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Research Article
Shuangjin Hemorrhoid Ointment and β-Sodium Aescinate Injection Alleviate Edema and Pain in Haemorrhoids Patients

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Abstract

Background and Objective: Haemorrhoids patients frequently experience pain, edema and local inflammation after automatic ligation of haemorrhoids. Reduction in postoperative edema and pain are important factors in postoperative treatment. This study examined the therapeutic efficacy of Shuangjin haemorrhoid ointment with β-sodium aescinate injection in treating postoperative edema and pain in patients with haemorrhoids. **Materials and Methods:** A total of 150 haemorrhoids patients who received automatic ligation were enrolled in the study. They were randomly assigned to the control group that received routine treatment (75 cases) and the research group that received Shuangjin haemorrhoid ointment and β-sodium aescinate (75 cases). The anal edge edema score, pain score, wound healing time and serum levels of β-endorphin (β-EP) and 5-hydroxytryptamine (5-HT) were compared between the two groups. **Results:** It was found that the anal edge edema score, pain score and serum levels of β-EP and 5-HT of the research group were statistically lower than the control group both on the fourth and seventh day of treatment ($p<0.05$). Meanwhile, the length of wound healing time of the research group was statistically shorter than the control group. **Conclusion:** The combined application of Shuangjin haemorrhoid ointment and β-sodium aescinate has significant benefits in treating anal edge edema and pain after automatic ligation of haemorrhoids.

Key words: Shuangjin haemorrhoid ointment, β-sodium aescinate, automatic haemorrhoid ligation, anal edge edema, pain

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Haemorrhoids are a common type of anorectal disease. Generally, haemorrhoids can be divided into three types: internal haemorrhoid, external haemorrhoid and mixed hemorrhoid[1]. The occurrence of haemorrhoids may stem from many factors, such as constipation, diarrhoea, low fibre intake, pregnancy, internal sphincter dysfunction, genetics, age and others[2,3]. The clinical manifestations of haemorrhoids include prolapsed anus, anal pain and swelling and blood in the stool. Haemorrhoids are prone to reoccur and can affect the quality of life of patients[4].

The treatment of haemorrhoids can be non-surgical or surgical. When non-surgical treatment cannot achieve satisfactory results, surgical treatment will be considered[5]. Automatic ligation of haemorrhoids (also known as Ruiyun procedure for haemorrhoids, RPH) is a common surgical method for haemorrhoids[6]. However, patients frequently experience pain, edema and local inflammation after the procedure. Edema, a common complication after anorectal surgery, can cause local swelling, pain aggravation and spasms of the internal sphincter[7]. Therefore, postoperative treatment of haemorrhoids should aim to reduce postoperative edema and provide pain relief.

Shuangjin haemorrhoid ointment is a common Traditional Chinese Medicine-based topical cream for haemorrhoids treatment. On the other hand, β-sodium aescinate is a natural herb extract that has been given to patients after surgery to improve postoperative inflammation and edema[8,9]. In this study, the combination of Shuangjin haemorrhoid ointment and β-sodium aescinate was used in the postoperative treatment of haemorrhoids patients and its effect on postoperative edema and pain of haemorrhoids patients was assessed to provide clinical evidence about this treatment.

MATERIALS AND METHODS

General design: A total of 150 patients who had been diagnosed with haemorrhoids and received automatic haemorrhoid ligation between January, 2018 and December, 2019 were enrolled as research subjects in Handan Hospital of Traditional Chinese Medicine. Out of all recruited subjects, 60 cases (40%) had second-degree haemorrhoids and 90 (60%) with third-degree haemorrhoids. In terms of types of haemorrhoids, 54 cases (36%) had internal haemorrhoids and 96 cases (64%) had mixed haemorrhoids. Patients were randomly divided into a control group that underwent routine treatment (75 cases) and a research group that underwent a combined treatment of β-sodium aescinate and Shuangjin haemorrhoid ointment (75 cases). The research study obtained the informed consent of all participants and has been reviewed and approved by the Ethics Committee from the Handan Hospital of Traditional Chinese Medicine. In the research group, there were 34 male and 41 female patients with an average age of 45.16±2.23 years and an average disease course of 7.13±1.93 years. In contrast, there were 32 male and 48 female patients in the control group, with an average age of 47.13±2.04 years and an average disease course of 6.62±1.48 years. There was no significant difference in the state of haemorrhoids and demographic information between the two groups ($p>0.05$).

