

# Morphological study on colonic pathology in ulcerative colitis treated by moxibustion

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## Abstract

**AIM** To observe the therapeutic effect of moxibustion on ulcerative colitis and its influence on the colonic mucosal morphology.

**METHODS** Forty-six patients with ulcerative colitis were randomly divided into the moxibustion with herbal medicine underneath group and the western medicine group. Thirty patients were treated with the above moxibustion and 16 patients with Salicylate fapyridine(SASP). The colonic mucosa of 13 patients in the moxibustion group was observed by colonoscopy before and after the treatment. Mucin was also analyzed by H.E and AB-PAS staining.

**RESULTS** Seventeen patients were clinically cured, 12 were improved and 1 unchanged in the moxibustion group. In the control group, 5 patients were clinically cured, 7 improved and 4 unchanged. Thirteen patients with active UC were taken as the subjects for histopathologic analysis in this study. The colonic mucosal lesions were remarkably improved and the characteristic of the mucin also changed. In most sections, the chronic inflammation of mucosa was greatly ameliorated ( $P<0.01$ ). The inflammatory cell infiltration much decreased

and neutrophils, disappeared in most sections ( $P<0.001$ ). The goblet cells significantly increased ( $P<0.001$ ); crypt paracrypt abscess or mucosal ulceration was seen ( $P<0.001$ ).

**CONCLUSION** The rate of cure of ulcerative colitis by moxibustion with herbal medicine beneath is superior to that by SASP. This sort of moxibustion can effectively improve the colonic mucosal lesions and restore the proportion of mucoprotein to near normal.

## INTRODUCTION

Chronic ulcerative colitis (UC) is autoimmune in nature<sup>[1-3]</sup>. Aminosalicyclic acid and corticosteroids are the drugs most commonly used in treatment of UC<sup>[4-19]</sup>, but long-term use may give rise to adverse effects. At present, many of them can be treated by combined western medicine and TCM<sup>[20-28]</sup>, or Chinese herbs<sup>[29-41]</sup> or acupuncture<sup>[42,43]</sup>. The present study is primarily aimed at the effectiveness of moxibustion on the morphological study of colonic mucosa in ulcerative colitis.

## SUBJECTS AND METHODS

### Subjects

Forty-six cases of UC were out-patients and in-patients who were diagnosed according to the diagnostic criteria established by National Academic Conference on Digestive System Diseases held in Taiyuan, 1993<sup>[3]</sup>, and were randomly divided into two groups: moxibustion with herbal medicine underneath (designated below as moxibustion) group and the SASP group. Differentiation of symptoms and signs by TCM was classified according to the criteria described in "Internal Medicine" edited by Shanghai College of TCM. The moxibustion group was made up of 30 cases, including 16 males and 14 females, mean age of 38.75 years (25-63). The course of illness ranged from 5 months to 18 years. The control group comprised 16 cases, including 9 males and 7 females with a mean age of 37 years (27-69), the course of illness ranged from 4 months to 17 years.

### Methods of treatment

**Method in the moxibustion group** Selection of

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acupoints: The main acupoints of the two groups: Zhongwan (RN 12), Qihai (RN 6) and Zusanli (ST 36 Bilateral); Dachangshu (BL 25 bilateral), Tianshu (ST 25, bilateral), and Shangjuxu (ST37, bilateral) were used alternately. Auxiliary acupoints was added to different clinical types: Pishu (BL 20) for deficiency of Spleen and Stomach; Shuifen (RN 9) for accumulation of damp-heat Ganshu and Pishu for stagnancy of Liver-qi and deficiency of Spleen; Guanyuan (RN 4) for deficiency of both Spleen-yang and the Kidney-yang, Zhongzhu (KI 15) for constipation and Yinbai (SP 1) for pus and bloody stool.

Preparation of medicinal pads for moxibustion: *Radix Aconiti Praeparata*, *Cortex Cinnamomi*, *Radix Salviae Miltiorrhizae*, *Flos Carthami*, *Radix Aucklandiae*, *Rhizoma Coptidis*, etc were respectively ground into fine powder and stored for use. *Rhizoma Coptidis*, *Radix Salviae Mitio rrhizae* and *Flos Carthami* were used as main ingredients for the type of accumulation of damp-heat, supplemented with an appropriate amount of *Radix Aucklandiae*; *Radix Aconiti Pracparata* was used as the main ingredient for other types of the syndrome, supplemented with a suitable amount of *Cortex Cinnamomi*, *Flos Carthami*, *Radix Salviae Miltiorrhizae* and *Radix Acucklandiae*. Each medicinal pad contained herbal powder 2.5g which was mixed up with rice wine 3g to make paste. The paste was then made into pads of 2.3cm in diameter and 0.5cm in thickness.

