RESEARCH ARTICLE

Comparison of effectiveness between two treatment methods for patients with anal fistula and their impact on serum IL-6 and SAA

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Abstract

Objective: Observation of the clinical effect of Jiedu Shengji ointment in treating anal fistula and its impact on serum interleukin-6 and serum amyloid A.

Methods: The study is a retrospective cohort study. The clinical comparative study was conducted at Baoding NO.1 Central Hospital, China, between April 2023 to March 2024, and comprised patients diagnosed with anal fistula who underwent surgery. The participants were assigned to control group A and intervention group B according to the treatment method. Control group A was treated with Vaseline gauze dressing, while intervention group B was treated with Jiedu Shengji ointment combined with Vaseline gauze. Treatment outcomes between the groups were compared. Data was analysed using SPSS 20.

Results: Of the 60 patients, 30(50%) were in group A; 20(66.6%) men and 10(33.3%) women with mean age 32.56±2.66 years (range: 22-43 years). There were 30(50%) patients in group B; 22(73.3%) men and 8(26.7%) women with mean age 32.14±2.35 years (range: 22-42 years). Total effective rate of treatment in group B was 26 (86.67%) compared to 19 (63.33%) in group A ($p<0.05$). After 7 and 14 days of treatment, the levels of interleukin-6 and serum amyloid A in group B were significantly better than those in group A ($p<0.05$). The wound bleeding score, wound healing time, and wound oedema score of group B were significantly better than those of group A ($p<0.05$). After treatment, the visual analogue scale and the Faecal Incontinence Severity Index scores of group B were significantly better than those of group A ($p<0.05$). After treatment, the levels of transforming growth factor-β and epidermal growth factor in group B were significantly better than those in group A ($p<0.05$).

Conclusion: Jiedu Shengji ointment demonstrated remarkable therapeutic efficacy in patients with surgical treatment for anal fistula.

Key Words: Anal fistula, Jiedu Shengji ointment, Clinical efficacy, IL-6, SAA.

(JPMA 75: 1224; 2025) **DOI: https://doi.org/10.47391/JPMA.20663**

Introduction

Anal fistula is abbreviated from anorectal fistula, and refers to a residual lesion caused by abscess rupture or incisional drainage around the anorectum, with clinical manifestations mainly including pus discharge, swelling, pain and itching.[1,2] Anal fistulas are one of the common diseases in proctology, with an incidence rate second only to haemorrhoids, and onset mainly in adults aged 20-40 years. According to incomplete statistics, the incidence rate of anal fistulas accounts for 1.67-3.60% of anorectal diseases in China.[3] In clinical practice, surgical destruction of the infected anal sinus, sufficient postoperative drainage, and regular dressing changes are the critical factors in the treatment of anal fistulas. However, due to the special lesion location, large wound surface area and complex structure of anal fistulas, postoperative wound repair and regeneration always take a long time, and the wounds are susceptible to infections, commonly manifested as wound pain, oedema, delayed healing, etc., which bring significant distress to the patients.[4] Traditional Chinese Medicine (TCM) boasts a longstanding history and extensive expertise in the treatment of anorectal conditions, including haemorrhoids, fistulas and postoperative wound healing. It has been well recognised by scholars and extensively applied in clinical practice, and has become a characteristic therapy in China.[5] Building on this foundation, the current study planned to scrutinize the clinical efficacy of Jiedu Shengji ointment in patients with anal fistulas, and its impact on serum interleukin-6 (IL-6) and serum amyloid A (SAA).

Patients and Methods

The study was a retrospective cohort study. The clinical comparative study was conducted at Baoding NO.1 Central Hospital, China, between April 2023 to March 2024. After approval from the institutional ethics review committee, the sample size was calculated with a 1:1 ratio using the formula n=2×(Uα+Uβ)2×P(1-P)/(P1-P2)2, with

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Submission complete: 26-06-2024 **First Revision received:** 24-09-2024

Acceptance: 31-05-2025 **Last Revision received:** 27-05-2025

P=(P1×n1+P2×n2)/(n1+n2), confidence level taken as bilateral α=0.05 and 1-β=0.8. After conducting a systematic literature review, literature similar to the current research plan was selected: P1=100%, n1=35, P2=77.1%, and n2=35.[6] Those included were patients diagnosed with anal fistula who underwent surgery. According to the treatment method, the participants were assigned to control group A which received dressing changes using Vaseline gauze, and intervention group B which was treated with Jiedu Shengji ointment in conjunction with Vaseline gauze. Written informed consent was obtained from all the participants. Patients with combined dysfunction of organs, such as the heart, liver and kidneys, with combined cognitive impairment, or surgical contraindications, and those who could communicate normally or were unwilling to participate were excluded.

