The retrospective evaluation of response to adalimumab and infliximab treatment in patients diagnosed with inflammatory bowel disease

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ABSTRACT

Objective: Inflammatory bowel disease encompasses two major form: Crohn's disease and ulcerative colitis. The Crohn's Disease Activity Index is used to determine the severity of disease activity in patients with Crohn's disease. On the other hand, the Truelove-Witts activity index is used to determine the severity of disease activity in patients with ulcerative colitis. Adalimumab and infliximab are biological agents used in the treatment of patients with inflammatory bowel disease. The aim of this study is to conduct a retrospective evaluation regarding the response to adalimumab and infliximab treatment in patients with inflammatory bowel disease.

Material and Methods: The data of the patients who were over the age of 18, diagnosed with inflammatory bowel disease, and followed up in the Gastroenterology Clinic and Outpatient Clinic of Fırat University Hospital between January 2008-April 2019 were assessed. Eighty patients who received adalimumab and infliximab treatment regularly for at least 4 weeks were included in the study.

Results: The Crohn's Disease Activity Index of patients who were diagnosed with Crohn's disease, and received adalimumab and infliximab treatment was compared, and it was found that it was significantly lower after the treatment (p <0.05). Truelove and Witts Activity Index of patients who were diagnosed with Crohn's disease, and received adalimumab and infliximab treatment were compared before and after the treatment, and it was found that it was significantly lower after the treatment (p <0.05).

Conclusion: The results showed that the recovery rate was %83.3 in crohn's disease and %84.6 in ulcerative colitis patients. Adalimumab and infliximab treatment was effective on the healing of active disease in patients with inflammatory bowel disease. It was also concluded that although the safety of adalimumab and infliximab was high, but few allergy, lymphadenopathy, and leukopenia side effects were observed.

Keywords: Inflammatory bowel disease, crohn disease activity index, Truelove-wittz index, adalimumab, infliximab

INTRODUCTION

Inflammatory bowel diseases (IBD) are intestinal inflammatory diseases that progress with chronic, relapse, and remission periods, can be associated with various intestinal and extraintestinal complications, and cannot be cured medically. Ulcerative colitis (UC) and Crohn's disease (CH) are the two major forms of IBD (1). The Crohn's Disease Activity Index (CHAI) is often used to determine the clinical severity of Crohn's disease. It is difficult to use in clinical practice because it cannot fully differentiate between symptoms and inflammation and is complex. Although numerous alternative indices have been used, none of them has been accepted as superior (2). The CHAI system calculates the index by scoring patients' features such as diarrhea status, antidiarrheal use, presence of abdominal mass, anemia, and weight loss from mild to severe (2, 3). The criteria defining ulcerative colitis activity were first defined by Truelove and Witts. In the Truelove-Witts index, stool blood, fever, anemia, pulse, erythrocyte sedimentation rate are evaluated as mild to severe (2). The criteria defining ulcerative colitis activity were first defined by Truelove and Witts. In the Truelove-Witts index, stool blood, fever, anemia, pulse, erythrocyte sedimentation rate are evaluated as mild to severe (2, 3). The CHAI system calculates the index by scoring patients' features such as diarrhea status, antidiarrheal use, presence of abdominal mass, anemia, and weight loss from mild to severe (2, 3). The criteria defining ulcerative colitis activity were first defined by Truelove and Witts. In the Truelove-Witts index, stool blood, fever, anemia, pulse, erythrocyte sedimentation rate are evaluated as mild to severe (2). The criteria defining ulcerative colitis activity were first defined by Truelove and Witts. In the Truelove-Witts index, stool blood, fever, anemia, pulse, erythrocyte sedimentation rate are evaluated as mild to severe (2). The criteria defining ulcerative colitis activity were first defined by Truelove and Witts. In the Truelove-Witts index, stool blood, fever, anemia, pulse, erythrocyte sedimentation rate are evaluated as mild to severe (2).
MATERIAL and METHODS

