Efficacy and Safety of Infliximab therapy in Inflammatory Bowel diseases in Iraqi patients.

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ABSTRACT

Background: Inflammatory bowel disease is a chronic disease need long-term use of steroids which have many disadvantages and side effects like irritation of the stomach lining, weight gain, increase in blood sugar and blood pressure levels and thinning of bones. Cytotoxic agents and, more recently, cyclosporine have emerged to become an important part of the therapeutic regimen for many autoimmune diseases. Nonetheless, these medications may still cause treatment-induced illness or even death. Infliximab is one of the biologic agents shown to be efficacious in the induction and maintenance of remission in patients with inflammatory bowel disease. It is a chimeric antibody to tumor necrosis factor-alpha (TNF-alpha). **Aim of the study:** To evaluate the patients with IBD treated with Infliximab in form of response, to lerability and safety. **Patients and methods:** A prospective study conducted at Baghdad teaching hospital during the period from the 1st of January 2013 to the 30th December 2013. A total of 50 patients who met the inclusion criteria were enrolled; 25 patients with ulcerative colitis and 25 patients with Crohn's disease. Patients were examined endoscopically and performed laboratory investigation. Infliximab was given in a dose of 5mg/kg in scheduled doses at weeks 0, 2 and 6 and a maintenance dose at 8 weeks interval and the patients were followed up, re-examined and investigated at each visit. Data collected by using a pre-constructed data collection sheet by history and clinical examination by expert professional gastroenterologist. Data were analyzed by using the statistical package for social sciences. **Results:** On treatment, a highly significant changes in the times of bleeding had been reported in both studied group (P=0.001), a highly significant improvement in bowel motion was also reported (P<0.001), 5 cases reported to be positive CRP all were converted negative at the third dose administration(P=0.001). A significant reduction in the mean ESR from the baseline had been reported in both studied group (P< 0.001). A significant increase in PCV from the baseline had been also reported (P<0.05). No significant changes had been observed in WBCs and platelets count (P>0.05). A significant weight gain amongstudied group had been found, the mean body weight at the baseline was 60.4 ±14.2 kg in UC group vs. 73.4 ± 19.1 kg at the last measurement (P=0.012), in theCD group; the mean body weight increased from 51.2 ± 13.9 kg at the baseline to70.6 ± 21.8 kg at the last measurement, (P=0.002).
Conclusion: Infliximab is a tolerable effective treatment in inflammatory bowel disease patients with severe disease form not responding to traditional treatment in both Crhon's disease and ulcerative colitis. The effect of infliximab was clear after short time through improvement in patients symptoms. No significantad verse effect had been developed due to initiation of Infliximab treatment and it was well tolerated by the patients.

Introduction:

Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), represents a chronic, relapsing and remitting inflammatory condition that effects individual throughout life. UC typically presents as a recurrent bloody diarrhea and abdominal pain. It is a diffuse mucosal and submucosal disease involving only the colon (1,2).CD is a chronic transmural disease causing inflammation in any segment of the alimentary tract, approximate 75% of the patients have small bowel involvement and 90% of these patients have disease in the terminal ileum. These two conditions share many common features-include chronic diarrhea, abdominal pain, gastrointestinal bleeding and weight loss. (1,2) Poorly controlled disease can result in the development of significant complications including intra-abdominal abscesses, intestinal perforation, fistulae, bowel obstruction, toxic megacolon, refractory rectal bleeding and repeated bowel resections resulting in short gut syndrome and malnutrition.(3)

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The etiology of IBD is still not very clear but different factors have been postulated as possible etiological agents; i.e. genetic factors, infective agents, immunological basis, smoking, medications and pathological factors. Medications like non-steroidal anti-inflammatory drugs (NSAIDS) can cause variety of effects in patients with IBD, including a symptomatic mucosal inflammation, strictures, obstruction and hemorrhage.(1) Alterations in the mucosal immune system are central to the pathogenesis of IBD. Inflammatory mediators such as cytokines, neutrophils, and reactive oxygen metabolites play a crucial role in the development and persistence of disease (4). Evidence suggests that the ensuing production of inflammatory cytokines can cause ulceration and increased intestinal permeability. Tumor necrosis factor appears to play a significant role in the pathogenesis; the uncontrolled immune system activation results in a sustained massive production of cytokines such as tumor necrosis factor (TNF) and interleukins. (5,6).

