Cell. Mol. Biol. (ISSN: 1165-158X)

Journal Homepage: www.cellmolbiol.org

Cellular and Molecular Biology

Original Article

# Huangbaiye Tuji combined with Longdan Xiegan Decoction for anal cryptitis: Analysis of clinical efficacy and its influence on disease recurrence

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**Article Info**

**Article history:**

**Received:** April 07, 2024
**Accepted:** May 05, 2024
**Published:** July 31, 2024

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**Abstract**

Given the rising incidence of anal cryptitis (AC) in recent years, it is of great significance to find an effective and safe treatment scheme to ensure the healthy life of patients. In this study, we explored the clinical efficacy of Huangbaiye Tuji combined with Longdan Xiegan Decoction (LDXGD) for AC and observed changes in patients' cellular immune function, which can provide a new reference for future treatment of AC. By comparison, we found that compared with Huangbaiye Tuji treatment alone, its combination with LDXGD had better clinical efficacy and high safety, contributing to more significant relief of inflammatory reaction and oxidative stress. In terms of immune function, the patients' humoral and cellular immunity were more effectively enhanced after the combination therapy. According to these results, it is recommended to use Huangbaiye Tuji combined with LDXGD in the treatment of AC.

**Keywords:** Huangbaiye Tuji, Longdan Xiegan Decoction, Anal cryptitis, Inflammatory response, Immune function

## 1. Introduction

Anal cryptitis (AC) is an acute/chronic inflammation of the anal sinuses and valves. The anatomical structure of the anal sinus makes it easy for fecal debris to accumulate here and block the orifice of the anal sinus, which will hinder the discharge of mucus secreted by anal glands and easily induce infection, causing AC and even anorectal diseases such as anal abscess or fistula in serious cases [1]. Clinically, AC is presented with incomplete defecation, pain, anal pruritus, etc., which generally last for a long time with repeated attacks, seriously affecting the normal life of patients [2]. As the early symptoms are not obvious, it is easy to be ignored by patients. As the disease progresses, AC can eventually lead to hemorrhoids, anal fistula, anal fissures, and other symptoms [3]. Antibiotics, as the traditional clinical treatment plan, can control the progression of AC, but they are usually difficult to achieve complete cure and carry a great risk of recurrence [4].

In traditional Chinese medicine, Huangbaiye Tuji is a common scheme for AC treatment, with its anti-inflammatory, antibacterial, antipyretic, and antiendotoxin effects demonstrated by pharmacological research [5]. At present, Huangbaiye Tuji has been proven to inhibit the growth and reproduction of infected bacteria and their RNA synthesis, eliminate edema, and accelerate the drying of the erosive surface of the damaged anal sinus [6]. However, its disadvantage is that the treatment progress is slow, usually taking 3-4 weeks to achieve the ideal treatment effect [7]. Hence, how to further enhance the efficiency of AC treatment is the focus of modern clinical research. Longdan Xiegan Decoction (LDXGD), which is recorded in the *Collection of Prescriptions with Notes*, is composed of Radix Gentianae, Fructus Gardeniae, Scutellaria baicalensis, akebia stem, Alisma orientalis, semen Plantaginis, Bupleurum chinense, Licorice pieces, Angelica sinensis, and Radix Rehmanniae. It has the functions of clearing heat from internal organs, purging excess fire in the liver and gallbladder, and clearing away dampness-heat of the liver channel, which is mainly used for treating inflammation syndrome of excess fire in the liver and gallbladder and

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**Doi:** http://dx.doi.org/10.14715/cmb/2024.70.7.17

syndrome of dampness-heat diffusing downward the liver meridian [8]. In diseases such as eczema and vaginitis, LDXGD has shown excellent therapeutic effects, greatly facilitating patient rehabilitation [9, 10]. But for AC, its application effect is still rarely reported.

Therefore, this study explores the clinical effect of LDXGD combined with Huangbaiye Tuji in the treatment of AC and observes the effect of this scheme on the cellular immunity of patients, thus providing new ideas and reference opinions for the future treatment of AC.

