 치료적 특성

<지도교수 천재희>

연세대학교 대학원 의학과

유은진

연구 배경: 본 연구는 염증성 장질환 환자의 이행 집단의 질병 특성 및 치료 결과를 평가하는 것을 목표로 하였다.
연구 방법: 18세 미만의 염증성 장질환 환자 (크론병, 궤양성 대장염, 베체트 장염) 진단을 받은 환자를 조사했다. 환자를 이행 집단 (집단 A, 최초 소아과에서 진단 후 성인 소화기내과에서 추적관찰)과 비이행 집단 (집단 B, 최초 소아과 혹은 성인 소화기내과에서 진단 후 이전 없이 각 과에서 추적관찰)의 두 가지 집단으로 분류했다.
연구 결과: 총 242명의 환자(집단 A[N=29, 12.0%], 집단 B[N=213, 88.0%)를 분석하였다. 집단 A 환자들이 집단 B에 비해 더 이른 나이에 진단되었으며 질병 악화 빈도, 장 관련 합병증, 총 입원 횟수, 응급실 입원 횟수가 집단 A에서 유의미하게 높게 나타났다. 다중 회귀 분석에 따르면 집단 A가 집단 B에 비하여 약물 비순응도 빈도가 낮았다. 또한 집단 A에서 이행 이후 총 입원 횟수, 응급실 입원 횟수, 질병 악화빈도, 약물 비순응도 등이 크게 개선되었다.
결론: 염증성 장질환 이행 집단은 비이행 집단에 비하여 더 심각한 질병 양상을 보였다. 또한 약물 비순응도는 이행 집단에서 낮게 나타났으며 이행 이후 여러 임상지표들이 개선되었다.

핵심되는 말: 이행 집단, 염증성 장질환, 약물순응도, 임상결과