Natural history studies of IBD have demonstrated high rates of steroid dependence and steroid refractoriness resulting in the need for surgical intervention even after just one course of corticosteroid treatment(7,8).

Although conventional corticosteroids have been a major component of acute inflammatory bowel disease management, they have many serious disadvantages; and toxicity is heightened with chronic steroid therapy. (9)

The recognition that earlier and more aggressive control of inflammatory disease leads to fewer complications, decreased morbidity and improved quality of life, has resulted in an explosion in research related to the development of novel therapeutic agents. (10,11) Medical treatment of IBD includes five major categories, namely anti-inflammatory drugs, immunosuppressant, biologic agents, antibiotics, and drugs for symptomatic relief. Several other pharmaceutical substances have been produced and studied in recent years, the implementation of which was the result of an increased knowledge of the underlying pathophysiological mechanisms. (12,13)

Before the era of biologic therapy and the use of immunosuppressant agents, clinicians relied heavily on corticosteroids for symptoms relief in IBD, as they are rapidly and consistently improve moderate to severe active ulcerative colitis and Crohn's disease, but they are ineffective in the maintenance of remission in either illness. (14)

Immunogenetic pathways associated with innate and adaptive immunity, cytokines secreted by innate and adaptive immune cells, epithelial and leukocyte factors, and structures on the endothelium that regulate the recruitment of leukocytes define pathways that could be therapeutic targets.

Biologic agent has been shown to be effective at inducing and maintaining clinical remission. These medications are engineered to target the immune system in a very specific way. Infliximab is one of the biologic agent shown to be efficacious in the induction and maintenance of remission. It specifically destroys a pro-inflammatory cytokine called tumor necrosis factor (TNF-α), which is up regulated in Crohn's diseaseand chronic ulcerative colitis.(15,16,17) The expansion of therapeutic options has been accompanied by the need for increased knowledge related to therapeutic dosing, medication related side effects, adverse events, and appropriate usage.

Aim of The Study:

Aim of this study designed to illustrate the role , efficacy and safety of Infliximab in treatment of IBD in patients who failed to respond to other types of treatment.

Patients and methods:

Study design, sample characteristics and data collection

This was a prospective study conducted at Baghdad teaching hospitalduring the period from the 1st of January 2013 to the 30th December 2013.

A total of 50 patients were included, 25 were proved to haveulcerative colitis (UC group) and the other 25 cases were proved to haveCrhon's diseases (CD group). In both groups the diagnosis was madeaccording to the clinical findings, and previous endoscopic examination byexpert professional Gastroenterologist with histopathological proof. The study was intended to enroll patients with proved diagnosis UC or CD regardless their age andsex were considered eligible and treated with Infliximab. The following patients were excluded: recent severe bacterial or viral infection, anaemia of other causes with anticipated need for blood transfusion, Haemolytic disorder, Haemoglobinopathy, Asthma, eczema or other atopic allergy, History of previous drugallergic reaction, Lupus erythematosus, Pregnancy, severe cardiac, severe hepatic or renal or psychiatric disorders, fibrostenotic stricturing crhon's disease, Patients with malignancy, Multiple sclerosis, Patients with positive HBs Ag , and active or latent TB.

Data were collected by using a pre-constructed data collection form,through a full history and clinical examination of the patients. Thecollected data included:the age, sex,address, age at diagnosis, duration of the disease, smoking, alcoholdrinking, family history of IBD ,medical , surgical and drug history andbody weight with measure of BMI. Laboratory investigations that were sent include:

hemoglobin, PCV, WBC, ESR, CRP, RBS,Blood urea, serum creatinine , TSB, SGPT, SGOT, ALP , ANCA andTuberculin skin test.

Radiological examination including ultrasonography, chestX-ray and CT scanning. Endoscopic findings of pre- and post treatment, indications for initiation of Infliximab therapy and dosage were assessed with reviewing of all symptoms.