**Method of moxibustion** Mugwort floss was made into moxacones, each being 2.1cm in base diameter, 2cm in height, and about 2g in weight, which were then placed on the medicinal pads and ignited. For deficiency of spleen and stomach, 3 moxa cones were used for each acupoint; for the type of accumulation of damp-heat, 2 cones were used for Dachangshu (BL 25), Tianshu (ST 25), Zhongwan (CV 12), Qihai (CV 6) and 4-7 cones for Zusanli (ST 36) and Shangjuxu (ST 37) until a strong warm sensation was felt by the patient; for stagnancy of liver-qi and deficiency of spleen, 3 cones were needed; for deficiency of both spleen-yang and kidney-yang, 3 cones were needed for the main acupoints and 4-7 cones for the auxiliary acupoints; for constipation, 2 cones were used on Zhongzhu (KI 3) and one cone was used on Tianshu (ST 25); and for serious pus and bloody stool, 4-7 moxacones were needed on Yinbai (SP 1). The treatment was given once daily, 12 treatments constituting a therapeutic course with an interval of 3 days between each two courses. After 5 courses of treatment the results were analyzed.

**Method in the control group** Patients were given Salicylazosulfapyridine 1g each time, 4 times a day at the beginning, and 0.5g each time, 4 times daily

in the convalescent period. After 3 months of treatment the results were analyzed.

### **Criteria for therapeutic effects**

Clinically cured: clinical symptoms and signs disappeared, and colomoscopy showed disappearance of ulceration of colonic mucosa without recurrence after follow-up for 6 months. Improved: symptoms and signs ameliorated significantly, colonoscopy indicated amelioration of mucosal pathological changes. Ineffective: Clinical symptoms, signs and colonoscopy showed no significant difference before and after treatment.

### **Indexes and methods of observation**

**Pathological observation of colonic mucosa** All specimens were taken from the most masked region or the edge of mucosal ulceration during colonoscopy. Three specimens were obtained in each patient, fixed with formalin, embedded in paraffin and sectioned, followed by H.E staining and pathologic observation.

### **Analysis of the mucin in colonic mucosa**

AB-HID and AB-PAS methods were used for the staining.

