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Therapeutic Effects of Mesalazine Enteric-Coated Tablets Combined with Low Molecular Heparin on Ulcerative Colitis and Influence on The Hypercoagulable State

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ABSTRACT

Objective: To evaluate the therapeutic effects of mesalazine enteric-coated tablets combined with low molecular heparin on ulcerative colitis and the influence on the hypercoagulable state.

Methods: A total of 100 patients suffering from ulcerative colitis and hospitalized in Department of Gastroenterology of our hospital from January 2017 to December 2019 were collected and divided into two groups (n=50) using a random number table. Control group was administered with mesalazine enteric-coated tablets and observation group was administered with mesalazine enteric-coated tablets combined with low molecular heparin. The overall response rate, symptom score, inflammatory factors in the serum, blood rheology indices, quality-of-life score, and incidence rate of adverse reactions were compared between the two groups.

Results: The overall response rate was 96.00% in observation group, higher than that in control group (82.00%) (P<0.05). The symptom scores involving abdominal pain, diarrhea and hematochezia after treatment were lower than those before treatment in the two groups (P<0.05), whereas they were lower in observation group than those in control group after treatment (P<0.05). C-reactive protein (CRP), interleukin-6 (IL-6) and procalcitonin (PCT) decreased significantly after treatment compared with those before treatment in the two groups, and observation group had lower CRP, IL-6 and PCT than control group after treatment (P<0.05). In comparison with those before treatment, there were significant decreases in hematocrit (HCT), erythrocyte sedimentation rate (ESR) and plasma viscosity (PV), after treatment in the two groups, and they were also lower in observation group than those in control group after treatment (P<0.05). The quality-of-life score after treatment was higher than that before treatment in the two groups (P<0.05), and the above score after treatment in observation group was higher than that in control group (P<0.05). No significant difference was found in the incidence rate of adverse reactions between the two groups, which was 6.00% in observation group and 4.00% in control group (P>0.05).

Conclusion: Mesalazine enteric-coated tablets combined with low molecular heparin in the treatment of ulcerative colitis can effectively alleviate relevant symptoms, reduce inflammatory response and hypercoagulable states and help improve the quality of life, with obvious efficacy, few adverse reactions and high safety.

KEYWORDS: gastroenterology; ulcerative colitis; mesalazine enteric-coated tablet; low molecular heparin

INTRODUCTION

Ulcerative colitis refers to the ulcerative lesion gastrointestinal tract diseases clinically. The

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occurred in colon; it is one of the common patients will have such symptoms as abdominal pain, diarrhea and hematochezia after the incidence of such a disease, which affects their daily life seriously and obviously decreases their quality of life [1-3]. Mesalazine enteric-coated tablets, a commonly used type of drug in treatment of ulcerative colitis in clinic, can alleviate symptoms in a certain degree [4]. However, some patients administered with mesalazine enteric-coated tablets alone manifest unsatisfactory efficacy. An existing study pointed out that low molecular heparin can effectively relieve the blood hypercoagulable states of the patients with ulcerative colitis to enhance the treatment efficacy [5]. Therefore, in this study, from January 2017 to December 2019, a total of 100 ulcerative co-colitis patients were collected and randomised in two groups (n=50) for a therapeutic effect combined to Low Molecule Heparin tablet on ulcerative colitis in the In-Patient Department of Gastroenterology of our hospital. The mesalazine enteric-coated tablets and mesalazine enteric-coated tablets combined with low molecular heparin in both groups were individually given. The

MATERIALS AND METHODS

Baseline clinical data

A total of 100 patients with ulcerative colitis hospitalised in our hospital's Department of Gastroenterology from January 2017 to December 2019 were assigned to two groups of 50 patients in each group using a randomised number table. The control group consisted of 27 males and 23 females aged 21-63 years, with an average age of (42.75 ± 8.37) years. The observation group consisted of 26 males and 24 females aged 21-64 years and (42,93 ± 8,45) years on average. Age and gender were comparable between both groups (P>0.05). This study was in accordance with the ethical principle set out in the Helsinki Declaration, and patients agreed to participate in the study with informed consent.

Inclusion criteria: (1) Patients who have been diagnosed with ulcerative colitis following clinical observation of symptoms, anorectal endoscopy and laboratory tests, (2) patients ≥ 20 years of age, and (3) those who have been conscious and have been able to coordinate to complete this study.

Exclusion criteria: (1) patients with severe hepatic or renal dysfunction, (2) patients with mental disorders, (3) patients with a history of drug allergy, (4) patients with other gastrointestinal disorders, or (5) patients who withdrew or did not complete treatment in the middle of the study.

