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Clinical efficacy of infliximab in Chinese patients with crohn's disease: a retrospective study.

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Abstract

Background: Infliximab (IFX) is used for the treatment of Crohn's disease (CD). However, there is still controversy on the efficacy and safety of IFX in CD patients. This study aimed to evaluate clinical efficacy and safety of IFX in Chinese CD patients.
Methods: Clinical data of 26 CD patients (16 males and 10 females) who received IFX treatment were retrospectively analyzed. C reactive protein (CRP) level, Crohn's disease activity index (CDAI) score and clinical remission were examined.
Results: Among 26 cases, 19 cases had inflammatory CD while 7 cases had fistulizing CD. At 14th week, CRP level and CDAI score decreased in all 26 patients. In addition, 16 achieved remission and remission rate was 61.5% at 14th week. At the end of follow-up, 14 patients achieved remission and remission rate was 53.9%. Among 7 patients with fistulizing CD, anal fistula was completely closed in 2 cases (28.6%) and partially closed in 5 cases (71.4%). Side effects were observed only in two patients, including one case of acute infusion reaction and one case of bellyache.
Conclusion: IFX could control inflammation, relieve syndrome and promote fistula closure in Chinese CD patients. IFX demonstrates good clinical efficacy and safety for CD treatment.

Keywords: Infliximab, Crohn's disease, Fistulizing crohn's disease, Fistula closure.

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Introduction

Crohn's disease (CD) is a form of inflammatory bowel disease that causes irritation in the gastrointestinal (GI) tract. CD mainly affects the lower small intestine or the colon [1]. The pathogenesis of CD remains not fully understood, but current theory is that CD develops from overactive T cell immune responses to a subset of enteric bacteria in genetically susceptible hosts, while environmental factors promote the progression of this disease [2]. Traditional pharmacological treatments for CD include 5-amino salicylic acid, corticosteroids, or immunosuppressive agents, but a considerable part of the patients develop no response to the drugs or are corticosteroid dependence. In recent years, a variety of biological agents have been developed for the treatment of CD. Among them, infliximab (IFX) is the first anti-tumor necrosis factor α (TNF-α) monoclonal antibody approved for CD therapy. However, there is still controversy regarding the efficacy and safety of IFX in CD patients [3]. In addition, few studies have reported the efficacy of IFX in Chinese patients with CD. Therefore, this study aimed to retrospectively evaluate clinical efficacy and safety of IFX in the treatment of Chinese CD patients.

Patients and Methods

Patients

From March 2012 to November 2013, 26 patients who were diagnosed as CD and received IFX (Janssen Pharmaceutical Co., Xian, China) treatment were included in this study, including 16 males and 10 females. CD was diagnosed based on conventional radiological, endoscopic, and histological criteria. IFX was administrated at 5 mg/kg dose in the first, the second and the sixth week, and then was administrated by intravenous injection every 8 weeks. All patients signed informed consent, and this study was approved by the Ethics Committee of the People's Hospital of Wuhan University.

Data collection

The data of all patients were collected, including the gender, age, the type and location of CD, CRP, clinical manifestations, anal fistula closure, and adverse reactions. Crohn's disease activity index (CDAI) was calculated before IFX treatment, 14 weeks after IFX treatment and at the end of follow-up.

Evaluation of treatment efficacy on CD

The efficacy of IFX treatment on CD was evaluated as described previously [4]. The efficacy was judged as good if

clinical symptoms of CD disappeared, X-ray or colonoscopy examinations revealed less inflammation, or CDAI score <150 points; the efficacy was judged as bad if clinical symptoms were not relieved, X-ray, endoscopy and pathological examinations revealed no improvement, or CDAI score >150 points.

Evaluation of fistula

The efficacy of IFX treatment on fistula was evaluated as described previously [5]. The efficacy was judged as good if the fistula was closed completely; as partial if the fistula had reduced drainage or smaller opening; as bad if the fistula drainage remained or developed new fistula.

Evaluation of adverse reactions

Any adverse events occurred during treatment were recorded. Adverse events included acute infusion reactions, abdominal pain, delayed hypersensitivity, infection and lymphoma.

Statistical analysis

All data were analyzed using SPSS 13.0 statistical software (SPSS Inc., Chicago, IL, USA). Numerical data were expressed as x ± s and analyzed by t-test, while categorical data were analyzed by x^2 test. P<0.05 was considered statistically significant.

Results

Basic data of the patients

Table 1. *Clinical data of the patients.*

		Total patients n=26	Inflammatory type n=19	Fistulizing type n=7
Gender	Male	16 (61.54%)	11 (42.31%)	5 (19.23%)
	Female	10 (38.46%)	8 (30.77%)	2 (7.69%)
Age (years)		31.21 ± 7.82	33.63 ± 6.54	29.26 ± 7.17
Age classification (years)				
A1: <18		1 (3.85%)	1 (3.85%)	0 (0%)
A2: 18-40		20 (76.92%)	14 (53.85%)	6 (23.08%)
A3: >40		5 (19.23%)	4 (17.39%)	1 (3.85%)
Disease locus				
L1: Intestinal		5 (19.23%)	4 (17.39%)	1 (3.85%)
L2: Intestinal colon		189 (69.23%)	13 (50.00%)	5 (19.23%)
L3: Colon		3 (11.54%)	2 (7.69%)	1 (3.85%)

A total of 26 CD patients were enrolled in this study, including 16 males and 10 females. Among them, 19 cases had inflammatory CD while 7 cases had fistulizing CD. The clinical data of 26 patients are shown in Table 1.