## **RESULTS**

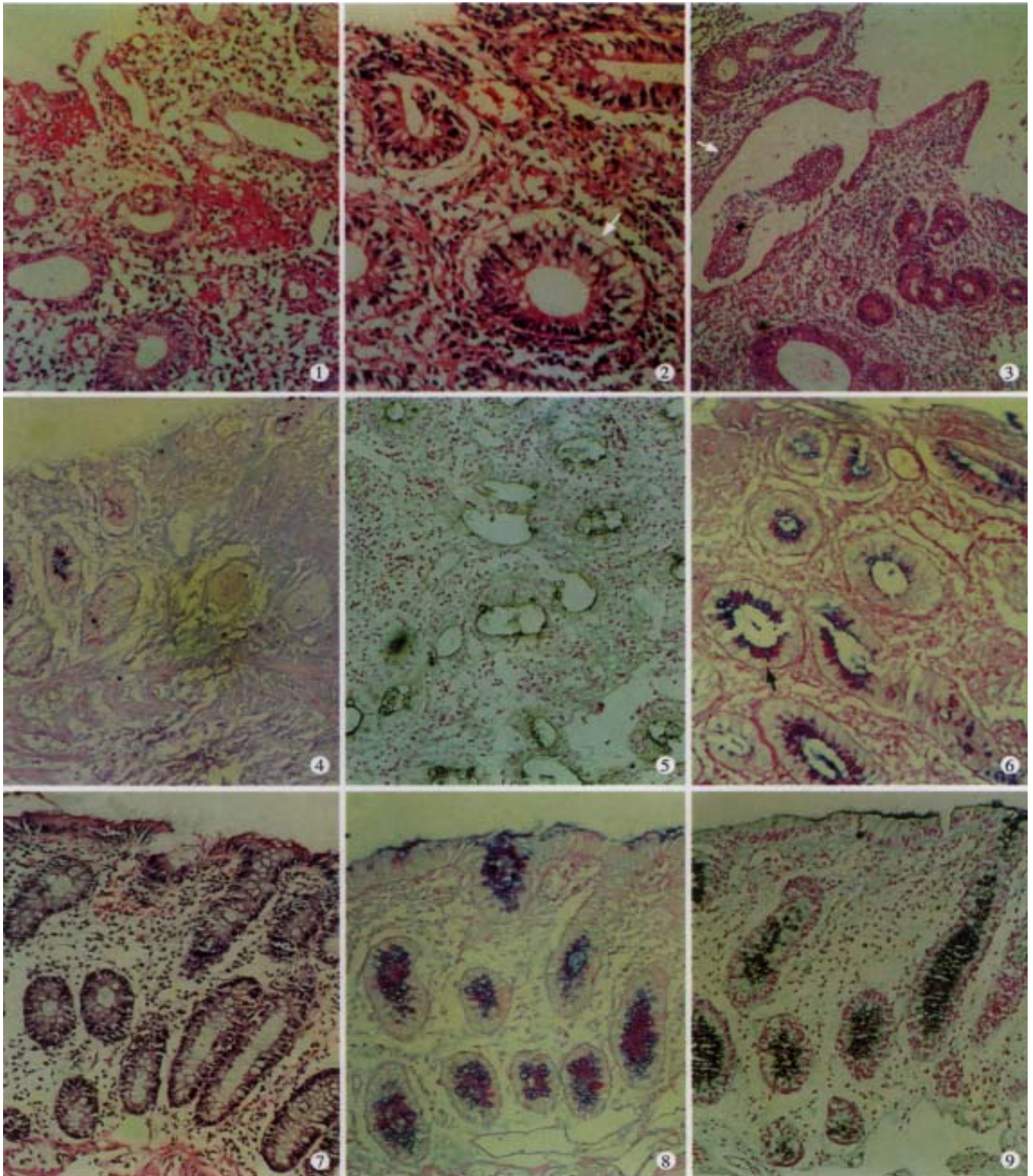
### **Analysis of therapeutic effects**

Seventeen patients were clinically cured, 12 were improved and one was ineffective, which made up 56.66%, 40.00%, and 3.33% respectively in the moxibustion group. In the control group, 5 patients were clinically cured, 7 improved and 4 ineffective, which accounted for 31.25%, 43.75%, 25.00% respectively. The cure rate in the moxibustion group was superior to that in the control group ( $P<0.01$ ).

### **Changes of colonic mucosal histopathology and mucin**

Thirteen patients with active UC were taken as the subjects for histopathologic analysis in this study.

**Pathological changes before treatment** The mucosa showed non-specific inflammation. The lamina propria showed hyperemia and edema with a great number of plasma cells, lymphocytes, mononuclear cells, neutrophils and eosinophils infiltration. The goblet cells in the body of the gland reduced in various extent, even disappeared, and replaced by columnar cells (Figures 1-3). Vacuoles, could be seen in the distal region of the nucleus (Figure 2). No mucin was present in the vacuoles. The lumen of gland became dilated, irregular or branched in some lesions, some regions were neplaced by immature glandulas body of smaller volume. The neutrophilic infiltration was present in the inter-epithelial cells



**Figure 1** The colonic mucosa shows hyperemia, edema and inflammatory cell infiltration. The goblet cells in the body of gland decrease remarkably, which are composed of columnar cells.

**Figure 2** The lesion is the same as above. The arrowhead shows an infranuclear vacuole.

**Figure 3** The lesion is the same as above. The arrowhead shows a crypt abscess. H.E.  $\times 100$

**Figure 4** The majority of acid mucin in the body of gland disappear. AB-PAS staining  $\times 100$

**Figure 5** The majority of mucin sulfate in the body of gland disappears. HID-AB staining  $\times 100$

**Figure 6** The mucin in the body of gland decreases. The amount of neutral mucin relatively increases (arrowhead). AB-PAS staining  $\times 100$

**Figure 7** The colonic mucosa shows mild hyperemia, with less mucosal inflammatory cell infiltration. The goblet cells in the body of gland show no reduction. H.E.  $\times 100$