Methods

In control group, mesalazine enteric-coated tablets (Jia Mu Si Luling Sunflower Pharmaceutical Group Co., Ltd., NMPN: H19980148) were administered orally for 2 weeks consecutively (1.0 g each time, 4 times per day). For 2 weeks, mesalazine enteric-coated tablets with low-mollecular heparin (GS K Tianjin Company Limited, NMPN: H20080480) had been treated in patients in the observation group. Specifically, mesalazine enteric-coated tablets were administered *as per* the methods in control group, and low molecular heparin was subcutaneously injected once a day (4100 U/time).

Observation indices

Comparison was made between the 2 groups of the total responses, symptom size, serum inflammatory factors, blood rheology indices, quality of life and the incidence rate of adverse reactions. Evaluation criteria for therapeutic effects [6]: (1) Cured: All the symptoms disappeared, and no abnormality was found by anorectal endoscopy. (2) Improved: All the symptoms were alleviated, and decreased area of colonic ulcer was detected by anorectal endoscopy. (3) Ineffective: All the symptoms were not alleviated, and the area of colonic ulcer had no change or was even increased. Overall response rate = cured rate + improved rate.

Symptom score: Visual Analog Scale (VAS) was used to assess the severity of abdominal pain, diarrhoea and hematochezia. The lowest score was 0 points and the highest score was 10 points. Higher scores meant more severe symptoms. Serum inflammatory factors were measured as the immune-reactive proteins, interleukin (IL-6) and procalcitonins. Blood rheology indices: Hematocrit (HCT) and erythrocytes (ESR) tested with a flow-cytometer and plasma viscosity (PV) was determined using a serum inflammatory factors, including immune-reactive turbidimetry, enzyme-linked immunosorbent assay, and immunochromatographic assays, respectively

Quality-of-life score [7]: The WHOQOL-BREF composed of four items such as physiology, psychology, environment and social relationship, was used for evaluation, each item was scored 0-100 points, and a higher score suggested better quality of life.

Statistical analysis

SPSS 26.0 has been used for statistical analyses. For square metering and for the quantitative data (t-test), numeric data (n) were tested. A major difference with P<0.05 was suggested.

RESULTS

Overall response rate

In the observational group, the overall response rates were 96.00 percent above that of the control group (82.00 percent) (P<0.05) (Table 1).

Table 1. **Overall response rates [n (%)]**

Group	n	Cured	Improved	Ineffective	Overall response rate
Control	50	20 (40.00%)	21 (42.00%)	9 (18.00%)	41 (82.00%)
Observation	50	25 (50.00%)	23 (46.00%)	2 (4.00%)	48 (96.00%) *

*P<0.05 *vs.* control group

Symptom scores

Following treatment, abdominal pain, diarrhoea, and hematochetia symptoms were lower after treatment in the two groups (P < 0.005) than before, compared to post-treatment control groups (P < 0.05) (Table 2).

Table 2. **Symptom scores ($\bar{x} \pm s$, point)**

Group	Time	Abdominal pain	Diarrhea	Hematochezia
Control (n=50)	Before treatment	6.35±1.39	6.18±1.42	5.92±1.27
	After treatment	4.98±1.13#	4.87±1.16#	4.66±1.05#
Observation (n=50)	Before treatment	6.26±1.41	6.04±1.53	5.81±1.32
	After treatment	3.87±0.94#*	3.72±0.98#*	3.61±0.90#*

#P<0.05 *vs.* before treatment within the group, *P<0.05 *vs.* control group.

Serum inflammatory factors

CRP, IL-6 and PCT after treatment in both groups were significantly lower than before, with CRP, IL-6 and PCT decreased compared to the control group (P<0.05), respectively following therapy (Table 3)

Table 3. **Serum inflammatory factors ($\bar{x} \pm s$)**

Group	Time	HCT (%)	ERP (mm/h)	PV (mp·s)
Control (n=50)	Before treatment	38.49±5.23	28.53±5.89	2.45±0.59
	After treatment	32.14±4.02#	22.06±5.23#	1.76±0.43#
Observation (n=50)	Before treatment	38.31±5.29	28.32±5.95	2.41±0.53
	After treatment	27.65±3.47#*	16.41±4.48#*	1.29±0.37#*

#P<0.05 *vs.* before treatment within the group, *P<0.05 *vs.* control group.

Blood rheology indices

Compared to previous treatments, the HCT, ESSR and PV after treatment in the two groups were decreased significantly, and HCT, ESR and PV were lower after treatment in the observation group than in the control group (P<0.05) (Table 4).

Table 4. **Blood rheology indices ($\bar{x} \pm s$)**

Group	Time	CRP (mg/L)	IL-6 (ng/L)	PCT (ng/mL)
Control (n=50)	Before treatment	9.83±1.61	26.54±3.09	1.95±0.34
	After treatment	8.20±1.47#	23.56±2.41#	1.62±0.31#
Observation (n=50)	Before treatment	9.72±1.64	26.29±3.15	1.93±0.37
	After treatment	6.69±1.29#*	20.34±2.10#*	1.30±0.29#*

#P<0.05 *vs.* before treatment within the group, *P<0.05 *vs.* control group.