This study was carried out retrospectively with the approval of Firat University Non-Interventional Research Ethics Committee dated 13/06/2019 and numbered 10/04. For this study, the data of the patients who were examined and treated in Firat University Hospital Gastroenterology clinic and outpatient clinic between January 2008 and April 2019 were analyzed. Patients with a diagnosis of inflammatory bowel disease who received adalimumab and infliximab treatment regularly for at least 4 weeks were included in the study. A total of 80 cases, 27 female and 53 male, whose file, clinical and laboratory information were accessed, were included in the study. Only patients aged 18 years and older were included in our study. In evaluating the response to adalimumab and infliximab treatment in the patients included in the study, the values of the parameters that increase due to inflammation and related to the activity of the disease were compared with the values before the treatment and after the treatment, and those who were found to be significantly decreased after the treatment were evaluated as responsive to the treatment. To evaluate the response to adalimumab and infliximab treatment in patients with a diagnosis of Crohn's disease, the Crohn's Disease Activity Index before and after treatment was calculated and compared (6). Crohn's patients according to CHAI; If CHAI <150, they were divided into 4 subgroups as in remission, CHAI 150-220 mild, CHAI 221-450 moderate, and CHAI >450 severely active. Patients with moderate or severe disease activity before treatment but with a Crohn's Disease Activity Index below 150 (in remission) or a decrease of more than 70 points after treatment with adalimumab and infliximab were considered responsive to treatment. In order to evaluate the response to adalimumab and infliximab treatment in patients with ulcerative colitis, the Truelove-wittz activity index before and after treatment was calculated and compared (7). According to the Truelove-wittz activity index before adalimumab and infliximab treatment, patients with severe or moderate disease activity and mild disease activity after treatment were evaluated as responsive to treatment. In addition, the rates of remission and non-remission were examined from the data of these patients. The rates of relapsed and non-relapsed patients were evaluated. Side effects, drug tolerance and intolerance rates, reasons for drug initiation, and other drug use rates were analyzed from patient files and data recorded in the system.

Statistical analysis

IBM SPSS Statistics Version 22.0 package program was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and continuous measurements as mean and standard deviation (median and minimum-maximum where appropriate). Chi-square test statistics were used to compare categorical measures between groups. Whether continuous measurements provided the assumption of normal distribution was tested with the Kolmogrov Smirnov test. Wilcoxon Signed Rank test was used to compare two dependent continuous measurements that did not show normal distribution. Statistical significance level was taken as 0.05 in all tests.

RESULTS

Of the 80 patients included in the study, 66.25% (n=53) were male and 33.75% were female. It was determined that 67.5% (n=54) of the patients had Crohn's disease and 32.5% (n=26) had ulcerative colitis. 68.5% (n=37) of Crohn's patients were male and 31.5% (n=17) were female. Of the ulcerative colitis patients, 61.5% (n=16) were male and 38.5% (n=10) were female (Table 1).

It was determined that 63.7% (n=51) of the patients received adalimumab treatment, and 36.3% (n=29) received infliximab treatment. It was determined that 70.4% (n=38) of Crohn's patients received adalimumab treatment and 29.6% (n=16) received infliximab treatment. It was determined that 50.0% (n=13) of ulcerative colitis patients received adalimumab treatment, and 50.0% (n=13) received infliximab treatment (Table 1).

The mean age of 80 patients in our study was 40.32±13.788 years, the mean age of Crohn's patients was 39.50±12.167 years, and the mean age of ulcerative colitis patients was 42.04±16.806 years (Table 2).

The mean duration of diagnosis was 54.79±19.976 months, and the mean duration of anti-TNF treatment was 24.68±9.245 months in Crohn's patients who received adalimumab treatment. Mean diagnosis time was 65.62±16.480 months and mean anti-TNF treatment duration was 28.25±6.608 months in Crohn's patients who received infliximab treatment.

The mean duration of diagnosis of ulcerative colitis patients receiving adalimumab treatment was 64.62±15.777 months, and the mean duration of anti-TNF treatment was 40.15±12.341 months. The mean duration of diagnosis of ulcerative colitis patients receiving infliximab treatment was 58.31±14.602 months, and the mean duration of anti-TNF treatment was 35.08±11.765 months (Table 2).

Considering the reasons for starting anti-TNF medication in Crohn's patients, it was observed that 24.7% (n=14) of untreated patients, 17.3% (n=10) of those who were unresponsive to treatment, and 58.0% (n=32) of those who were steroid dependent.

