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Effects of combined therapy of traditional Chinese medicine and western medicine on platelets, coagulative functions and inflammatory cytokines with ulcerative colitis

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ABSTRACT

Objective: To explore the effects of combined therapy of traditional Chinese medicine and western medicine on platelets, coagulative functions and inflammatory cytokines in patients with ulcerative colitis (UC). **Methods:** A total of 267 patients with UC were collected. 137 patients were treated with combined therapy of traditional Chinese medicine and western medicine as experimental group and 130 patients were treated with only western medicine as controls. Platelet count, coagulation function indexes and inflammatory cytokines were measured before and 15 d after the treatment. **Results:** No significantly differences were found in all indexes before treatment between two groups. After different treatments, platelet count (PLT), platelet distribution width (PDW) were significantly decreased in both groups, but mean platelet volumn (MPV) were significantly increased than before treatment. PLT and PDW were significantly lower and MPV were significantly higher in experimental group than control group. Fibrinogen (Fib) and D-dimer (DD) decreased significantly after treatment. Fib and DD in experimental group were significantly lower than controls. No significantly differences were found in activated partial thromboplastin time (APTT) and prothrobin time (PT). Tumor necrosisi factor-α (TNF-α), interleukin-6 (IL-6) and interleukin-8 (IL-8) decreased significantly in both group after treatment. TNF-α, IL-6 and IL-8 were significantly lower in experimental group than controls. **Conclusion:** Combined therapy of traditional Chinese medicine and western medicine can more effectively improve the cogulation, fibrinolysis and inflammation in patients with UC than only western medicine therapy.

1. Introduction

Ulcerative colitis (UC) is a chronic nonspecific inflammation of intestine, its incidence rate is rising in China and one of the modern refractory disease listed by WHO[1]. Rapid onset of Western medicine therapy, but long-term use of drug has side effects and poor patient compliance[2]. Traditional Chinese medicine therapy is mainly removing heat and dampness, soothing liver and strengthening spleen and warming spleen and stomach for dispelling cold[3]. We used oral administration of Western medicine combined with traditional Chinese medicine enema for UC patients treatment. Through a series of indexes of peripheral blood detection before and after treatment, we aims to explore the effects of combined therapy of traditional Chinese medicine and western medicine on platelets, coagulative functions and inflammatory cytokines in patients with ulcerative colitis (UC).

2. Data and methods

2.1. General information

A total 267 cases patients with UC who admitted to the hospital of traditional Chinese Medicine Hospital Affiliated to Xinjiang

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Medical University from December 2012 to December 2015 were selected. All patients were in accordance with the diagnostic criteria of Digestive Disease Branch of the Chinese Medical Association in 2007 Ji'nan meeting[4], and completed colonoscopy. According to the classification of the disease, mild 73 cases, moderate 91 cases and severe 103 cases; The lesions were 146 cases in straight sigmoid colon, 76 cases in the left colon and 45 cases in the whole colon. All patients did the relevant examination to exclude the associated systemic diseases which affect the outcome of the indexes and no use of drugs with effect on coagulation function within the past 3 months. According to the voluntary, patients were divided into two groups. The observation group used combination therapy of traditional Chinese and Western Medicine, a total of 137 cases, including 76 male and female 61 cases, age from 17 to 74 years old, with an average (43.16±8.28) years. The control group used simple western medicine therapy, a total of 130 cases, including 73 male and female 57 cases, age from 18 to 72 years old, with an average (42.79±8.19) years. There were no significant differences in gender, age, and other information between the two groups (P>0.05).

2.2. Methods

2.2.1. Treatment program

The observation group was given oral administration of Western medicine add traditional Chinese medicine decoction enema treatment. Western medicine was Etiasa (mesalazine, manufacturers: France love the hair pharmaceutical company), 4 times a day, each time 1g, with meals to take; Traditional Chinese medicine enema prescription: phellodendron, garden burnet, Bletilla hyacinthina Reichb, pseudo-ginseng powder, Fructus Mume, radix salviae miltiorrhizae, Rhizoma Coptidis, myrobalan flesh and pearl powder, each 10 g, pan fried two times and mixed, concentrated into 200 mL, carried out enema after bowel movements every night, the drug retention time was at least 20 min. The control group was given simple western medicine oral therapy, given Editha, 4 times a day, each time 1g, with meals to take.

