

Clinical study of herbal mixture “Diding Oral Medicine” as an alternative to preventative antibiotics in perioperative hemorrhoids

A CARE-compliant article

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Abstract

To study the clinical effects of Diding Oral Medicine as an alternative to preventative antibiotics in perioperative hemorrhoids.

From August 2017 to February 2018, a total of 214 patients who were treated with external exfoliation and internal ligation of mixed hemorrhoids in our hospital were divided into the control group and experimental group by way of stratified random (107 cases in each group). Patients in the control group were given antibiotics preventatively before operation, while patients in the experimental group took Diding Oral Medicine before operation, and the white blood cell count, neutrophil count, wound recovery, pain score, anal bulge score, and pathogen culture of wound secretions were compared between the 2 groups.

There was no significant difference in white blood cell count and neutrophil count between both groups before and after operation ($P > .05$). The wound seepage score, wound edema score, and wound area score in the experimental group were lower than those in the control group, and the wound healing in the experimental group was shorter than that in the control group (all $P < .05$). The pain score and anal bulge score of the experimental group were decreased significantly compared to the control group ($P < .05$). In addition, the detection rate of pathogenic bacteria in the experimental group was downregulated significantly compared to the control group ($P < .05$).

The Diding Oral Medicine has prominent bacteriostatic and antibacterial effects on patients with hemorrhoids during perioperative period, and promotes wound healing, reduces pain stress, and anal bulge.

Abbreviations: SD = standard deviation, VAS = Visual Analogue Scale.

Keywords: antibacterial effects, antibiotics, bacteriostatic effects, Diding Oral Medicine, hemorrhoids, pain stress, perioperative period, wound healing

1. Introduction

Hemorrhoids are one of the most common gastrointestinal diseases with a high prevalence. The occurrence of hemorrhoids is

usually higher in certain jobs such as drivers and office workers.^[1] Factors such as improper diet, abnormal excrement, bad excrement habit, heredity, anal cecal structure, and other chronic diseases may lead to this disease.^[2] Hematochezia and pain are the early symptoms, while perianal itching and prolapse of hemorrhoids may occur in the later stage.^[3] This disease has a serious impact on the daily life of patients and may induce a variety of complications, ranging from iron-deficiency anemia to cardiovascular and cerebrovascular diseases, which may threaten life.^[4] It should be noted that hemorrhoids in anorectal diseases is the most prone to postoperative infection, so it is of important clinical significance to take prevention measures in the perioperative period of hemorrhoids, in order to guarantee the smooth implementation of treatment and improve the safety of patients.^[5]

According to the current knowledge, management of hemorrhoids includes modification of the dietary and lifestyle, medications, and radical surgery.^[6] The recommended principle of clinical treatment for hemorrhoids is conservative treatment for the patients with no symptoms or no radical cure, while for patients with severe symptoms, surgical removal or collapse of the hemorrhoids and embolization should be selected.^[7] Preventive use of antibiotics to prevent infection is a routine treatment for hemorrhoids patients during perioperative period.^[8] However, it should be noted that there has been a serious abuse of antibiotics in recent years, because antibiotics not only lead to impaired liver and kidney functions of patients, but also

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result rapid drug resistance, and they are not favorable for follow-up treatment.^[9] Therefore, many researchers look for traditional medicines as a potential resource for hemorrhoids treatment.

Chinese herbal medicine originated in China is a complementary alternative medicine, which uses medical plants, minerals, and animal parts to prevent or treat diseases.^[10] In recent years, Chinese herbal medicines such as Liang-Xue-Di-Huang Decoction and Liuhe Dan have been widely used to treat or prevent or treat more and more hemorrhoids patients.^[11,12] Diding Oral Medicine used in this study was prepared in our hospital, which consisted of different kinds of Chinese medicines such as violet, Honey-suckle stem, *Sanguisorba officinalis*, *Hairyvein agrimony*, *Oldenlandia diffusa*, *Sophora pseudoacacia*, *Radix paeoniae alba*, Semen cannabis, and Common vladimiria root. In the present study, the effects of Diding Oral Medicine as an alternative to preventative antibiotics in perioperative hemorrhoids patients were evaluated in our hospital.