Treatment methods: Both groups of haemorrhoid patients were treated with automatic haemorrhoid ligation and received the same routine treatment after the operation. Routine treatment included postoperative anti-infection, potassium permanganate solution (1:5000) sitz bath and fumigation-washing and defecation care. In addition to the routine treatment, the research group was given Shuangjin haemorrhoid ointment and β-sodium aescinate. The Shuangjin haemorrhoid ointment was applied to the postoperative wound twice a day and covered by sterile gauze. β-sodium aescinate was given daily through intravenous injection of a solution consists of 20 mg of β-sodium aescinate in 250 mL of 0.9% sodium chloride. Both groups of patients were treated for one week.

Observational indexes: Clinical outcomes were compared between the two groups, including the anal edge edema score, pain score and wound healing time. Postoperative anal edge edema was assessed using a scoring system of 0–4, where 0 represents no edema and 1, 2, 3 and 4 represent edema with 25, 50, 75 and 100% of anal edge, respectively. Pain score was evaluated using the Visual Analogue Scale (VAS)[10] between 0-10, where 0 represents no pain and 10 represents severe and intolerable pain. Wound healing was recorded from one day after operation to the day of complete wound healing.

Pain-related factors: Peripheral venous blood was obtained on the day of operation, then 4 and 7 days after the operation. Blood was allowed to coagulate for 30 min and was centrifuged at 3,000 rpm min^{-1} for 10 min. The serum was obtained and tested for levels of β-EP (β-endorphin) and 5-HT (5-hydroxytryptamine) by Enzyme-Linked Immunosorbent

Assay (ELISA). All assays were performed using the Human β-EP ELISA kit and Human 5-HT ELISA kit (Bio-Techne, USA) according to the manufacturer's protocol.

Statistical analysis: Numerical data were presented as mean±standard deviation. Significance was determined by the Student *t*-test or one-way analysis of variance followed by a post hoc least significant difference test using the SPSS 20.0 software. A $p<0.05$ was considered statistically significant.

RESULTS

Comparison of the anal edge edema score between the control and research groups: As shown in Table 1, there was no statistical difference in anal edge edema score between the control group (1.95±0.52) and the research group (2.07±0.47) before treatment ($p>0.05$). On the 4th day of treatment, the anal edge edema score of the control group was significantly lower than before treatment (1.44±0.50 vs. 1.95±0.52, $p<0.05$) and the anal edge edema score of the research group was significantly lower than before treatment (1.13±0.34 vs. 2.07±0.47, $p<0.05$). On the 7th day of treatment, the anal edge edema score of the control group was significantly lower than before treatment (1.03±0.50 vs. 1.95±0.52, $p<0.05$) and the anal edge edema score of the research group was significantly lower than before treatment (0.76±0.46 vs. 2.07±0.47, $p<0.05$). When comparison was made between the control and research groups, the research group had more significant improvement in anal edge edema than the control group on the 4th day of treatment (1.13±0.34 vs. 1.44±0.50, $p<0.05$) and the 7th day of treatment (0.76±0.46 vs. 1.03±0.50, $p<0.05$).

Comparison of the pain score between the control and research groups: As shown in Table 2 there was no statistical difference in the pain scores between the control group (5.56±1.27) and the research group (5.73±0.88) before treatment ($p>0.05$). On the 4th day of treatment, the pain score of the control group was significantly lower than before treatment (4.03±0.94 vs. 5.56±1.27, $p<0.05$) and the pain score of the research group was significantly lower than before treatment (3.35±0.71 vs. 5.73±0.88, $p<0.05$). On the 7th day of treatment, the pain score of the control group was significantly lower than before treatment (2.75±0.72 vs. 5.56±1.27, $p<0.05$) and the pain score of the research group was significantly lower than before treatment (1.93±0.58 vs. 5.73±0.88, $p<0.05$). In addition, the pain score of the research group was significantly lower than that of the control group both on the 4th day of treatment (3.35±0.71 vs. 4.03±0.94, $p<0.05$) and the 7th day of treatment (1.93±0.58 vs. 2.75±0.72, $p<0.05$).