Initiation of Infliximab treatment, scheduled follow up and clinical assessment

After the completion of the clinical assessment and investigations of the patients Infliximab treatment was initiated in scheduled doses to begin infusions at 5 mg/kg with induction infusions at weeks 0, 2, and 6, followed by maintenance therapy every 8 weeks up to one year of the study. All the cases were followed up according to the scheduled infliximab doses, ateach visit the cases were assessed by history and clinical examination. Prior to giving the treatment checking the following: Changes in symptoms ; diarrhea ,bleeding and abdominal pain by taking full history from the patients , also patients were asked about any adverse reaction. Physical examination including the general status of the patients, vitalsigns and abdominal examination for tenderness or masses .Laboratory investigations: A sample of venous blood was drawn from each patients and sent for laboratory investigations including Hemoglobin, PCV, WBC count, platelets count, ESR , CRP , RFT & LFT.

Initiation of the scheduled dose of the infusion of infliximab wasperformed while the patient under observation to check for infusion hypersensitivity and adverse reaction. At each visit patient's weight was measured .All these data were reported in the case sheet of the patient and kept forthe next dose time.

Evaluation of disease severity and activity

According to the Crohn's Disease Activity Index (CDAI), remission ofCrohn's disease is defined as CDAI below 150. Severe disease was definedas a value of greater than 450.**(18)**Most major research studies onmedications in Crohn's disease define response as a fall of the CDAI ofgreater than 70 points than baseline CDAI.(18, 19).The Mayo score, was used for UC, that ranges from 0 to 12, with higher scores indicating moresevere disease. This score can be used for both initial evaluation andmonitoring treatment response.

(20) Ethical considerations

The study protocol was approved by local committee of scientific council of internalmedicine of the Arab board of health specializations, and the agreement of administration of Baghdad teaching hospital was obtained . The study participantswere informed about the nature of study, the expected benefits andhazards were explained to them prior to participate in this study.All patients were informed to contact gastroenterology out patient's clinic immediately when he/she developed an adverse effect.

Data management and Statistical analysis

At the last point of follow up which end at the 30th December 2013,after at least 6 months of follow up, data of all patients were entered and analyzed by using the statisticalpackage for social sciences (SPSS) version 20, IBM, US, 2010. Descriptivestatistics were presented as mean± standard deviation (SD), frequencies(numbers) and proportions(%). Students test was used to compare two means, chi square test was used to compare frequencies in addition to assess the significance of changes in times of diarrhea, bleeding and changes inpositivity of CRP. Analysis of variances (ANOVA) test was used to assess the changes in ESR, PCV, Platelets, WBC count and body weight. Level of significance (P.value) was set at < 0.05 as cutoff point for significance. Finally data and findings were presented in tables and figures with explanatory paragraphs.

Results:

The general characteristics of enrolled patients are shown in table 1. There was no significant difference between groups in mean age and age at time of diagnosis . No significant effect infrequency distribution according to gender, smoking and family history ($p> 0.05$); however, the disease duration was significantly longer in ulcerative colitis than in Crohn's disease ($p< 0.05$). Types and severity of diarrhea are shown in table 2.

No significant difference was observed between both groups regarding occurrence of diarrhea, its type or its severity ($p> 0.05$). Distribution of symptoms and findings of physical examination of patients is shown in table 3. There was no significant variation between study groups ($p> 0.05$). Medications are shown in table 4 with lack of significant variation between study groups ($p> 0.05$). Endoscopic findings are shown in table 5 with significant improvement in both study groups. Improvement of the patients with the infliximab administration according to the disease activity scores are shown in table 6. According to Mayo Scoring System for Assessment of Ulcerative Colitis activity which there was a significant reduction in the mean UC activity scores of the UC patients, the mean Mayo score was 7.0 ± 1.9 at the baseline (pre-treatment) reduced dramatically with the subsequent doses of infliximab to reach (1.5 ± 0.10) after the last dose , while in CD , the DAI was 242 ± 83 at the baseline (pre-treatment) reduced dramatically to 21 ± 6 after the last dose.