The diagnostic criteria used as per TCM as well as the Western medicine.[7,8]

Both groups underwent surgical treatment by the same team of doctors. On the second day after surgery, the wounds were cleaned with normal saline-soaked cotton balls and disinfected with iodophor-coated cotton balls after each bowel movement in both groups. Group A was subjected to dressing changes once in the morning and again in the evening. Group B also received the therapy twice daily. The main TCM components of Jiedu Shengji ointment included Radix lithospermi, Angelica sinensis, Angelica dahurica, Glycyrrhiza uralensis, frankincense (processed with vinegar), calomel, etc. Both cohorts were treated for 2 courses, with continuous treatment for 7 days constituting one course. The therapeutic effect was categorised as cure meaning dramatic disappearance of main clinical symptoms and complete healing of wounds; marked improvement meaning notable improvement of main clinical symptoms and partial wound healing; improvement meaning improvement of main clinical symptoms, although wounds remained unhealed; and ineffective meaning no improvement or aggravation of main clinical symptoms. The overall effectiveness rate was a combination of cure rate, marked improvement rate and improvement rate, and was expressed as a percentage of the total.[9]

For the comparison of serum indicators, 5mL of venous blood was drawn from each individual prior to therapy, 7 and 14 days after the initiation of the treatment. IL-6 values were detected using an enzyme-linked immunosorbent assay (ELISA) assay (Wuhan ADANTI Biotechnology Co., Ltd., China). SAA concentration was measured with colloidal gold (Hunan Beixier Biotechnology Co., Ltd., China).

Comparison of wound healing was done on the basis of wound bleeding score, wound healing time, and wound oedema score of the two cohorts. The scoring criteria for wound bleeding (at day 14 after treatment) [10 was bleeding volume <1mL = 0, 1-10mL = 1, and ≥10mL = 2. In terms of wound oedema score (at day 14 after treatment), mild oedema = 2, obvious oedema = 4, and severe oedema = 6. The period for wound healing was defined as the duration (in days) from the completion of the surgical procedure to the complete healing of the wound.

Anal function and pain degrees were assessed using the visual analogue scale (VAS) and the Faecal Incontinence Severity Index (FISI) before and following therapy.[11,12] The VAS score correlated positively with the level of anal pain, whereas the FISI score had an inverse relationship with anal function.

For the comparison of growth factor degrees pre- and post-therapy, serum concentrations of transforming growth factor-beta (TGF-β) and epidermal growth factor (EGF) in both the groups were measured before and after treatment using a Western blot assay (Shanghai Univ Biotech Co., Ltd., China).

Data was analysed using SPSS 20. Categorical data was presented as frequencies and percentages, and was assessed using the chi-square test. Quantitative data with a normal distribution was expressed as mean ± standard deviation, and inter-group comparisons were performed using independent-sample t-test. For data that did not have a normal distribution, median and interquartile range (IQR) values were used. Rank-sum test was employed to examine the ranked data. P<0.05 was taken as statistically significant.

Results

Of the 60 patients, 30(50%) were in group A; 20(66.6%) men and 10(33.3%) women with mean age 32.56±2.66 years (range: 22-43 years). There were 30(50%) patients in group B; 22(73.3%) men and 8(26.7%) women with mean

Table-1: Intergroup comparison of baseline data.

Group	Gender		Average	Type of anal fistula	
	Male (n)	Female (n)	age (year)	Complex (n)	Simple (n)
Control group (n = 30)	20(66.7)	10(33.3)	32.56 ± 2.66	18(60.0)	12(40.0)
Observation group (n = 30)	22(73.3)	8(26.7)	32.14 ± 2.35	15(50.0)	15(50.0)
χ2/t	0.317		0.648	0.606	
P	0.573		0.519	0.436	

Table-2: Comparison of efficacy between the groups

Group	Efficacy				Overall effective rate (n, %)
	Cured	Remarkably effective	Effective	Invalid	
Control group (n = 30)	1(3.3)	8(26.7)	10(33.3)	11(36.7)	19(63.3)
Observation group (n = 30)	4(13.3）	9(30.0)	13(40.0)	4(13.3)	26(86.7)
χ2	14.527				
P	<0.001				

values in group B were 15(50%) and 15(50%). The comparison of baseline data between the groups showed no significant difference (p>0.05) (Table 1).