When the reasons for starting anti-TNF drugs in ulcerative colitis patients were examined, it was observed that 30.8% (n=8) of untreated patients, 15.4% (n=4) of unresponsive patients and 53.8% (n=14) of those who were steroid dependent (Table 3).

While 31.6% (n=12) of the Crohn's patients who received adalimumab treatment had a severe course before treatment, 55.3% (n=21) had moderate disease activity and 13.2% (n=5) had a moderate disease activity. It was mild and there were no patients in remission. After the treatment, while there were no patients with severe disease activity, 7.9% (n=3) had moderate disease activity, 50.0% (n=19) had mild disease activity, and 42.1% had mild disease activity. Before adalimumab treatment, 31.6% (n=12) of patients had severe disease activity but did not have severe disease activity after treatment, 55.3% (n=21) patients had moderate disease activity before treatment, while disease activity was moderate after treatment.
Disease activity according to the Crohn's disease activity index after treatment compared with before treatment, because the number of patients with a low level of disease was 7.9% (n=3) and 42.1% (n=16) were in remission after treatment while there was no patient in remission before treatment. The decrease in their levels was statistically significant (p<0.05) (Table 4).

Before treatment, 50.0% (n=8) had severe disease activity, 43.8% (n=7) had moderate disease activity, and 6.2% (n=1) of CD who received infliximab treatment. Disease activity was mild, and there were no patients in remission. After infliximab treatment, 62.5% (n=10) were in remission, 31.25% (n=5) had mild disease activity, 6.25% (n=1) had moderate disease activity, and It was observed that there was no patient with severe disease activity.

While the disease activity was moderate in 43.8% (n=7) of the patients before treatment, it decreased to 6.2% (n=1) after treatment. Although 50.0% (n=8) of the patients had severe disease activity before the treatment, there were no patients with severe disease activity after infliximab treatment, and while the patient was not in remission before the treatment, 62.5% (n=10) of the patients were in remission after the treatment. An increase in the number of patients in remission and a decrease in the number of patients with moderate and severe disease activity were statistically significant after infliximab treatment compared to before treatment (p<0.05) (Table 5).

While 46.2% (n=6) of ulcerative colitis patients who received adalimumab treatment had a severe course before treatment, 46.2% (n=6) had moderate disease activity, 7.6% (n=1) had disease. The activity was mild. After adalimumab treatment, there were no patients with severe disease activity, 15.4% (n=2) had moderate disease activity, and 84.6% (n=11) had mild disease activity.

Before adalimumab treatment, 46.2% (n=6) of patients had severe disease activity but did not have severe disease activity after treatment, 46.2% (n=6) of patients with moderate disease activity before treatment and moderate disease activity after treatment Since the number of patients with the high level of disease was 15.4% (n=2), the decrease in the disease activity levels according to the Truelove-wittz index was statistically significant after the treatment when compared with the pre-treatment status (p<0.05) (Table 6).

While 38.5% (n=5) of ulcerative colitis patients who received infliximab treatment had a severe course before treatment, 53.8% (n=7) had moderate disease activity and 7.7% (n=1) had a severe course. After the treatment activity was mild. After infliximab treatment, there were no patients with severe disease activity, 15.4% (n=2) had moderate disease activity, and 84.6% (n=11) had mild disease activity.

Before infliximab treatment, 38.5% (n=5) of patients had severe disease activity but did not have severe disease activity after treatment, 53.8% (n=7) of patients with moderate disease activity before treatment, but moderate disease activity after treatment Since the number of patients with the high level of disease was 15.4% (n=2), the decrease in the disease activity levels according to the Truelove-wittz index was statistically significant after the treatment when compared with the pre-treatment status (p<0.05) (Table 7).

Among non-penetrating, non-stricted Crohn's disease patients, 56.2% (n=9) of those who received adalimumab treatment and 60.0% of those who received infliximab treatment had abdominal pain, fever, diarrhea complaints regressed after anti-TNF treatment, and their clinic status improved. The complaints of nausea, vomiting, abdominal pain and cramping due to stricture were regressed after anti-TNF treatment in 60.0% (n=6) of patients with Crohn's stricture who received adalimumab treatment and 66.7% (n=2) of those who received infliximab treatment.

Fistula development was observed in 25.0% (n=20) of Crohn's patients and followed up as fistulizing Crohn's disease.