2. Materials and methods

2.1. Patients

From August 2017 to February 2018, a total of 214 patients who were treated with external exfoliation and internal ligation of mixed hemorrhoids in our hospital were divided into the control group and experimental group by way of stratified random. Written informed consent will be obtained from each patient. Inclusion criteria:

1. Patients met diagnostic criteria for hemorrhoids in Diagnosis and Treatment Guidelines for Hemorrhoids^[13] established by The American Society of Colon and Rectal Surgeons;
2. Patients conformed to the indications of mixed hemorrhoids external exfoliation and internal ligation for treatment;
3. All patients were operated by the same doctor;
4. Patients and their family members were fully aware of the study plan, signed the informed consent and cooperated in the operation.
5. Patients without recent history of antibiotic use before the admission to the hospital.

Exclusion criteria:

1. Combined with other anal diseases;
2. Combined with immune system diseases;
3. Combined with mental disorders;
4. Combined with serious blood diseases, portal hypertension, and cardio-cerebrovascular diseases;
5. Lack of general information led to failure of data analysis.

2.2. Treatments

Control group: preventative giving 1.5 g of cefazolin sodium for injection (national drug approval H31020824) produced by Shanghai Xinya Pharmaceutical Co., Ltd. (China), and 0.25 g of metronidazole for injection (national drug approval H20041392) produced by Jilin Jinsheng Pharmaceutical Co., Ltd. (China), all were given by single intravenous drip half an hour before operation.

Experimental group: oral administration of Diding Oral Medicine 10 mL each time and 3 times each day. The prescription consisted of violet (85 g), honey-suckle stem (350 g), *Sanguisorba officinalis* (85 g), *Agrimonia pilosa* (85 g), *Hedyotis diffusa* (85 g), *Sophora japonica* (85 g), *Paeonia lactiflora* (85 g), Semen cannabis

(85 g), *Sanguisorba officinalis* (85 g), Sodium benzoate (2.4 g), and ethyl hydroxybenzoate (0.2 g) (total weight 1032.6 g). The water decoction filtrate was concentrated to a clear paste with a relative density of 1.06. After cooling, ethanol was added until the alcohol content reached 50%. After standing for 72 hours, the supernatant was taken back to ethanol, and 800 mL of water was added. After cooling for 24 hours, the mixture was filtered, and the water was added to 1000 mL 3 times in the middle and late.

Evaluation of the white blood cell count and neutrophil count:

The white blood cell count and neutrophil count were measured through blood routine examination in both groups.

2.3. Evaluation of the wound recovery

The wound recovery of both groups was evaluated on the wound seepage score, wound edema score, wound area score, and wound healing time. The evaluation criteria included^[14]:

1. Wound seepage score: no seepage or 1 piece of gauze without permeation indicated zero point; permeating 1 piece of gauze but not permeating 2 pieces of gauze indicated 1 point; permeating 2 pieces of gauze but not permeating 3 pieces of gauze indicated 2 points; permeating 3 pieces of gauze or more indicated 3 points.
2. Wound edema score: no edema indicated zero point; slight swelling in the skin pattern indicated 1 point; no visible skin striations and moderate swelling indicated 2 points; dermatoglyph disappeared; and severely swelling indicated 3 points.
3. Wound area score: wound healing indicated zero point; wound area no more than 2 cm² indicated 1 point; the wound area between 2 and 4 cm² indicated 2 points, and the wound area exceeding 4 cm² indicated 3 points.
4. Wound healing time is the time when the wound being covered by the epithelial tissue completely.

2.4. Evaluation of the pain score and anal bulge score

The pain score and anal bulge score were recorded in the control group and experimental group. The pain score was evaluated by Visual Analogue Scale (VAS) with a score of 0–10 points. The higher the score was, the stronger the pain was. The score of anal dilatation was developed to quantify the symptoms according to the Guiding Principles for Clinical Research on New Chinese Medicines.^[15] The evaluation criteria were as follows: no felling of anal distension and fullness score indicated zero point; slight swelling of anus indicated 1 point; obvious anus distension and fullness, and remission after rest indicated 2 points; severe anal distension and continuous fullness indicated 3 points.