## 2. Materials and methods

### 2.1. Study participants

This study included 92 AC patients admitted to our hospital from May 2021 to October 2022 and randomized them into a research group (n=46) and a control group (n=46) that were treated with Huangbaiye Tuji and LDXGD plus Huangbaiye Tuji, respectively. The Ethics Committee of our hospital approved the study, and all study subjects signed the informed consent form.

### 2.2. Criteria for patient enrollment and exclusion

Inclusion criteria: anal distension, pain, wet anus, foreign body sensation, and mucus in feces; obvious tenderness, depression, or induration of anal recess, as well as anal papilla edema and tenderness; anal sinus congestion and edema, with dark color and discharge of secretions, or accompanied by hypertrophy of anal papilla by anal endoscopy; age > 18 years old; complete medical records. Exclusion criteria: serious diseases of the heart, liver, kidneys, etc.; disturbance of consciousness or lack of active cooperation; pregnant and lactating women; anal fistula, hemorrhoids, anal fistula, intestinal polyps, or other anorectal diseases; allergy history or allergies to the study medication.

### 2.3. Methods

Both groups were treated by retention enema with Huangbaiye Tuji. After the patient emptied his or her bowels, the anus was washed with warm water and wiped with a clean, dry towel. After heating the Compound Huangbaiye Tuji (Shandong Hanfang Pharmaceutical Co., Ltd., Z10950097) to 37-38℃, 30mL of it was sucked up with a sterile syringe that was connected to a disposable sputum suction tube. The patient was placed in the left lateral position, with the perianal sphincter relaxed. The sputum suction tube was then gently inserted into the rectum by 5-7cm through the anus, and the syringe was slowly pushed to inject the medicine into the anus. The patient changed his/her position every 30min to keep the drug in the anus for 3-4 hours. The drug was given as a bolus injection once in the morning and once in the evening, with 7 days as a course of treatment for 28 days. On this basis, the research group was additionally treated with LDXGD. 6g each of stir-fried Radix Gentianae and Licorice pieces, 15g each of Scutellaria baicalensis and Fructus Gardeniae, as well as 9 g each of Alisma orientalis, Herba Houttuyniae, Radix Puerariae, Radix Angelicae Sinensis, Caulis Akebiae, Radix Rehmanniae, and Radix Angelicae Dahuricae were decocted with 500mL of water, and the decoction was taken orally once in the morning and evening for 28 days.

### 2.4. Clinical efficacy evaluation

The efficacy was evaluated after treatment with reference to the AC clinical guidelines [11]. Cure: all clinical symptoms disappeared, and the anal sinus returned to normal by anal endoscopy. Marked effectiveness: the clinical symptoms basically disappeared, and there was no congestion in the anal sinus. Improvement: symptoms improved with mild sinus congestion. Ineffectiveness: symptoms and signs did not change. Total effective rate = (cure+marked effectiveness+improvement) cases / total number of people ×100%.

### 2.5. Sample collection and testing

The patients' fasting venous blood was collected before and after treatment and divided into two parts, and the serum was separated by centrifugation after standing at room temperature for 30 min. TNF-α, IL-2, IL-6, IL-10, SOD, and MDA were detected by ELISA, and immunoglobulin (Ig) A/G/M/E was measured by immunoturbidimetry. The other portion was used for flow cytometry detection of T lymphocyte subsets $CD3^+$, $CD4^+$, and $CD8^+$, and $CD4^+/CD8^+$ was calculated.

### 2.6. Prognostic follow-up

All patients were followed up for one year by regular review, with a follow-up interval of no more than 2 months, and the one-year recurrence rate was recorded.

### 2.7. Outcome measures

The clinical efficacy and adverse reactions of the two groups were observed. The inflammatory reaction (TNF-α, IL-2, IL-6, and IL-10), oxidative stress (SOD and MDA), humoral immunity (IgA/G/M/E), and cellular immunity ($CD3^+$, $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$) were compared between the two groups before and after treatment. Finally, the AC recurrence rate was analyzed.