The 60.0% (n=12) of fistulizing Crohn's patients received adalimumab and 40.0% (n=8) received infliximab treatment. Fistula healed in 58.4% (n=7) of fistulizing Crohn's patients who received adalimumab treatment, and 41.6% (n=5) did not. The fistula of 62.5% (n=5) of fistulizing Crohn's patients who received infliximab treatment healed, 37.5% (n=3) did not (Table 8).

Colonoscopy findings performed before anti-TNF treatment in 24.0% (n=13) of Crohn's patients and 46.1% (n=12) of ulcerative colitis patients and were compared with colonoscopy findings, at least 3 months after anti-TNF treatment. Other patients could not be compared because they did not have colonoscopy results after anti-TNF treatment.

While there were aphthous ulcers, erosions, and fistulas in the colonoscopy finding of Crohn's patients before the treatment, whose colonoscopy results were compared, the colonoscopy findings improved in 57.2% (n=4) of those who received adalimumab treatment and 83.3% (n=5) of those who received infliximab treatment.

In ulcerative colitis patients whose colonoscopy results were compared, while there were aphthous ulcers, active colitis, and pseudopolyps in their colonoscopy examination before treatment, the findings in the colonoscopy after treatment in 50.0% (n=4) of those who received adalimumab treatment and in 50.0% (n=2) of those who received infliximab treatment were improved (Table 9).

It was observed that 42.1% (n=16) of Crohn's patients who received adalimumab treatment entered remission, and 62.5% (n=10) of those who received infliximab treatment. The rate of remission of ulcerative colitis patients who received adalimumab treatment and those who received infliximab treatment was 84.6% (n=11). It was observed that 18.4% (n=7) of Crohn's patients who received adalimumab treatment relapsed after remission and 25.0% (n=4) of those who received infliximab treatment relapsed after remission. Relapse was observed in 15.4% (n=2) of ulcerative colitis patients after both adalimumab and infliximab patients entered remission (Table 10).
Table 1. Gender and treatment data of the patients (n=80)

|                     | Male                   | Female                 | Those receiving adalimumab therapy | Those receiving infliximab therapy |
|---------------------|------------------------|------------------------|-----------------------------------|-----------------------------------|
| Crohn's patients(n=54) | 37 (68.5)              | 17 (31.5)              | 38 (70.4)                         | 16 (29.6)                         |
| Ulcerative colitis patients(n=26) | 16 (61.5)              | 10 (38.5)              | 13 (50.0)                         | 13 (50.0)                         |

Table 2. Diagnosis period, treatment duration, and age data of the patients (n=80)

|                     | Diagnosis time Average (Moon) | Anti-TNF treatment duration Average (Moon) | Age average (Year) |
|---------------------|-------------------------------|---------------------------------------------|-------------------|
| Crohn's patients(n=54) | Adalimumab (n=38) 54,79±19,976 | 24,68±9,245                                  | 39.50±12,167      |
|                     | Infliximab (n=16) 65,62±16,480 | 28,25±6,608                                  |                   |
| Ulcerative colitis patients(n=26) | Adalimumab (n=13) 64,62±15,777 | 40,15±12,341                                  | 42,04±16,806      |
|                     | Infliximab (n=13) 58,31±14,602 |                                            |                   |

Table 3. Data on the reasons for starting anti-TNF medication (n=80)

|                     | Untreated | Unresponsive to treatment | Steroid dependent |
|---------------------|-----------|---------------------------|-------------------|
| Crohn's patients(n=54) | 14 (24.7) | 10 (17.3)                 | 32 (58.0)         |
| Ulcerative colitis patients(n=26) | 8 (30.8) | 4 (15.4)                  | 14 (53.8)         |

Table 4. Comparison of Crohn's disease activity index in patients with adalimumab treated Crohn's disease (n=38)

|                     | Before treatment | Post treatment | p value |
|---------------------|------------------|----------------|---------|
|                     | CHAI n (%)       | CHAI n (%)     |         |
| Severe (>450)       | 12 (31.6)        | 0 (0.0)        | <0.001  |
| Moderate (220-450)  | 21 (55.3)        | 3 (7.9)        | <0.001  |
| Mild (150-220)      | 5 (13.2)         | 19 (50.0)      | <0.001  |
| in remission (<150) | 0 (0.0)          | 16 (42.1)      | <0.001  |