2.2.2. Detection methods

Platelet and correlation coefficient were detected by Japanese Sysmex company's automatic blood cell analyzer (model: XS-800I) with matching reagent; Coagulation function indexes were determined by the Japanese Sysmex company's fully automatic coagulation analyzer (model: CA-1500) and the matching reagents; TNF-α, IL-6 and IL-8 were measured using the German SIEMENS automatic immunoassay analyzer (model: Immune 1000) and the matching reagents. A total of three venous blood were taken 48 h after admission, 15 d after treatment, and used for the blood platelets and the related parameters, blood coagulation function and inflammatory factors detection.

2.3. Statistical treatment

Using SPSS 19.0 software for statistical analysis, the measurement data were expressed by (Mean ± SD), the observation group and the control group were compared using independent sample t test, the same patient before and after treatment were compared using paired t test, P<0.05 was considered the difference to be statistically significant.

3. Results

3.1. Comparison the platelet and platelet related parameters of the two groups before and after treatment

Before treatment, there had no significant differences in platelet count (PLT), platelet distribution width (PDW) and mean platelet volume (MPV) between the observation group and the control group (P>0.05). After different treatments, PLT, PDW were significantly decreased in both groups, while MPV were significantly increased than before treatment (P<0.05). PLT and PDW in the observation group were significantly lower that in the control group (P<0.05), while MPV were higher than that in the control group, but the difference had no statistical significance (P>0.05). See table 1.

Table 1.
Comparison the platelet and platelet related parameters of the two groups before and after treatment.

Group	n	Time	PLT ($\times10^9$/L)	MPV (fL)	PDW (fL)
Observation	137	Before treatment	326.42±70.52	7.62±.3.33	17.92±3.28
		After treatment	288.61±69.31[ab]	8.92±3.25[a]	14.33±2.94[ab]
Control	130	Before treatment	316.77±69.37	7.75±2.99	18.18±3.42
		After treatment	302.16±70.16[a]	8.69±3.18[a]	15.82±3.09[a]

Ps: Compared with before treatment, [a]P<0.05; Compared with the control group after treatment, [b]P<0.05.

3.2. Comparison the coagulation function of the two groups before and after treatment

Before treatment, there had no significant differences in fibrinogen (Fib), partially activated prothrombin time (APTT), prothrombin time (PT) and D- dimer (DD) levels between the observation group and the control group (P>0.05). After different treatments, Fib and DD were significantly decreased in both groups (P<0.05) and Fib and DD in the observation group were significantly lower that in the control group (P<0.05), while APTT and PT had no significant differences between the two groups before and after treatment (P>0.05). See table 2.

3.3. Comparison the inflammatory factors levels of the two groups before and after treatment

Before treatment, there had no significant differences in the inflammatory factors TNF- α , IL-6 and IL-8 between the observation group and the control group (P>0.05). After different treatments, TNF- α , IL-6 and IL-8 were significantly decreased in both groups (P<0.05) and TNF- α , IL-6 and IL-8 in the observation group were significantly lower that in the control group (P<0.05). See table 3.

4. Discussions

UC is a chronic nonspecific inflammatory disease caused by a variety of causes, with lifelong recurrent infection and can occur at any age. Western medicine believes that the cause of this disease is not yet clear, and often considered it related to abnormal immune and inflammatory mediators[5]. The traditional Chinese medicine believes that it related to emotional hurt, eating disorders, emotional feelings of evils and the weakness of the spleen and stomach[6]. In the treatment, western medicine mainly with oral aminosalicylic acid, antibiotics and steroids drugs, after treatment remission, surgical treatment can be carried out[7]. Recent studies have reported the use of immunosuppressive agents, immunomodulatory agents, inflammatory inhibitors and other drugs, but the curative effect and side effect has not yet clear [8]. Traditional Chinese medicine considered that in acute attack stage, the main is to clear away heat and dampness, in Relief period, the main is to strengthening the spleen and replenishing qi[9,10]. However, there are some limitations in simple use of Western medicine or traditional Chinese medicine treatment, and the combination of traditional Chinese and Western medicine therapy makes up the deficiency of single therapy.