Changes in BMI with the subsequent administration of Infliximab Doses are shown in table 7. During the follow up period, there was a significant weight gain in both studied group, with the subsequent doses, the mean weight at the baseline was 60.4 ± 14.2 kg in UC group increased significantly to reach 73.4 ± 19.1 kg at the last measurement (*P*=0.012), the same trend with more significance had been observed in the CD group; the mean body weight increased from 51.2 ± 13.9 kg at the baseline to reach 70.6 ± 21.8 kg at the last measurement, (*P*=0.002).

Table 1:Demographic characteristics of patients

Characteristic	Ulcerative colitis *n* = 25	Crohn's disease *n* = 25	*p*
Gender			
Male, *n* (%)	12 (48.0 %)	10 (40.0 %)	0.780 C
Female, *n* (%)	13 (52.0 %)	15 (60.0 %)	NS
Age (years)			
Mean ±SD	35.70 ±11.8	38.70 ±10.5	0.350 I
Range	18-53	18-54	NS
Age at time of diagnosis (years)			
Mean ±SD	30.20 ±12.00	33.90 ±10.80	0.260 I
Range	13-50	13-50	NS
Smoking			
Current smoker, *n* (%)	2 (8.0 %)	5 (20.0 %)	0.290 C
Ex-smoker, *n* (%)	20 (80.0 %)	15 (60.0 %)	NS
Non-smoker, *n* (%)	3 (12.0 %)	5 (20.0 %)	
Family history			
n (%)	0 (0.0 %)	3 (12.0 %)	0.070 C NS
Disease duration (years)			
Median	5	3	0.023 M
Range	1-30'	1-18'	S

n: number of cases; **SD**: standard deviation; **C**: chi-square test; **I**: independent samples t-test; **M**: Mann Whitney U test; **NS**: not significant at $p > 0.05$; **S**: significant at $p \leq 0.05$

Table 2:Distribution of types and times of diarrhea among studied Group

Characteristic	ulcerative colitis *n* = 25	Crohn's disease *n* = 25	*p*
Frequency of diarrhea *n* (%)	25 (100.0)	25 (100.0)	---
Types			
Bloody, *n* (%)	23 (92.0 %)	21 (84.0 %)	0.380 C
Mucous, *n* (%)	1 (4.0 %)	2 (8.0 %)	NS
Watery, *n* (%)	1 (4.0 %)	2 (8.0 %)	
Severity			
< 4, *n* (%)	4 (16.0 %)	5 (20.0 %)	0.360 C
> 4, *n* (%)	21 (84.0 %)	20 (80.0 %)	NS

n: number of cases; C: chi-square test; NS: not significant at p> 0.05

Table 3:Distribution of symptoms and findings of physical examination of patients

Characteristic	ulcerative colitis *n* = 25	Crohn's disease *n* = 25	*p*
Abdominal pain	25 (100.0 %)	25 (100.0 %)	---
Weight loss	20 (80.0 %)	19 (76.0 %)	0.730 C NS
Tensmus	16 (640.0 %)	17 (68.0 %)	0.250 C NS
Hematemesis	0 (0.0 %)	3 (12.0 %)	0.240 C NS
Malena	4 (16.0 %)	3 (12.0 %)	0.500 C NS
Hematochezia	3 (12.0 %)	4 (16.0 %)	0.500 C NS
Vomiting	1 (4.0 %)	5 (20.0 %)	0.190 C NS
Arthralgia	3 (12.0 %)	4 (16.0 %)	0.500 C NS
Pallor	12 (48.0 %)	13 (52.0 %)	0.500 C NS

Data were expressed as number (%); n: number of cases; C: chi-square test; NS: not significant at p> 0.05

Table 4: Distribution of medications used by patients

Characteristic	ulcerative colitis *n* = 25	Crohn's disease *n* = 25	*p*
Steroid	20 (80.0 %)	24 (96.0 %)	0.190 C NS
Aminosaicylic acid	22 (88.0 %)	19 (76.0 %)	0.270 C NS
Azathioprine	21 (84.0 %)	20 (80.0 %)	0.710 C NS
Folic acid	23 (92.0 %)	22 (88.0 %)	0.400 C NS
Metformin	2 (8.0 %)	2 (8.0 %)	0.600 C NS
Antihypertesnive	2 (8.0 %)	2 (8.0 %)	0.600 C NS