Table 5. Comparison of Crohn's disease activity index in Crohn's patients who received infliximab treatment (n=16)

|                     | Before treatment | Post treatment | p value |
|---------------------|------------------|----------------|---------|
|                     | CHAI n (%)       | CHAI n (%)     |         |
| Severe (>450)       | 8 (50.0)         | 0 (0.0)        | <0.001  |
| Moderate (220-450)  | 7 (43.8)         | 1 (6.25)       | <0.001  |
| Mild (150-220)      | 1 (6.2)          | 5 (31.25)      | <0.001  |
| in remission (<150) | 0 (0.0)          | 10 (62.5)      | <0.001  |

Table 6. Comparison of the Truelove-wittz index of ulcerative colitis patients who received adalimumab treatment (n=13)

|                     | Before treatment | Post treatment | p value |
|---------------------|------------------|----------------|---------|
|                     | Truelove-wittz indeksi n (%) | Truelove-wittz indeksi n (%) |         |
| Severe              | 6 (46.2)         | 0 (0.0)        | <0.001  |
| Moderate            | 6 (46.2)         | 2 (15.4)       | <0.001  |
| Mild                | 1 (7.6)          | 11 (84.6)      | <0.001  |

Table 7. Comparison of the Truelove-wittz index of ulcerative colitis patients treated with infliximab (n=13)

|                     | Before treatment | Post treatment | p value |
|---------------------|------------------|----------------|---------|
|                     | Truelove-wittz indeksi n (%) | Truelove-wittz indeksi n (%) |         |
| Severe              | 5 (38.5)         | 0 (0.0)        | <0.001  |
| Moderate            | 7 (53.8)         | 2 (15.4)       | <0.001  |
| Mild                | 1 (7.7)          | 11 (84.6)      | <0.001  |
DISCUSSION

Delayed diagnosis and inadequate treatment of inflammatory bowel diseases cause high morbidity, mortality and serious increases in health expenditures. Therefore, these patients should be diagnosed in a timely manner and the parameters indicating the activation of the disease should be carefully monitored. The Crohn’s Disease Activity Index (CDAI) is often used to determine the clinical severity of Crohn’s disease (6). Although numerous alternative indices have been used instead, none of them has been accepted as having superiority (6).

The criteria for defining ulcerative colitis activity were first defined by Truelove and Witts (7). Disease activity is evaluated as mild–moderate–severe according to diarrhea, blood in stool, fever, anemia, pulse values in the Truelove-Witts index.

It was observed that Crohn’s disease activity index levels in patients with Crohn’s disease were significantly lower after adalimumab and infliximab treatment than before treatment.

To evaluate the response to adalimumab and infliximab treatment in ulcerative colitis patients, we compared the Truelove-Witts activity index levels before and after treatment. Truelove-Witts activity index levels in ulcerative colitis patients were found to be significantly lower after adalimumab and infliximab treatment than before treatment.

Although ulcerative colitis and Crohn’s disease are two different clinical entities, the same drugs are used to treat both diseases. Despite many studies, there is no specific treatment for these patients. The mainstays of treatment are 5-ASA derivatives, corticosteroids, immune modulatory agents (6-mercaptopurine, azathioprine, and methotrexate) and biological agents (8, 9).

Biological agents are effective in corticosteroid-dependent or refractory disease and cause improvement in the natural course of the disease. Anti-TNF agents (Adalimumab, Infliximab, Golimumab, Sertolizumab) and anti-integrins (Natalizumab and Vedolizumab) are used as biological agents (9).
Adalimumab treatment is started at 160 mg SC, continued at 80 mg SC two weeks later, and 40 mg SC two weeks later. In maintenance therapy, 40 mg SC is administered every 2 weeks. It has been shown that remission can be achieved in the majority of patients in the first 4 weeks when these doses are used. Infliximab 5 mg/kg IV infusion (at weeks 0, 2, and 6; then maintenance therapy every 8 weeks).

The ACCENT I study is a multicenter study evaluating the efficacy of infliximab treatment (9-11). In the arm in which the initial clinical response was evaluated, 83% of the 573 patients included in the study responded. This response was seen in 27% of patients at week 2, 69% at week 10, 38% of patients were in remission.