2.5. Evaluation of the detection rate of pathogenic bacteria

The secretions on the wound of the control group and experimental group were collected for examination, and microbial culture was conducted for both groups. Pathogen identification and isolation were conducted with automatic microbial assay instrument, and the detection rate of pathogenic bacteria was calculated.

2.6. Statistical analysis

Statistical Product and Service Solutions (SPSS) version 17.0 software (SPSS, Inc., Chicago, IL) was used for data analysis. Sex

Table 1**Comparison of general information of patients in experimental group and control group (n, %, $\bar{x} \pm s$).**

Groups	Cases	Gender		Age (years)	Degree of disease	
		Male	Female		Grade-III	Grade-IV
Experimental group	107	62 (57.94%)	45 (42.06%)	42.28 ± 4.53	48 (44.86%)	59 (55.14%)
Control group	107	66 (61.68%)	41 (38.32%)	43.02 ± 5.11	51 (47.66%)	56 (52.34%)
$t\chi^2$	–	0.291	1.121	0.158		
<i>P</i>	–	0.590	0.264	0.691		

Table 2**Comparison of white blood cell count and neutrophil count in the experimental group and control group ($\bar{x} \pm s$).**

Groups	Cases	White blood cell count ($\times 10^9/L$)		Neutrophil count (%)	
		Before operation	After operation	Before operation	After operation
Experimental group	107	9.91 ± 2.31	10.54 ± 3.40	71.98 ± 6.39	76.25 ± 6.75
Control group	107	9.63 ± 2.14	10.42 ± 3.87	72.44 ± 6.80	76.81 ± 6.46
<i>t</i>	–	0.920	0.241	0.510	0.620
<i>P</i>	–	0.359	0.810	0.611	0.536

ratio, disease index, and pathogen detection rate were analyzed by Chi-Squared test, and expressed as a percentage. Age, white blood cell count, neutrophil count, wound seepage score, edema scores, the area of the wound, wound healing time, pain score, and the anus belly score were evaluated by *t* test and expressed as mean ± standard deviation (SD). *P* < .05 indicated the statistically significant data difference.

3. Results

3.1. Characteristics of patients

The baseline data of the study subjects were shown in Table 1. There were 107 cases (62 males, 45 females) in the experimental group, and 107 cases (66 males, 41 females) in the control group. The age of 42.28 ± 4.53 years old and 43.02 ± 5.11 years old in the experimental group and control group, respectively. A total of 48 (44.86%) cases belonged to Grade-III, and 59 (55.14%) belonged to Grade-IV in the experiment group. A total of 51 (47.66%) cases belonged to Grade-III, and 56 (52.34%) belonged to Grade-IV in the control group. However, there were no statistical differences in sex ratio, age, and degree of disease between the control group and experimental group (*P* > .05).

3.2. Evaluation of white blood cell count and neutrophil count in both groups

White blood cell count and neutrophil count were evaluated in the control group and experimental group, and shown in Table 2. The comparison between both groups showed that there were no

statistically significant differences in white blood cell count and neutrophil count between the 2 groups before and after operation (*P* > .05).

3.3. Analysis of wound recovery in both groups

Wound recovery including the wound seepage score, wound edema score, and wound area score was analyzed in the control group and experimental group, as shown in Table 3. The comparison between the 2 groups showed that the wound seepage score, wound edema score, and wound area score in the experimental group were lower than those in the control group (*P* < .05). The wound healing time in experimental group (10.12 ± 1.14 d) was shortened compared to the control group (14.62 ± 1.57 d), which made statistically significant differences (*P* < 0.05).

3.4. Analysis of pain score and anus swelling score in both groups

As demonstrated in Figure 1, the pain score and anal anus swelling score of the experimental group were lower than those of the control group, and the data difference made statistical significances (*P* < .05):

3.5. Analysis of the detection rate of pathogenic bacteria of wound secretions in both groups

Wound secretions were collected for pathogen culture in the experimental group and control group. A total of 2 patients in the

Table 3**Comparison of wound recovery in the experimental group and control group ($\bar{x} \pm s$).**