Total effective rate of treatment in group B was 26 (86.67%) compared to 19 (63.33%) in group A (p<0.05) (Table 2).

Before treatment, IL-6 and SAA values were not significantly different (p>0.05). After 7 and 14 days of treatment, the levels of IL-6 and SAA in group B were significantly better than those in group A (p<0.05) (Table 3).

Table-3: Comparison of serum indicators between the groups at baseline and post-intervention

Score	IL-6（ng/L）			SAA（ug/mL）		
	Before treatment	7 d after treatment	14 d after treatment	Before treatment	7 d after treatment	14 d after treatment
Control group (n = 30)	72.15±7.24	56.32±4.88	13.76±1.88	17.54±2.11	15.64±1.88	12.02±1.36
Observation group (n = 30)	73.21±7.19	42.14±3.69	8.67±1.10	18.01±2.18	13.24±1.47	8.45±1.03
T	0.569	12.695	12.799	0.849	5.508	11.462
P	0.572	<0.001	<0.001	0.400	<0.001	<0.001

IL-6: Interleukin-6, SAA: Serum amyloid A.

Table-4: Comparison of wound healing between the groups

Group	Wound bleeding score (point)	Wound oedema score (point)	Wound healing time (d)
Control group (n = 30)	2.14±1.06	3.75±1.68	18.25±2.05
Observation group (n = 30)	1.24±0.88	1.59±0.65	12.33±1.54
T	3.578	6.568	12.646
P	0.001	<0.001	<0.001

The wound bleeding score, wound healing time, and wound oedema score of group B were significantly better than those of group A (p<0.05) (Table 4).

Prior to treatment, VAS and FISI scores between the cohorts were not significantly different (p>0.05). Following the therapy, VAS and FISI scores of group B were significantly better than those of group A (p<0.05) (Table 5).

Table-5: Comparison of anal function and pain scores between the groups

Group	VAS (score)			FISI (score)		
	Before treatment	After treatment	Difference (score)	Before treatment	After treatment	Difference (score)
Control group (n = 30)	3.85±1.25	3.12±1.12	-0.62±0.05	5.34±1.65	3.54±1.04	-1.85±1.03
Observation group (n = 30)	3.88±1.33	2.54±1.07	-1.33±0.12	5.36±1.62	2.41±0.97	-2.94±1.12
T	0.090	2.051	29.914	0.047	4.352	3.924
P	0.929	0.045	<0.001	0.962	<0.001	<0.001

VAS: Visual analogue scale, FISI: Faecal incontinence severity index.

Table-6: Comparison of growth factor levels between the groups at baseline and post-intervention.

Group	TGF-β（ug/L）		EGF（ug/L）	
	Before treatment	After treatment	Before treatment	After treatment
Control group (n = 30)	0.20±0.02	0.42±0.06	0.15±0.02	0.55±0.06
Observation group (n = 30)	0.21±0.02	0.74±0.08	0.16±0.02	0.77±0.08
T	1.936	17.527	1.936	12.050
P	0.058	<0.001	0.058	<0.001

TGF-β: Transforming growth factor-beta, EGF: Epidermal growth factor.

Prior to treatment, TGF-β and EGF values were not significantly different between the cohorts (p>0.05). After treatment, the levels in group B were significantly better than those in group A (p<0.05) (Table 6).

age 32.14±2.35 years (range: 22-42 years). In group A, there were 12(40%) patients with complex anal fistulas and 18(60%) with simple anal fistulas. The corresponding

Discussion

At present, surgery is the main treatment for anal fistulas in China as well as internationally. However, due to the special location of lesions, wound suturing is generally not performed in patients with anal fistulas after surgical treatment, which leads to a large postoperative wound surface area and a high risk of infections at the surgical site, causing a negative impact on wound healing. In cases of severe infections, the wounds are difficult to heal and some are even unhealed, resulting in serious adverse effects on patients' lives.[11,12] TCM believes that although anal fistula surgery can remove pathological products, there are still residual toxins left. In addition, surgical treatment may cause damage to patients' meridians, collaterals, skin and muscles, as well as Qi and blood stasis. After surgery, dampness-heat pathogenic factors can stagnate Qi and blood, invade tissues, meridians and collaterals, as well as cause Qi and blood stasis, leading to difficulty in surgical wound healing.[13] Consequently, TCM advocates clearing heat and expelling dampness, reducing swelling and relieving pain, and producing muscle with astringents to promote surgical wound healing.