In our study, 83.3% of Crohn's patients and 84.6% of ulcerative colitis patients responded to infliximab treatment at 4 weeks. In our study, 84.6% of ulcerative colitis patients who received infliximab and 62.5% of Crohn's patients who received infliximab entered remission. In addition, 25.0% of Crohn's patients who received infliximab and 15.4% of ulcerative colitis patients in our study could not tolerate infliximab treatment.

When the response rate to infliximab treatment was compared with the ACCENT I study; With the ACCENT I study, the response rate to treatment was found to be close, but the response to treatment was earlier. In terms of remission rates, when compared to the ACCENT I study, the rate of remission was higher in our study. In a study involving a total of 317 patients in Korea in 2016, the clinical results and response rates of induction and maintenance therapy with infliximab were evaluated (12). At 14 weeks, 89.2% of these patients achieved clinical response, 60.0% developed remission, and 11% of the patients could not tolerate infliximab treatment. Compared to this study conducted in Korea in 2016, in our study, the rate of remission was higher for those who received infliximab, the rate of intolerance to infliximab was higher, and the rate of response to infliximab treatment was lower.

The safety and efficacy of adalimumab were evaluated in the CLASSIC I study, a previous phase 3 placebo-controlled study. Anti-TNF therapy was included in the study in 299 patients with naive Crohn's disease, and it was found to be more effective in inducing remission than placebo (13). In this study, 36% of patients were in remission at week 4, and 52% of them responded to treatment. Following the CLASSIC I study, the more recent CLASSIC II study was a smaller, placebo-controlled, randomized study of 55 patients. In this study, 65% of the patients responded to adalimumab treatment at week 10, and 46% were in remission (14).

In our study, response was obtained in 83.3% of Crohn's patients and 84.6% of ulcerative colitis patients at 4 weeks. In our study, 84.6% of ulcerative colitis patients and 42.1% of Crohn's patients who received adalimumab were in remission. When compared to the CLASSIC I and CLASSIC II study; In our study, although ulcerative colitis patients had a higher remission rate, Crohn's patients had a lower remission rate and a higher response rate to adalimumab treatment.

A multicenter (52 centers in the USA, Canada, Belgium, and France), randomized, placebo-controlled GAIN study was conducted to evaluate the efficacy and safety of adalimumab. 301 adult patients were included and remission rates at week 4 were evaluated. The 21% of patients in the adalimumab group and 7% of those in the placebo group were in remission at week 4. 52% of the patients in the adalimumab group and 34% of the patients in the placebo group responded to treatment at week 4 (15).

One hundred thirty-five patients were included in the study and mucosal healing and Crohn's disease activity indices at 12 weeks were examined. In 47% of the patients, the Crohn's disease activity index decreased significantly at 12 weeks, and 35% of them were in remission (16). When the GAIN and EXTEND study was compared with our study, both the rates of remission and the response rate to adalimumab treatment were higher in our study. A study with a total of 310 patients was conducted in 2018. At the end of the 96th week, 39.0% of the patients responded to the treatment, 26.5% went into remission, and 11% of the patients were excluded from the study because they could not tolerate the drug (17). Compared with our study; In this study, the duration of treatment was longer, and the rate of response and remission to adalimumab treatment was higher in our study. In a study published in 2019, Crohn's disease activity indexes were measured in patients receiving adalimumab at 14 weeks following induction therapy, and their rates of remission were compared with those treated with placebo. The 36% of the patients were in remission in the 4th week, and 9% could not tolerate the drug (18).

When compared with this study, the rate of remission was found to be higher in ulcerative colitis patients who received adalimumab in our study. In our study, 13.1% of Crohn's patients and 23.1% of ulcerative colitis patients who received adalimumab treatment could not tolerate the drug. The rate of those who could not tolerate adalimumab treatment was higher in our study compared to these two studies published in 2018 and 2019.

To evaluate the efficacy of infliximab therapy in patients with fistulizing Crohn's disease, the ACCENT II study was conducted involving 282 adult patients. This is a multicenter, randomized, placebo-controlled study (19). In the ACCENT II study, 60.7% of patients who received infliximab at week 10 had closed fistulas. In our study, 62.5% of patients with fistulizing Crohn's disease who received infliximab treatment had their fistula healed. After infliximab treatment, fistula healing rates in our study and in the ACCENT II study were found to be close to each other. The CHARM-I study resulted in fistula closure in 36% of patients receiving 40 mg adalimumab every other week and in 46% of patients receiving 40 mg adalimumab weekly (20). In our study, fistula healing rates were found to be higher than in the CHARM-I study, since 58.4% of fistulizing Crohn's patients who received adalimumab treatment healed their fistula.