Quality-of-life score

In contrast to prior therapy in both groups (P<0.05), the quality-of - life score was increased after therapy and the above after therapy in observation group was higher than in the control group (P<0.05) (Table 5).

Table 5. **Quality-of-life scores ($\bar{x} \pm s$, point)**

Group	Time	Physiology	Psychology	Environment	Social relationship
Control (n=50)	Before treatment	70.29±5.09	70.58±5.14	71.20±5.38	70.02±5.03
	After treatment	76.94±6.48#	77.05±6.17#	78.04±6.32#	77.35±6.53#
Observation (n=50)	Before treatment	70.45±5.04	70.75±5.19	71.39±5.47	70.25±5.10
	After treatment	84.57±7.01#*	84.39±6.76#*	85.90±6.91#*	85.52±6.84#*

#P<0.05 *vs.* before treatment within the group, *P<0.05 *vs.* control group.

Incidence of adverse reactions

Following administration, there were 2 cases of ecchymosis and 1 case of nausea in the observation group as well as 1 case of nausea and 1 case of vomiting in the control group. There was no significant difference in the incidence rate of adverse reactions between the two groups of 6.00 per cent in the observation group and 4.00 per cent in the control group (P>0.05).

DISCUSSION

Ulcerative colitis is a kind of gastrointestinal tract lesion with a high morbidity rate, and its major clinical feature is focal and ulcerative lesions in colon. In recent years, more and more people have been diagnosed with ulcerative colitis due to changes of dietary structures and habits. At the onset of ulcerative colitis, patients will have abdominal pain, diarrhea, hematochezia and other symptoms. But as the disease develops, the expansion of focal and ulcerative lesions in colon is easy to cause intestinal perforation and necrotic lesions, even damage the skin, joints and other tissues in some patients, and lead to systemic symptoms such as high fever and fatigue, thereby bringing serious physical and mental damage to patients [8-10].

Active treatment of ulcerative colitis is supported in clinic, but the pathogenesis of the disease is unclear despite the hypotheses that ulcerative colitis is mostly associated with inflammation, infection and imbalance of intestinal flora [11]. Mesalazine enteric-coated tablets are a kind of aminosalicylic acid preparation which is the main drug for the treatment of ulcerative colitis in clinical practice. After oral administration, mesalazine enteric-coated tablets will delay the release of efficacy. Moreover, they are barely absorbed in the small intestine and primarily enter the colon to decompose into 5-aminosalicylic acid rapidly, which can form complexes with intestinal connective tissues. Besides, it can retain in such tissues for a long time to inhibit the activity of pathogens in the colon, reduce the release of inflammatory factors, and correct the imbalance intestinal floras into a balanced state, thus controlling the condition of the disease [12].

The emerging ulcerative colitis, with the exception of inflammation and infections, has been clinically established in recent years. Ulceratory colitis patients are usually in hypercoagulated conditions, so the search of effective therapeutics for ulcerative colitis for "hypercoagulable blood-relieving states" may be seen as a breakthrough in the clinical treatment of this condition. Low heparin molecular is one of the most common anticoagulants in clinical practise. The medicine can influence coagulation factors IIa and Xa to prevent activation and aggregation of platelets and reduce the risk of thrombosis and resistance of blood flow in the vessels, so that the hypercoagulable state of the blood can be alleviated [13]. The results of this study were as follows : (1) The overall response rate of the observer group was 96.00%, which was higher than that of the control group (82.00%), whereas the symptoms including abdominal pain , diarrhoea and hematochezia were lower for the observational group than those of the control group after therapy (P<0.05). (2) CRP, IL-6, and PCT were lower than those of a control group in the observation group after treatment (P<05); this indicates that low molecular heparin in combination with entero-coated tablets with tablelazine can significantly decrease inflammatory factors. (3) HCT, ESR and PV were decreased in observation group, compared to P < 0,05 in post-control group, showed that low-molecular heparin may decrease patients ' blood viscosity, improve hemorrheology and promote patient relief from hypercoagulable conditions. (4) Following treatment, a higher quality of life-score than a control group showed the observation group (P<0.05). That is mainly due to the increase in the efficacy and better control of the illness of tablelazine enteric-coated tablets combined with low molecular heparin, which reduce the adverse health effects on the patients ' quality of life. (5) The rate of incidences of adverse effects (e.g. 6.00 per cent against 4.00 per cent) between the observation group and control group (P>0.05) shows that low molecular heparin has good safety without increased adverse reactions with tablelazine enteric-capped tablets.

In conclusion, tablelazine enteric-coated tablets combined with low molecular heparin can efficiently relieve significant symptoms, decrease inflammatory and hypercoagulable conditions, contribute to improved quality of life with apparent efficacy, low adverse effects and good safety.

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