ORIGINAL ARTICLE

Response of biological agents (inflixmab, adalimumab) in treatment of inflammatory bowel diseases (IBD)

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Abstract:

Objective: To assess the response of biological agents in inflammatory bowel diseases (IBD)

Study design: Randomized Controlled Trail (RCT)

Place and duration: The study was conducted in King Salman Armed Forces Hospital,Tabuk, Kingdom of Saudi Arabia(K.S.A) for the time period of one year (June 2015-June 2016).

Material and Methods: The study was a randomized controlled trail with 1:1:1 ratio of three groups. The interventions were given as following, group 1 was given infliximab 10mg/kg, group 2 was given adalimumab 160mg while group 3 was placebo. The sample size calculated for this study was 36. Data was analyzed using SPSS software version 20.0. An independent T-test was performed to observe the results before and after intervention.

Results: Total 36 patients were included in this study with 1:1:1 in each group. The mean age of all patients in group 1(infliximab) was 22±10.2 SD while in group 2 (Adalimumab) the mean age was 25.3±1.3 SD and in group 3 (placebo) the mean age was 28.9±13.4 SD. The study found that maintenance of remission varies from moderate to severe in study participants. after intervention there were 50% patients with few ulcers, 10% with impoved vascularity, 15% with improved vascularity and few ulcers, 25% with decreased strictures and few ulcers (p<0.002, 95%CI).

Conclusion: Biological agents had a positive response in treatment of inflammatory bowel disease. These agents are responsible for reducing mucosal healing while infliximab is associated with better results for the treatment of Crohn's disease and ulcerative colitis.

Keywords: Crohn's disease and ulcerative colitis, biological agents, ulcers, vascularity, infliximab, adalimumab

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Introduction:

Inflammatory bowel diseases (IBD) including crohn's diseases and ulcerative colitis are chronic relapsing diseases worldwidely.[1] Crohn's disease is a transmural inflammation associated with an imbalance in pro and anti inflammatory process in human body.[2] Majority of patients with inflammatory bowel disease develop complications like strictures, fistulas, penetration of bowel wall with obstruction and abscess.[3] Another major form of inflammatory bowel diseases is ulcerative colitis. It consists of chronic inflammation involving both colon and rectum in human gastrointestinal system. Worldwide significant morbidity is associated with ulcerative colitis. The incidence and prevalence of ulcerative colitis is increasing day by day with time.[4]

The ulcerative colitis is associated with bloody diarrhea with and without mucous, weight loss, fever and abdominal pain. Ulcerative colitis involve dys-regulated immune response within large bowel under an unknown environmental stimulus.[5] Infliximab is a chimeric monoclonal and anti TNF IgG1 antibody that had an approved efficacy of remission maintenance and induction in patients associated with refractory luminal and fistulizing Crohn's disease.[6] It is associated with endoscopic healing. Evidence exist that remission rate 29% was found to be in patients treated with infliximab as compared to those who have given placebo after 54 weeks.

Table 1: Characteristics and dosage of three groups interventions

Drug	Route of administration	Induction	Maintenance
Group 1 (infliximab)	IV	5mg/kg (0-2week)	5mg/kg (2-4 week)
Group 2 (adalimumab)	SC	160mg(0-2week)	80 mg(2-4 week)
Group 3 placebo	IM	1ml saline	1 ml saline

(P<0.001)

Table 2:

	Before intervention			After intervention		
Intervention	Hb d/Dl	ESR mm/h	CRP mg/Dl	Hb d/Dl	ESR mm/h	CRP mg/Dl
Group 1, (N=12)(infliximab)	8.5	55	6.8	12.5	20	0.92
Group 2, (N=12)(Adalimumab)	9.0	66	7.9	11.0	25	1.0
Group 3, (N=12)(placebo)	7.8	55	8.0	7.9	50	7.9

While in 44% of patients mucosal healing was found as compared to those whom placebo was given.[7] Adalimumab is a fully humanized monoclonal anti TNF IgG1 antibody. It is proved to be a biological agent with very low immunogenicity. The CHARM trail proved that remission rate was higher with adalimumab after every week and response range from moderate to severe.[8]

This study was conducted to assess the response of biological agents in inflammatory bowel diseases (IBD).

Patients and Methods:

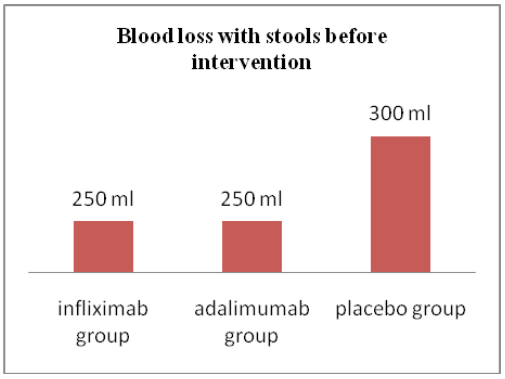
After taking ethical approval from ethical review board, the consent forms were taken from all participants. The study was a randomized controlled trail with 1:1:1 ratio of three groups. The interventions were given as following, group 1 was given infliximab 10mg/kg, group 2 was given adalimumab 160mg while group 3 was placebo. The study was conducted in King Salman Armed Forces Hospital, Tabuk, Kingdom of Saudi Arabia (K.S.A). The sample size calculated for this study was 36 with 80% power of two sided test and 5% significance level using WHO calculator. The three groups were followed 4 months (16 weeks) and measured for the induction, maintenance, number of stools per day, stool cal protection level, Hb d/Dl, ESR mm/h, CRP mg/Dl and colonoscopy results. Patients with age > 18 years and both genders were included in study. While the exclusion criteria was patients with planned bowel surgery, current diagnosis of fulminant colitis, patients with ulcerative proctitis, recent history of infection requiring antimicrobial therapy and current diagnosis of intermediate colitis. The study time period was one year (June 2015-June 2016). A pretested questionnaire was used for patient evaluation. Data was analyzed using SPSS software version 20.0. Descriptive statistics (percentages, mean, SD) was used to describe the data. Results were reported in percentages, tables and charts for different variables according to nature of variable. An independent T-test was performed to observe the results before and after intervention.