**Figure 8** The reduction of acid mucin is not obvious. AB-PAS staining  $\times 100$

**Figure 9** No reduction of mucin sulfate occurs. HID-AB staining  $\times 100$



**Table 1a The histologic changes of 13 cases with UC**

	n	Chronic mucosal inflammation				Neutrophil infiltration reduction				Decrease of goblet cells			
		-	+	++	+++	-	+	++	+++	-	+	++	+++
Before treatment	13	0	0	4	9	0	1	5	7	0	1	5	7
After treatment	13	1	11	1	0	10	3	0	0	7	4	2	0

$\chi^2$  test:  $\chi^2=20.69$ ,  $P<0.001$ ;  $\chi^2=21.09$ ,  $P<0.001$ ;  $\chi^2=16.71$ ,  $P<0.001$

**Table 1b Histologic changes of 13 cases with UC**

	n	Neutrophil infiltration in the interepithilium				Crypt abscess, abscess near crypt and ulceration of mucosa			
		-	+	++	+++	-	+	++	+++
Before treatment	13	3	5	5	0	1	2	6	4
After treatment	13	10	2	1	0	13	0	0	0

$\chi^2$  test:  $\chi^2=7.07$ ,  $P<0.01$ ;  $\chi^2=18.78$ ,  $P<0.001$ .

in majority of sections. Most of sections showed crypt abscesses (Figure 3), abscesses near crypts and ulceration of the mucosa. The amount of mucin in the body of the gland of the colonic mucosa in all patients decreased or decreased remarkably. As to the change of the mucin characteristic, most of the acid mucins in the body of gland disappeared (Figure 4). Most of AB-PAS staining was negative, mucin sulfate in the body of gland disappeared (Figure 5). HID-AB staining became hypochromatic. As the mucin in the body of gland decreased, the amount of neutral mucin increased relatively (Figure 6).

**Changes after moxibustion treatment** The mucosal inflammatory lesions in the majority of sections from the 13 patients with active UC abated remarkably. No hyperemia and edema were seen. Inflammatory cell infiltration decreased. In the majority of sections, neutrophil infiltration disappeared. Crypt abscesses, abscesses near crypts and ulceration of the mucosa were not seen. The reduction of the goblet cells in the body of gland was not obvious (Figure 7). The amount of mucin in the body of gland was almost normal. AB-PAS staining showed no obvious reduction in acid mucin (Figure 8). HID-AB staining showed no reduction in mucin sulfate (Figure 9).

**The occurrence and severity of the main pathologic lesions before and after treatment** (Table 1a,ab).

## DISCUSSION

The clinical manifestations of UC is non-specific, and the disease is usually diagnosed by fibercolonoscopy and biopsies<sup>[44-51]</sup>. All sections were examined and reexamined by the same pathologist. The sections showed typical pathologic features of UC, such as chronic mucosal inflammation, neutrophil infiltration, reduced goblet cells, crypt abscesses, mucosal ulceration.

In recent years, many studies on the change of colonic mucus were carried out. It was suggested that it might be the prodromal change of carcinoma of large intestine. As we all know, UC is a precancerous lesion of colon carcinoma. In this group, most mucin sulfate in glandular body disappeared whereas neutral mucin was relatively increased. We also found that the reduction of mucin was associated with the degree of local inflammation, the more severe the inflammation, the more obvious the reduction of mucin. The mucosa in this region also showed certain histologic characteristics: The goblet cells in the glandular body decreased remarkably or disappeared. With appearance of simple columnar cells which were lack of mucin section. The lumen of some mucosal glands became dilated, branched or irregularly arranged.

According to TCM, chronic non-specific ulcerative colitis belongs to the category of "Changpi" (bloody stool) and "Xiuxie" (diarrhea), and results from deficiency and hypofunction of spleen and stomach, accumulation of damp-heat, stagnancy of the liver-qi and deficiency of spleen, or insufficiency of spleen-yang and kidney-yang. In this study, good curative effect was achieved by the treatment of the moxibustion. The results showed that this moxibustion has the function of warming yang, promoting flow of qi and blood, improving the lesional blood circulation, and is helpful to hemostasis and the absorption of inflammatory products, and eventually attains the goal of the neogenesis of granulated tissue in the region of ulceration, and the repair of mucosal epithelium.

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