In our study, the combination of traditional Chinese and Western medicine treatment program was oral administration of Western medicine plus enema. In the rapid remission of clinical symptoms, at the same time, through the traditional Chinese medicine conditioning, can significantly improve the efficacy. The effective components of mesalazine is 5-ASA, mainly effect on small intestine and colon, through inhibiting the formation and release of inflammatory mediators to improve UC symptoms and slow down the process. Compared with the traditional salazosulfapyridine (SASP), one more 5-ASA molecule can improve the curative effect and reduce the adverse reaction of the drug[11]. Traditional Chinese medicine enema prescription was phellodendron, garden burnet, Bletilla hyacinthina Reichb, pseudo-ginseng powder, Fructus Mume, radix salviae miltiorrhizae, Rhizoma Coptidis, myrobalan flesh and pearl powder, it has the effects of clearing away heat and toxic material, regulating qi blood and heal sore muscle, drugs can directly arrive the lesion, its effective components directly in the intestinal absorption, improve the drug concentration in the lesion site, while protecting the intestinal ulcer surface, improving local blood circulation and promoting ulcer healing.

In UC activity period, endothelial cell injured and platelet activated, the activated platelets can stimulate the secretion of inflammatory factors, which aggravate the inflammatory reaction and the progress of disease. According to the research, UC patients blood is in hypercoagulable state, the occurrence probability of thrombotic disease increased, which is one of the causes of death in patients with UC[12,13]. Studies have shown that platelet count increased, the proportion of small platelets increased and the platelet volume distribution was not uniform in UC activity period, suggesting that platelet plays an important role in the development of UC[14]. Our study showed that the platelet and platelet related parameters were significantly improved after different treatment schemes, it was consistent with literature reports[12-14], after treatment of combined traditional Chinese and Western medicine therapy, each index was

Table 2.
Comparison the coagulation function of the two groups before and after treatment.

Group	n	Time	Fib (g/L)	APTT (s)	PT (s)	DD (μg/L)
Observation	137	Before treatment	4.63±1.22	30.11±6.51	12.02±1.22	606.18±113.52
		After treatment	3.05±0.95^{ab}	29.36±5.98	11.91±1.06	239.68±68.25^{ab}
Control	130	Before treatment	4.66±1.25	30.33±6.24	11.95±1.21	603.34±111.73
		After treatment	3.84±1.03^{a}	29.63±5.73	11.86±0.98	341.42±78.01^{a}

Ps: Compared with before treatment, ^{a}P<0.05; Compared with the control group after treatment, ^{b}P<0.05.

Table 3.
Comparison the inflammatory factors levels of the two groups before and after treatment.

Group	n	Time	TNF- α (ng/mL)	IL-6 (ng/mL)	IL-8 (ng/mL)
Observation	137	Before treatment	264.89±77.58	195.32±58.35	203.46±41.64
		Aftertreatment	125.37±52.16^{ab}	101.14±55.61^{ab}	93.01±12.98^{ab}
Control	130	Before treatment	261.77±76.36	193.28±61.41	203.92±41.20
		Aftertreatment	186.39±62.84^{a}	157.12±53.14^{a}	123.63±26.60^{a}

Ps: Compared with before treatment, ^{a}P<0.05; Compared with the control group after treatment, ^{b}P<0.05.

significantly better than simple western medicine, which indicated that this therapy can effectively improve the platelet abnormal state in UC patients.

Coagulation function detection is the most direct indicator to reflect the high coagulation state in patients. Studied showed that intestinal inflammation can activate coagulation and fibrinolysis cascade, D-two dimer, fibrinogen and other products tend to promote platelet function and aggravate the course of disease[15,16]. Our study found that the fibrinogen and D-two dimer were significantly decreased after treatment, while the combination of traditional Chinese and Western medicine treatment decreased more significantly, which indicated that this therapy was more effective than western medicine oral therapy in improving the high coagulation and secondary fibrinolysis in patients with UC and slowing down the progression of UC.

One of the important causes of UC is the imbalance between pro-inflammatory and anti-inflammatory cytokines *in vivo*. TNF-α, IL-6, and IL-8 are produced by activated mononuclear macrophages, and can cause gut inflammation and the onset of UC, so they can be used for UC condition judgment[17,18]. TNF-α, IL-6 and IL-8 were all significantly increased in the UC activity period[19,20]. Our study showed that after treatment, the inflammation factor levels were significantly decreased, and the combination of traditional Chinese and Western medicine treatment decreased more significantly, which indicated that this therapy has powerful anti-inflammatory effect, can significantly reduce the intestinal mucosa tissue inflammatory injury. In summary, combined therapy of traditional Chinese medicine and western medicine can more effectively improve the cogulation, fibrinolysis and inflammation in patients with UC than only western medicine therapy. But because the observation time is only 15 d after treatment, the indexes has not completely returned to normal levels, so its long-term efficacy and the observation of UC recurrence still needs further research.

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