Groups	Cases	Wound seepage score (points)	Wound edema score (points)	Wound Area score (points)	Wound healing time (d)
Experimental group	107	1.26 ± 0.21	1.10 ± 0.33	1.36 ± 0.29	10.12 ± 1.14
Control group	107	1.71 ± 0.45	1.58 ± 0.40	1.94 ± 0.41	14.62 ± 1.57
<i>t</i>	–	9.374	9.575	11.947	23.991
<i>P</i>	–	0.000	0.000	0.000	0.000

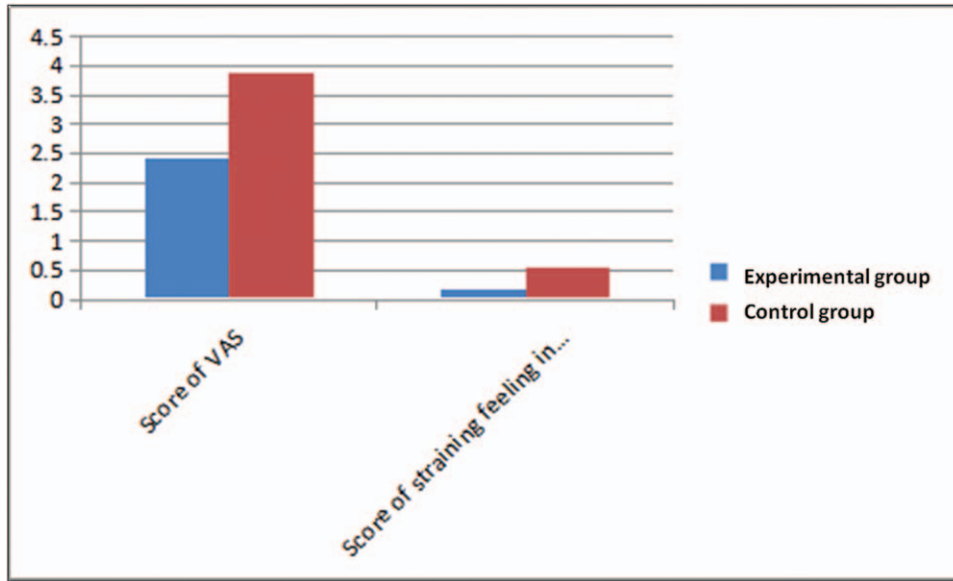


Figure 1. Comparison of pain score and anus swelling score in the experimental group and control group.

experimental group were detected of pathogenic bacteria, with a detection rate of 1.87% and 9 patients in the control group were detected of pathogenic bacteria, with a detection rate of 10.28%. The comparison between the 2 groups showed that the detection rate of pathogenic bacteria in the experimental group was lower than that in the control group ($\chi^2=6.198, P=.013$), and the difference made statistical significance ($P<.05$), as shown in Figure 2.

4. Discussion

Hemorrhoids are an anorectal disease with typical symptoms of pain caused by hematochezia, prolapse, and incarceration of internal hemorrhoids or mixed hemorrhoids.^[1-3] Antibiotics are usually given to the patients in conventional antiinfection treatment.^[16,17] However, the unreasonable application of antibiotics has become increasingly serious in recent years, which increases the drug resistance of pathogenic bacteria and even the emergence of multidrug resistant bacteria.^[18] In order to explore the effect of this prescription alone in patients with

hemorrhoids and further popularize the application of Diding Oral Medicine consisted of Chinese medicines, this study took patients proceeding mixed hemorrhoids external exfoliation and internal ligation in our hospital, and found that this kind of medicine is effective as an alternative to preventative antibiotics in perioperative hemorrhoids.

Notably, many experts and scholars have carried out detailed studies on traditional Chinese medicine in replacing antibiotics to treat hemorrhoids in China.^[19-21] Wu et al proposed the use of Liuhe Pill Ointment to prevent infection in patients with hemorrhoids, and the results showed that, compared to the control group, the score of wound edema and pain, the length of hospital stay and wound healing time in the study group treated with Liuhe Pill Ointment were shortened.^[20] Shi et al used Blood-cooling Rehmannia Soup as the main drug for hemorrhoids treatment, and showed that the score of anal distension after 14day treatment was significantly lower while the score of the life quality was higher than that after 7day of treatment.^[21] Diding Oral Medicine a key prescription in our hospital was used in this study, which was originally syrup and has been gradually