Data were expressed as number (%); n: number of cases; C: chi-square test; NS: not significant at p> 0.05

Table 5: Endoscopic findings of patients

Characteristic	Previous endoscopy *n* = 25	Post treatment endoscopy *n* = 25
Ulcerative colitis		
Grade 0	0 (0.0 %)	17 (68.0 %)
Grade I	0 (0.0 %)	8 (32.0 %)
Grade II	0 (0.0 %)	0 (0.0 %)
Grade III	9 (36.0 %)	0 (0.0 %)
Grade IV	16 (64.0 %)	0 (0.0 %)
Crohn's disease		
Colonic	16 (64.0 %)	16 (64.0 %)
Cecal	9 (36.0 %)	9 (36.0 %)
Fistulating	5 (20.0 %)	2 (8.0 %)
Not fistulating	20 (80.0 %)	23 (92.0 %)

Data were expressed as number (%); Grade 0: Normal; Grade I: loss of normal vascular pattern or granularity; Grade II: granular mucosa with contact bleeding; Grade III: Spontaneous bleeding; Grade IV: Ulceration

Table 6:Improvement of the patients with the infliximab administrationaccording to the disease activity scores

Characteristic	ulcerative colitis *n* = 25	Crohn's disease *n* = 25
Baseline	7.0 ±1.9	242 ±83
Dose 1	7.0 ±1.5	180±61
Dose 2	5.0 ±1.4	150 ±30
Dose 3	1.5 ±0.75	120 ±22
Dose 4	1.5 ±0.6	80 ±20
Dose 5	1.5 ±0.11	60 ±10
Dose 6	1.5 ±0.10	21 ±6

Table 7:Changes in BMI with the subsequent administration of InfliximabDoses

Characteristic	Ulcerative colitis *n* = 25	Crohn's disease *n* = 25
Baseline	19.9 ±4.7	17.3 ±4.7
Dose 1	22.4 ±5.3	20.2 ±3.8
Dose 2	23.2 ±4.6	22.8 ±4.8
Dose 3	24.1 ±6.1	23.4 ±7.3
Dose 4	24.2 ±6.3	23.8 ±7.4
Dose 5	24.5 ±5.8	24.5 ±6.6
Dose 6	24.8 ±6.0	25.3 ±5.4
p	0.002	0.001

Discussion:

Infliximab (IFX) has become a cornerstone treatment in IBD and canbe successively administered with excellent tolerability in IBD patients **Katsanos K. et al (21)**. During the period of one year , 50 Iraqipatients with IBD of two groups UC and CD groups with 25 patients ineach , the mean age of the patients ranged between 18 and 54 years with amean of 35.7 ± 11.8 years and 38.7± 10.5 years, respectively, the age andage at diagnosis distribution revealed that 80% of the cases in bothstudied groups between 21 and 50 years . Thisfinding consistent with other studies and published literatures,**FerranteM et al**. **(22)**reported a median age of 38 years with a range of (27.4 - 52.2)years among 121 UC patients. Also our findings agreed that of **Molnar T etal**. **(23)**(Hungary, 2008) who reported a mean age of 39 years in 50 patientswith Crohn's disease and the range was (20 56) years. Many studies referred that IBD are most commonly diagnosed in late adolescenceand early adulthood, but diagnosis may occur in all ages **Katsanos K et al (21).** The gender of the studied groups, females were slightly more than males, in UCgroup male to female ratio was 0.9, and it about 0.7 in CD group, but of no statically significant differences . These findingsare close to that previously found by **Assche et al**. **(24)**and **Katsanos K etal (21)** , male to female ratio in these two studies were 1.1 and 1.3,respectively.The current study showed that 80% of the UC patients were ex-smokers,and 12% were non-smokers while 8% were current smokers thisindicated that current smoker were less likely to have UC. In CD cases,60% were ex-smoker, 20% were non-smoker and 20% were current smokers with no significant difference in between both groups. This consistent with that reported in United Kingdom in 2010 by **Aldhous MC et al (25)** in that study , ulcerative colitis was found more prevalent among ex-smokers and nonsmokers, whereas Crohn's disease is more prevalent among smokers . Smokers are 40% less likely to develop ulcerative colitis compared to those who have never smoked. Surgical history was positive in 32 patients, 2 of them had right hemicolectomy and ileostomy, one patient had colonic resection and one patient of CD had intestinal obstruction ended with laprotomy , the remaining patients had positive surgical history not related to the GIT; which reported in 25 patients represented 50% of the total patients in this study, nonetheless, no significant difference had been found in between UC and CD groups.