Comparison of the β-EP and 5-HT level between the control and research groups: As shown in Table 3 there was no statistical difference in serum levels of β-EP between the control group (93.26±12.86) and research group (95.55±11.93) before treatment ($p>0.05$). On the 4th day of treatment, the β-EP level of the control group was significantly lower than before treatment (85.46±11.89 vs. 93.26±12.86, $p<0.05$) and the β-EP level of the research group was significantly lower than before treatment (80.51±10.50 vs. 95.55±11.93, $p<0.05$).On the 7th day of treatment, the β-EP level of the control group was significantly lower than before treatment (71.73±10. vs. 93.26±12.86, $p<0.05$) and the β-EP level of the research group was significantly lower than before treatment (62.67±9.77 vs. 95.55±11.93, $p<0.05$). In addition, the serum β-EP level of the research group was significantly lower than that of the control group both on the 4th day of treatment (80.51±10.50 vs. 85.46±11.89, $p<0.05$) and the 7th day of treatment (62.67±9.77 vs. 71.73±10.24, $p<0.05$).

As shown in Table 4 there was no statistical difference in serum levels of 5-HT between the control group (193.43±18.91) and the research group (187.18±19.80) before treatment ($p>0.05$). On the 4th day of treatment, the 5-HT level of the control group was significantly lower than before treatment (181.90±15.04 vs. 193.43±18.91, $p<0.05$) and the 5-HT level of the research group was significantly lower than before treatment (170.44±18.02 vs. 187.18±19.80, $p<0.05$). On the 7th day of treatment, the 5-HT level of the control group was significantly lower than before treatment (159.00±14.23 vs. 193.43±18.91, $p<0.05$) and the 5-HT level of the research group was significantly lower than before treatment (143.29±16.18 vs. 187.18±19.80, $p<0.05$). In addition, the serum 5-HT level of the research group was significantly lower than that of the control group both on the 4th day of treatment (170.44±18.02 vs. 181.90±15.04, $p<0.05$) and the 7th day of treatment (143.29±16.18 vs. 159.00±14.23, $p<0.05$).

Comparison of the wound healing time between the control and research groups: As shown in Table 5, the wound healing time in the control group was significantly longer than that in the research group (19.07±3.40 vs. 14.96±3.35, $p<0.05$).

Table 1: Comparison of the anal edge edema scores between the control and research groups

	Before treatment	4th day of treatment	7th day of treatment
Control group	1.95±0.52	1.44±0.50*	1.03±0.50*&
Research group	2.07±0.47	1.13±0.34*#	0.76±0.46*#&

*p<0.05 compared with before treatment, #p<0.05 compared with the control group, &p<0.05 compared with the 4th day of treatment

Table 2: Comparison of the anal pain scores between the control and research groups

	Before treatment	4th day of treatment	7th day of treatment
Control group	5.56±1.27	4.03±0.94*	2.75±0.72*&
Research group	5.73±0.88	3.35±0.71*#	1.93±0.58*#&

*p<0.05 compared with before treatment, #p<0.05 compared with the control group, &p<0.05 compared with 4th day of treatment

Table 3: Comparison of serum β-EP level between the control and research groups

	Before treatment	4th day of treatment	7th day of treatment
Control group	93.26±12.86	85.46±11.89*	71.73±10.24*&
Research group	95.55±11.93	80.51±10.50*#	62.67±9.77*#&

*p<0.05 compared with before treatment, #p<0.05 compared with the control group, &p<0.05 compared with 4th day of treatment

Table 4: Comparison of serum 5-HT level between the control and research groups

	Before treatment	4th day of treatment	7th day of treatment
Control group	190.43±18.91	181.90±15.04*	159.00±14.23*&
Research group	187.18±19.80	170.44±18.02*#	143.29±16.18*#&

*p<0.05 compared with before treatment, #p<0.05 compared with the control group, &p<0.05 compared with 4th day of treatment