In the current study, the control cohort underwent dressing alterations using Vaseline gauze, while the observation cohort received therapy with Jiedu Shengji ointment combined with Vaseline gauze dressing. The results showed that the overall effective rate was 86.67% and 63.33% in the observation and control cohorts, respectively ($p<0.05$). Across all the parameters assessed, the intervention group had better outcome than the control group.

The main TCM components of Jiedu Shengji ointment include Radix lithospermi, Angelica sinensis, Angelica dahurica, Glycyrrhiza uralensis, frankincense (processed with vinegar), calomel, etc. Radix lithospermi has the functions of cooling the blood, promoting blood circulation, detoxifying and promoting eruption. Angelica sinensis has been recorded as a medicinal herb in the first pharmacological treatise in China, Sheng Nong's Herbal Classic, with significant effects and an ability to regulate and nourish blood. Most TCM formulas contain Angelica sinensis, and it is said that it is used in nine out of 10 formulas. Glycyrrhiza uralensis has the effects of clearing away heat and toxic material, and relieving spasms and pain. Besides, it can also harmonise various medicines. As stated in the Compendium of Materia Medica, Angelica dahurica exhibits properties that include alleviating pain and expelling wind, eliminating dampness and reducing leucorrhoea, decreasing swelling and promoting pus discharge, as well as relieving itching. In the current study, the intervention group exhibited markedly higher overall efficacy and wound healing compared to the control cohort. This notable difference can be attributed primarily to the beneficial impact of TCM components found in Jiedu Shengji ointment, which possess advantageous properties, such as dampness elimination, blood circulation, heat dissipation, enhancement, inflammation reduction, pain alleviation, and tissue contraction. Consequently, these properties play an integral role in stimulating wound healing and enhancing the overall effectiveness of treatment among the patients. Furthermore, IL-6, a regulatory factor governing immune and inflammatory responses within the body, serves as a noticeable biomarker signifying inflammation in the body .[14] IL-6 production contributes to the body's defence and recovery during infection and tissue damage, but excessive synthesis of IL-6 can lead to severe inflammatory diseases.[15,16] In this study, before treatment, and on days 7 and 14 after treatment, there was a significant decrease in IL-6, which may be related to the components for promoting blood circulation, removing stasis, stopping bleeding, and producing muscle in Jiedu Shengji ointment. This result fundamentally aligns with earlier findings.[17] SAA, an acute-phase reactive protein, is derived from a precursor and is closely associated with inflammatory reactions and the severity of injuries. According to relevant data.[18], the serum SAA levels of patients with anal fistulas are significantly higher compared with the normal population. The TCM ingredients in Jiedu Shengji ointment have a certain anti-inflammatory effect. They promote wound recovery by inhibiting inflammatory responses at the site of the anal fistula, thereby reducing the patients' serum SAA to a relatively normal level. In the current intervention group, Jiedu Shengji ointment combined with Vaseline gauze dressing had a significant effect on reducing postoperative pain, and also basically restored the anal function to normal in the patients. There is relevant research.[19,20] indicating that serum TGF-β and EGF are involved in the repair of human traumatic wounds. Serum TGF-β can promote wound repair by transforming and activating signalling proteins to precipitate the substrate. EGF is a factor that promotes the proliferation of vascular pericytes, and also has the function of wound repair.

The current study has limitations of having a small sample size, and a single-centre design. Also, there may be selection bias in the sample. Future studies should have larger sample sizes raised from multiple centres and assessed prospectively.

Conclusion

Jiedu Shengji ointment was found to have significant efficacy in patients with anal fistulas undergoing surgical treatment. It could promote wound healing, and also improved serum indicator levels in the patients.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: This study is supported by S&T Program of Baoding（NO.2241ZF237.

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AUTHOR'S CONTRIBUTION:

YL: Design, preparation and agreement to be accountable for all aspects of the work.

YH: Collected and analysed clinical data.

SC & XZ: Significantly revision.

All authors read and approved the final manuscript.