In a study of 15 patients treated with infliximab, all patients underwent colonoscopy at weeks 0, 24, and 54. Complete mucosal healing was achieved at the 24th week in 53.3% of the patients and at the 54th week in 60% of the patients (21). In our study, colonoscopy data obtained at least 3 months after treatment showed improvement in colonoscopy after treatment in 83.3% of Crohn's patients and 50.0% of ulcerative colitis patients who received infliximab treatment. Compared to this study, in our study, patients with Crohn's had higher recovery rates at colonoscopy, and lower rates of ulcerative colitis patients.
In a study conducted with patients receiving adalimumab treatment, an improvement in colonoscopy was observed in 49.5% of the patients at 52 weeks (22). In our study, 57.2% of Crohn's patients who received adalimumab treatment and 50.0% of ulcerative colitis patients improved in colonoscopy, and the recovery rate was higher in our study.

A study was conducted comparing anti-TNF agents in 1459 patients with Crohn's disease receiving infliximab therapy and 871 patients receiving adalimumab therapy. Anti-TNF treatment was responded to in 49% of patients receiving infliximab and 47% of patients receiving adalimumab after 26 weeks of treatment, and it was observed that there was no significant difference in efficacy between adalimumab and infliximab (23). Among Crohn's patients, those with ileum, colon and ileocolonic involvement responded to anti-TNF therapy, but no response was observed in those with upper GIS involvement. In ulcerative colitis patients, those with proctitis, left colon involvement, and pancolitis responded to anti-TNF therapy (23). In our study, it was observed that 84.6% of ulcerative colitis patients who received both adalimumab and infliximab received a response to anti-TNF therapy. On the other hand, 62.5% of Crohn's patients who received infliximab and 42.1% of those who received adalimumab responded to Anti-TNF therapy, and those who received infliximab had more response to Anti-TNF therapy than those who received adalimumab. In our study, patients with Crohn's disease with upper GIS, ileum and colon involvement responded to anti-TNF therapy, while those with colonic involvement did not respond. Among the ulcerative colitis patients in our study, those with proctitis and left colon involvement responded to anti-TNF therapy, but no response was observed in those with pancolitis.

In a study involving 115 patients with Crohn's disease, 44% of those who discontinued infliximab treatment relapsed after 1 year (24). Relapse occurred within two years in 50 percent of these patients who were in clinical remission who discontinued anti-TNF therapy (25). In our study, the recurrence rate at the 24th week of treatment was 15.4% in ulcerative colitis patients and 20.4% in Crohn's patients. Both ulcerative colitis patients and Crohn's patients developed earlier and at a higher rate.

The difference in response to anti-TNF therapy, remission, recovery rates in colonoscopy, and recurrence rates between our study and the studies in the literature may differ in patients' characteristics (ethnicity, indications for biologic therapy, disease severity) or study design (study inclusion, disease activity, duration of treatment). It may be related to the differences.

CONCLUSION

Crohn's disease activity index in patients with Crohn's disease and Truelove-witts activity index in ulcerative colitis patients were significantly lower than before treatment after adalimumab and infliximab treatment. After adalimumab and infliximab treatment, the significant decrease in parameters such as erythrocyte sedimentation rate, C-reactive protein, leukocyte, neutrophil/lymphocyte ratio, which are important in disease activation, and a significant increase in hemoglobin levels, and because of this significant decrease in disease activity levels, both adalimumab treatment, and infliximab treatment are inflammatory. It is understood that it plays an active role in the recovery of active disease in the treatment of bowel disease. In addition, patients with ulcerative colitis who received adalimumab and those who received infliximab were in remission at a similar rate, whereas Crohn's patients who received infliximab entered remission more often than those who received adalimumab. In both ulcerative colitis patients and Crohn's patients, a proportion of those who go into remission develop relapse after treatment. Adalimumab and infliximab treatment are highly reliable and have low rates of side effects.

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