Table 5: Comparison of wound healing time between the control and research groups

	Cases	Time of wound healing (min-max, d)
Control group	75	19.07±3.40 (13-28)
Research group	75	14.96±3.35* (10-22)

*p<0.05 compared with before research group

DISCUSSION

Doctors employ a variety of methods to treat haemorrhoids based on patient conditions[11,12]. When surgical procedure is needed, postoperative complications such as edema can cause additional pain, prolonged wound healing and even reduce the intended benefit of surgical treatment[13,14]. Edema may be caused by several factors, such as damage to the anal canal, tissue inflammation, abnormalities of microcirculation, increased vascular permeability, lymphatic drainage disorder, liquid retention and thrombosis[15]. Hence, the treatment of postoperative edema will focus on improving microcirculation and reducing inflammation.

The main medicinal ingredients of Shuangjin haemorrhoid ointment include mint, honeysuckle, rhubarb, gardenia and cibotium barometz. Shuangjin haemorrhoid ointment provides anti-itch and anti-inflammatory effects, reduce swelling and promote blood circulation[16]. β-sodium aescinate is extracted from Chinese buckeye seeds, which has demonstrated pharmacological benefits of relieving tissue edema and inflammation, recovering vascular permeability and improving microcirculation[17]. In rats with experimental traumatic brain injury, β-sodium aescinate treatment helped improve neurological function, decrease cerebral edema and attenuate brain lesion[18]. Zhang and colleagues reported that β-sodium aescinate treatment could control and improve wound healing in diabetic rats by regulating inflammation and oxidative stress[19].

In this study, external applications of Shuangjin haemorrhoid ointment combined with intravenous injection of β-sodium aescinate have received good clinical results. Their combined use on haemorrhoids patients effectively improves their postoperative anal edema and pain. In addition, the anal edema score and pain score of the research group were significantly lower than those in the control group both on the 4th and the 7th day of treatment. Wound healing time was also significantly shorter in the research group than that in the control group. The mechanistic action of the two drugs may be related to their ability to reduce inflammation and promote wound healing.

Pain is a defence mechanism in response to damage of the body[20]. β-EP is one of the opioids produced by the endogenous opioid system in response to pain, which produces several effects, including analgesia[21,22]. 5-HT is another molecule involved in the pain and inflammatory

response and plays a role in numerous physiological and behavioural disorders, such as major depression, anxiety and obesity[23,24]. 5-HT is also a strong vasoconstrictor that can aggravate tissue ischemia, hypoxia and even necrosis[25]. In this study, combined treatment of Shuangjin haemorrhoid ointment and β-sodium aescinate injection statistically reduced levels of serum β-EP and 5-HT. The decrease in β-EP and 5-HT levels further provided evidence for the anti-inflammatory, analgesic and stress-reducing effects of the two drugs.

CONCLUSION

In conclusion, it was demonstrated that the combined application of Shuangjin haemorrhoid ointment and β-sodium aescinate injection has effectively improved the postoperative anal edema, pain and wounding healing time of haemorrhoids patients. In addition, the combined treatment also decreased the serum levels of β-EP and 5-HT, which are two Indicators of pain and stress. Shuangjin haemorrhoid ointment and β-sodium aescinate, when used together, have significant benefits in treating anal edge edema and pain after automatic haemorrhoid ligation. This treatment method is worth promoting in clinical practice.

SIGNIFICANCE STATEMENT

This study discovered that the combined application of Shuangjin Haemorrhoids Ointment and β-sodium aescinate injection can be beneficial for the postoperative treatment of haemorrhoids patients. This study will help future researchers uncover integrative treatment options-based on Chinese and Western medicine of postoperative haemorrhoids that many researchers were not able to explore. Thus, a new theory on treating postoperative haemorrhoids with integrative medicine may have arrived at this study.

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Cuihong Zhao and Lanjun Li participated in conception and design of this study. Cuihong Zhao, Wei Shen and Yun Lin collected and analyzed the date. Cuihong Zhao drafted the manuscript. Lanjun Li revised the manuscript. All authors gave the final approval and agreed to be accountable for all aspects of the work.

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