In the study of **Baumgart D. C. et al. (26)** in 2007, no patient had history of appendectomy , so they suggested that appendectomy might be protective against UC while the opposite is true for CD where it Is associated with raised risk of strictures.

The current study found none of the UC patients as well as only 2 (8%) of the CD patients had positive family history of IBD . This disagreed with what reported in previous studies (may be due to small number of patients) , which weresuggested a genetic basis for IBD, including familial clustering and racial and ethnic differences in risk for IBD. Studies have shown that 5% to 20% of affected individuals have a first degree relative (parents, child, 1 or sibling) with one of the diseases and suggesting a strong genetic component **Baumgart D. C. et al. (26)** and **Loftus E.(27) .**

Before starting biolobical therapy ,the median duration of the UC was 5 years and in CD group it was 3 years with, this finding in line with that found by **Sprakes M. et al. (28)** who reported median disease duration of 6 years, similarly other study conducted by **De Vos M. et al**. **(29)**found the mean disease duration of 6 years in UC. The present study found that all the UC and CD patients had one or more symptoms included bloody diarrhea; which was found in 92% of UC group and 48% of CD group, mucinous and watery diarrhea in only one (4%) of UC patients and 2 CD patients (8%), Weight loss reported in 80%and 76%, rectal pain in 64% and 36%, tenesmus in 48% and 32%, melena in 16% and 12%, Hematochezia in 12% and 16%, Vomiting in 4% and 20%, , Arthralgia in 12% and 16%, pallor in 48% and 52%, tenderness of abdomen in 28% and 20% of UC and CD patients, respectively. Hematemesis was only found in 12% of CD patients, while none of the patient had abdominal mass. This consistent with the natural history and clinical features of the IBD that mentioned in other studies and literatures which showed that UC and CD patients could presented with GI tract inflammation symptoms and or extra GI tract symptoms **Van A.G. et al (30).** In the current study, steroids, Amino-salicylic acid, azathioprine in addition to folic acid were used in majority of cases, some of them were used combinations of these medications, which were expected and consistent with that published about the treatment of IBD; where CD has similarities with UC treatment, and the traditional medical treatment had limited therapeutic efficacy and not curative with non-specific effects on the immune system, leading to significant systemic side effects, thus these drugs are effective in only few IBD patients to maintain remission and stop flare ups, this agreed what was reported in **Baumgart D et al.**

study (Germany, 2007).**(31).**The current study reported that during the scheduled visits of the patients for administration of IFX and follow up , all the vital signs and the laboratory investigations were within the normal levels in both UC and CD patients.

The endoscopic examination prior to administration of IFX revealed that 16 of the 25 UC cases had grade III or IV colitis, and all the CD cases had severe disease form, the endoscopic examination post treatment with biological therapy showed a significant improvement in all cases; all the UC patients had grade 0 (68%) or I (32%) at the last endoscopic examination and the CD group showed statistically significant improvement (92%) in their endoscopic findings including the decreasing in fistula size and reductionof inflammation .

In addition to the significant endoscopic improvement, a dramatic symptomatic improvement had been reported in almost all cases; even before a new endoscopic findings were obtained .

During the follow up period, there was a significant weight gain in both studied group, with the subsequent doses, the mean body weight in UC group at the baseline was 60.4 ± 14.2 kg and 73.4 ± 19.1 kg at the last measurement (*P*=0.012), the same had been observed in the CD group; the mean body weight was 51.2 ± 13.9 kg at the baseline and 70.6 ± 21.8 kg at the last measurement, (P=0.002). A significant reduction in bleeding per rectum had been reported in all cases in both UC and CD groups; Prior to administration of IFX, all patients experienced bleeding 2 -3 times improved dramatically after the first dose and none of the patients reported bleeding at the third dose. On the other hand, a significant reduction in bowel motion had been found in all cases; bowel motion\day, reduced subsequently with administration of each dose from 4/day prior to the induction of IFX to reach only 1-2 times\day at the 4th dose.