Results:

Total 36 patients were included in this study with 1:1:1 in each group. The mean age of all patients in group 1(infliximab) was 22±10.2 SD while in group 2 (Adalimumab) the mean age was 25.3 ±11.3 SD and in group 3 (placebo) the mean age was 28.9±13.4 SD. There were 33% males and 67% females in group 1, 20% males and 80% females in group 2, 44% males and 56% females in group 3.

Out of all 36 patients 80% patients were diagnosed with crohn's disease while 20% were diagnosed with ulcerative colitis. The study found out that mean stool cal protection before intervention was 800 md/L±33.2 SD, 1,000 md/L±32.1SD and 11200 md/L±34.4 SD in infliximab, adalimumab and placebo respectively while after intervention the stool cal protection was found to be 100 md/L±8.4 SD, 350±9.2 SD and 500±10.5 SD respectively.

The present study found out that before intervention there were 40% patients presenting with ulcer plus stricture and vascularity, 10% presenting with pale mucosal few stricture, 15% vascularities with few ulcers while 10% with stricture ulceration, 10% stricture, ulcer, vascularity and only 5% ulceration massing. While after intervention there were 50% patients with few ulcers, 10% with improved vascularity, 15% with improved vascularity and few ulcers, 25% with decreased strictures and few ulcers (p<0.002, 95% CI). The study found out mean number of stools



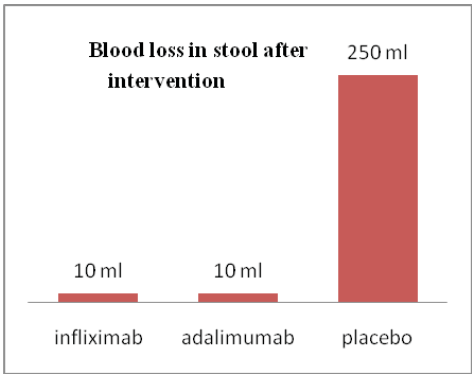


Figure 1: blood loss with stools before and after interventions

at 0 week were 8/d with 250 ml blood (22.3SD), 7/d with 250 ml blood (23.1 SD) and 8.5/d 300 ml blood (28.1SD) before intervention in infliximab group, adalimumab group and in placebo group respectively. While after intervention the mean no. of stools were 1/d with no blood (8.9 SD), 2/d with no blood (9.9 SD) and 7/d with 250 ml blood (23.4 SD) in infliximab, adalimumab and placebo group respectively. The study found that maintenance of remission varies from moderate to severe in study participants.

Discussion:

Present study was conducted to assess the response of biological agent in treatment of inflammatory bowel diseases. It was found that there is a positive response ($p<0.00$) in treatment of inflammatory bowel disease including Crohn's diseases and ulcerative colitis. While similar studies reported that infliximab induced a positive response ($p<0.001$) in treatment of crohn's disease.[9] The present study found that infliximab and adalimumab had maintenance of remission from moderate to severe in inflammatory bowel diseases. Evidence exit that 30% patients with an induction therapy of infliximab showed a clinical remission as compared to placebo group ($p=0.003$).[10]

Present study proved that Hb d/Dl, ESR mm/h and CRP mg/Dl in infliximab group were 12.5, 20 and 0.29 while in adalimumab group 11.0, 25 and 1.0 in placebo group 7.9, 50 and 7.9 after intervention. Similar studies reported that mucosal healing was observed in 27% patients with adalimumab.[11] While another study reported that complete closure of fistulas was observed in 33% of patients with adalimumab.[8] The present study found out that before intervention there were 40% patients presenting with ulcer plus stricture and vascularity, 10% presenting with pale mucosal few stricture, 15% vascularities with few ulcers while 10% with stricture ulceration, 10% stricture, ulcer, vascularity and only 5% ulceration massing. While after intervention there were 50% patients with few ulcers, 10% with improved vascularity, 15% with improved vascularity and few ulcers, 25% with decreased strictures and few ulcers ($p<0.002$, 95% CI). While similar studies reported that the in infliximab group decrease in ulcer was found to be in 30% of patients and reduction in vascularity was observed in 44% patients as compared to placebo.[12]

Limitation: Due to limited time period and resources the study was not able to find exact remission period that need a longer duration of follow up.

Conclusion:

Biological agents had a positive response in treatment of inflammatory bowel disease. These agents are responsible for reducing mucosal healing while infliximab is associated with better results for the treatment of crohn's disease and ulcerative colitis.

Conflict of interest: None

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Role and contribution of authors:

Dr Waseem Babur, Consultant Internal Medicine, Department of Medicine, King Salman Armed Forces Hospital, Tabuk, Kingdom of Saudi Arabia, Designing, data collection & analysis

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Dr Mubasher Hassen, Specialist Internal Medicine, Department of Medicine, King Salman Armed Forces Hospital, Tabuk, Kingdom of Saudi Arabia, conception & acquisition of data

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