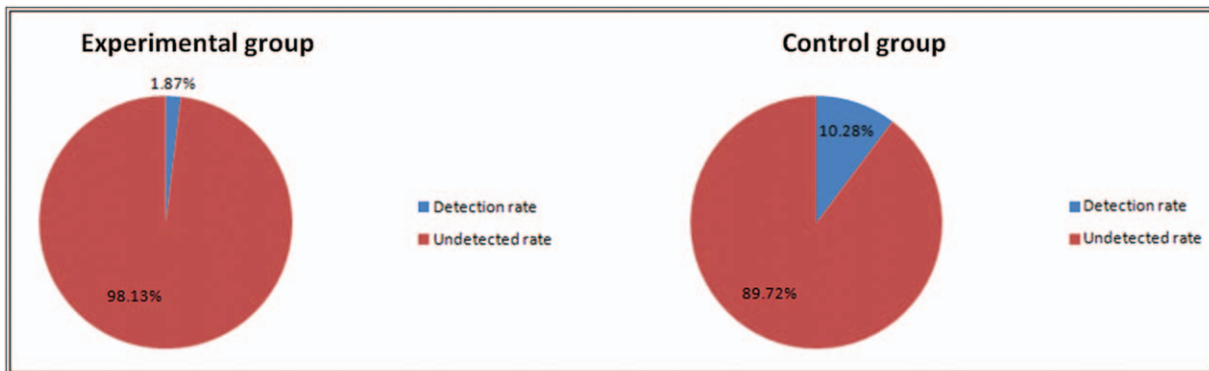


Figure 2. Comparison of pathogen culture results of wound secretions in the experimental group and control group.

improved to sugar free oral liquid in order to meet the needs of patients. This prescription has been applied in our hospital for more than 10 years, benefiting more than tens of thousands of patients.

Diding Oral Medicine consists of Chinese violet, Honeysuckle stem, *Sanguisorba officinalis*, *Hairyvein agrimony*, *Oldenlandia diffusa*, *Sophora pseudoacacia*, *Radix paeoniae alba*, Semen cannabis, and Common vladimiria root among which, Chinese violet has an effect of detumescence and blood cooling, inflammation resistance and virus suppression, acting as the Jun (emperor) component. Honeysuckle stem and *Oldenlandia diffusa* have an effect of clearing away heat and toxic materials, regulating the immune, acting as ministerial drug. *Sanguisorba officinalis*, *Sophora pseudoacacia* and *Radix paeoniae alba* have an effect of dispelling stasis and relieving pain, hairyvein agrimony has an effect of astringency and hemostasis. Semen cannabis has an effect of laxation and defecation, while common vladimiria root has an effect of promoting qi circulation to relieve pain, acting as conducting component.^[22,23] Therefore, the entire prescription of this study has an effect of relieving swelling and pain, clearing away heat and toxic materials, cooling blood, and relaxing the bowels, so as to promote the rehabilitation, restrain the reproduction of pathogenic bacteria, and reduce the adverse stress.^[22,23] This study showed no significant difference in white blood cell count and neutrophil count between the 2 groups before operation, and there was no significant difference in the 2 indexes after operation, suggesting that the antiinfection effect of Diding Oral Medicine was close to antibiotics. The comparison showed that the wound seepage score, wound edema score, wound area score, wound healing time, pain score, anal bulge score and the detection rate of pathogenic bacteria in the experimental group were all downregulated compared to the control group.

There are still several limitations in this study. First, the effects of Diding Oral Medicine were only studied in hemorrhoids patients in perioperative period, other periods of hemorrhoids needs to be further investigated. Second, only 214 patients were involved in this study, Diding Oral Medicine would be clinically practiced in more big samples. Third, although Diding Oral Medicine has been used directly in clinical practice in our hospital, it was still necessary to prove the efficacy and safety of this Chinese prescription in other hospitals.

5. Conclusions

In conclusion, Diding Oral Medicine given to hemorrhoids patients in perioperative period has significant antibacterial effects, and can promote wound healing, reduce pain stress and anal bulge. This study confirms that Diding Oral Medicine can be implemented as a new medical therapy to hemorrhoid in China.

Author contributions

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