This is consistent with that reported by **Lichlenstein G et al** (USA 2002) **(32)** who reported normal or near normal bowel motion in 67% of the cases treated with IFX as compared to 32% in placebo group, and 76% of IFX group didn't had rectal bleeding at the week 12 of treatment.

CRP was positive in 5 cases (2 UC and 3 CD) all were negative after the third dose, , on the other hand the current study found a significant reduction in ESR as compared to baseline values; the mean ESR in UC group was 25.6 prior to induction of IFX and 11.1 after the 4th dose, in the CD cases the mean ESR was 24.9 at the baseline and 9 after the 4th dose of IFX.

These findings indicated a significant reduction in disease activity and consistent with that reported by **Vermeire S et al. (USA, 2006) (33)** who reported that decrease in CRP in response to therapy is objective evidence that the drug has a beneficial effect on gut inflammation and disease activity. In addition they concluded that using CRP and ESR together considered a good marker for disease activity and response to treatment. The current study found a significant increase in PCV had been reported during the follow up period, in both UC and CD groups the mean PCV at the baseline vs. the last dose was (37.2 vs. 48.5) in UC group and (37 vs. 47.6) in CD group respectively and this attributed to the significant reduction in bleeding and anemia.

No significant changes had been reported in WBC or Platelets counts in both studied groups with consequent doses of IFX, indicated the safety and effectiveness of IFX, nonetheless, severe infusion reaction had been reported in only one case in whom the infusion was stopped and hydrocortisone injection and antihistamine medications were given, additionally, mild skin reaction was reported in one UC patient (4%).

These findings are consistent with a study conducted by **Fidder et al**. (Belgium, 2009) **(34)** who reported skin eruption in 20% of 150 patients treated with IFX and most cases responded to topical steroids and severe infusion reaction was reported in only two patients in whom IFX to be discontinued. According to the findings of the present prospective study, at the last point of follow-up in December, 31, 2013(after one year of treatment) it had been observed that infliximab therapy induced a significant endoscopic improvement, sustained clinical benefit as determined by continued improvement in symptoms and last endoscopic examination. The least incident adverse effect and the laboratory findings indicated the safety and tolerability of infliximab. In a study conducted in Belgium in 2008, **Ferrante M et al(22)**reported that over a follow-up period of 17 - 49.8 months, 68% of the cases with initial response to IFX had a sustained clinical response. studies reported that clinical improvement was observed as early as week 2.In Netherlands in 2011, **DeVose M et al (29)**demonstrated, a very fast effectiveness of treatment observed 2 weeks after the first infusion and additional effect of second (and third) infusions was observed and predicted a remission at week 10. **Molnar T et al** (Hungary, 2008) **(23)**studied 50 CD cases and found that Infliximab induction therapy resulted in a beneficial effect lasting for at least 1 year in 44% of CD patients and 57.9% with luminal disease remained in steroid-free complete remission, while the fistulae persisted closed in only 35.5% of those presented with fistula.

Conclusions:

- Infliximab is a tolerable effective treatment in inflammatorybowel disease patients with severe disease form notresponding to traditional treatment in both Crhon's diseaseand ulcerative colitis.
- In most cases the effect of infliximab was clear after shorttime through improvement in patients symptoms.
- No significant adverse effect had been developed due toinitiation of Infliximab treatment and it was well tolerated bythe patients (Infusion reaction was

Reported in only onepatient and mild skin eruption and hypersensitivity reportedin another one patient).

Recommendations:

- Use of Infliximab in treatment of severe inflammatory boweldisease refractory to traditional treatment.
- Infliximab should be available to those cases for whomneed it is highly indicated.
- Further studies with larger sample size and longer follow upperiod are highly suggested for further evaluation of theefficacy and safety of Infliximab.

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