Efficacy of IFX treatment

At 14th week, CRP level and CDAI score decreased in all 26 patients compared to before treatment (P<0.05, Table 2). In addition, 16 patients achieved remission and remission rate was 61.5% at 14th week. At the end of follow-up, CRP level and CDAI score decreased in all 26 patients compared to before treatment (P<0.05, Table 3). In addition, 14 patients achieved remission and remission rate was 53.9%.

Table 2. *CRP level and CDAI score at 14 week after IFX treatment.*

	CRP level		CDAI score	
Time	Inflammatory type	Fistulizing type	Inflammatory type	Fistulizing type
	n=19	n=7	n=19	n=7
0 week	33.23 (7.23, 61.8)	31.31 (6.83, 59.21)	360.9 ± 131.2	354.1 ± 128.4
14th week	3.61(1.89, 7.64)	3.54 (1.64, 6.98)	162.2 ± 85.3	148.3 ± 75.3
P value	<0.05	<0.05	<0.05	<0.05

CRP: C reactive protein; CDAI: Crohn's disease activity index

Among 7 patients with fistulizing CD, anal fistula was completely closed in 2 cases (28.6%) and partially closed in 5 cases (71.4%). The time for IFX treatment was significantly longer for 7 patients with fistulizing CD than for 19 cases with inflammatory CD (37.13 weeks vs. 24.84 weeks, P<0.05).

Table 3. CRP level and CDAI score at the end point of follow-up after IFX treatment.

	CRP level		CDAI score	
Time	Inflammatory type	Fistulizing type	Inflammatory type	Fistulizing type
	n=19	n=7	n=19	n=7
0 week	33.23 (7.23, 61.8)	31.31 (6.83, 59.21)	360.9 ± 131.2	354.1 ± 128.4
endpoint	3.45 (1.92, 6.54)	3.36 (1.56, 6.33)	146.5 ± 79.3	140.1 ± 72.8
P value	<0.05	<0.05	<0.05	<0.05

CRP: C reactive protein; CDAI: Crohn's disease activity index

Adverse effects of IFX treatment

Among 26 patients treated with IFX, 2 patients developed side effects. One case had acute infusion reaction with local neck rash, and the rash disappeared after intramuscular injection of phenergan. The other case had bellyache, and the pain relieved without treatment.

Discussion

IFX is a human mouse chimeric monoclonal antibody against TNF-α and has therapeutic effects on inflammatory diseases by antagonizing the inflammatory factor TNF-α. IFX is the first novel biologics approved by the US Food and Drug Administration (FDA) for CD treatment. A large randomized controlled study confirmed that IFX was effective for the treatment of patients with active CD and fistulizing CD [4].

In this study, we found that short-term IFX treatment could reduce CRP levels, indicating that IFX has good effect in controlling CD by inhibiting inflammatory response. IFX led to remission rate of 61.5% after 14 weeks treatment and remission rate of 53.9% at the follow-up endpoint. These data are consistent with the literature [4]. A recent study reported that the combined use of IFX and immunosuppressant for one year could successfully treat CD, but CD recurred in nearly 50% of patients within 1 to 2 years after the use of IFX was stopped (5). Therefore, longer follow-up studies are needed to validate the efficacy of IFX on CD.

Depending on the nature of the disease, CD can be divided into inflammatory and fistulising CD. Selective treatment of high-risk patients for CD by IFX could change the disease course and promote the healing of the mucosa [6]. In this study we showed a higher response rate of anal fistula to IFX therapy in 7 patients with fistulising CD, in that anal fistula was completely closed in 2 cases (28.6%) and partially closed in 5 cases (71.4%).

IFX has been documented to cause a variety of adverse reactions including acute infusion reactions, delayed hypersensitivity, and drug-induced lupus, infection, lymphoma and other malignancies. In this study, we only found acute infusion reactions and acute abdominal pain as the adverse reactions of IFX therapy and the incidences of these reactions (4.35%) were similar to those reported in previous studies [7,8]. In addition, two cases of adverse reactions did not severely affect the patients. And we found no severe infection or malignancy in all patients after IFX therapy. This may be related to our comprehensive assessment of the patients before their enrolment, or the limited duration of our follow-up. Long-term follow-up studies are necessary to confirm that IFX could not induce serious adverse reactions in Chinese patients with CD.

This study has some limitations. First, we did not include a placebo control group. Second, our study was not blinded. Third, the sample size is relatively small. We could only enroll 26 CD patients in this study. Further studies with larger sample size are needed to evaluate the efficacy and safety of IFX in Chinese CD patients.

In conclusion, our data suggest that IFX could control inflammation, relieve syndrome and promote fistula closure in Chinese CD patients. IFX demonstrates good clinical efficacy and safety for CD treatment.

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