### 2.8. Statistical methods

Data were input into SPSS24.0 for statistical analyses, and a minimum significance threshold of $P<0.05$ was used. Count data were represented by [n(%)] and the inter-group differences were identified by the chi-square test. Measurement data, expressed by ( $\chi \pm s$), were analyzed between groups using the independent sample t-test and within groups using the paired t-test.

## 3. Results

### 3.1. Comparison of clinical data

Patient age, sex, disease course, and other clinical data were statistically analyzed, with no marked inter-group differences identified (P>0.05), confirming comparability (Table 1).

### 3.2. Comparison of clinical efficacy

After treatment, the total effective rate of the research group was 86.96%, higher compared with the control group (69.57%, P<0.05), indicating that LDXGD combined with Huangbaiye Tuji has a better clinical effect on AC (Table 2).

### 3.3. Comparison of safety

By counting the adverse reactions in the treatment process, it was found that the incidence of adverse reactions was 10.87% in the research group and 13.04% in the

**Table 1.** No difference in clinical data.

| | Control group (n=46) | Research group (n=46) | $t/\chi^2$ | P |
|---|---|---|---|---|
| Age | 42.63±7.58 | 43.91±6.79 | 0.855 | 0.395 |
| Disease course (years) | 3.26±1.10 | 3.30±1.01 | 0.197 | 0.844 |
| Sex | | | 0.821 | 0.365 |
| male | 34 (73.91) | 30 (65.22) | | |
| female | 12 (26.09) | 16 (34.78) | | |
| Smoking | | | 0.045 | 0.833 |
| yes | 20 (43.48) | 19 (41.30) | | |
| no | 26 (56.52) | 27 (58.70) | | |
| Drinking | | | 0.453 | 0.501 |
| yes | 13 (28.26) | 16 (34.78) | | |
| no | 33 (71.74) | 30 (65.22) | | |
| Family history of disease | | | 0.713 | 0.398 |
| yes | 4 (8.70) | 2 (4.35) | | |
| no | 42 (91.30) | 44 (95.65) | | |

**Table 2.** Better clinical efficacy in research group.

| Group | Cure | Marked effectiveness | Improvement | Ineffectiveness | Total effective rate |
|---|---|---|---|---|---|
| Control group (n=46) | 7 (15.22) | 24 (52.17) | 9 (19.57) | 6 (13.04) | 40 (86.96) |
| Research group (n=46) | 3 (6.52) | 15 (32.61) | 14 (30.43) | 14 (30.43) | 32 (69.57) |
| $\chi^2$ | | | | | 4.089 |
| P | | | | | 0.043 |

**Table 3.** No difference in safety.

| Group | Abdominal Pain | Nausea and vomiting | Diarrhea | Skin rash | Fever | Total incidence |
|---|---|---|---|---|---|---|
| Control group (n=46) | 1 (2.17) | 2 (4.35) | 1 (2.17) | 1 (2.17) | 1 (2.17) | 6 (13.04) |
| Research group (n=46) | 1 (2.17) | 1 (2.17) | 1 (2.17) | 0 (0.0) | 2 (4.35) | 5 (10.87) |
| $\chi^2$ | | | | | | 0.103 |
| P | | | | | | 0.748 |

control group. No significant inter-group difference was found in the incidence of adverse reactions (P>0.05), demonstrating an equivalent treatment safety profile in the two groups (Table 3).

### 3.4. Comparison of inflammatory reaction

The two groups showed no marked difference in pre-treatment inflammatory reaction (P>0.05). After treatment, TNF-α, IL-2, and IL-6 in both groups decreased, while IL-10 increased (P<0.05). Among them, the post-treatment TNF-α, IL-2, and IL-6 in the research group were (102.74±25.76)ng/L, (96.49±9.91)μg/L and (93.30±17.52) ng/L, all lower compared with the control group; while the L-10 was (227.02±41.91)ng/L after treatment, which was higher versus the control group (P<0.05). It shows that LDXGD combined with Huangbaiye Tuji has a better anti-inflammatory effect on AC (Figure 1).

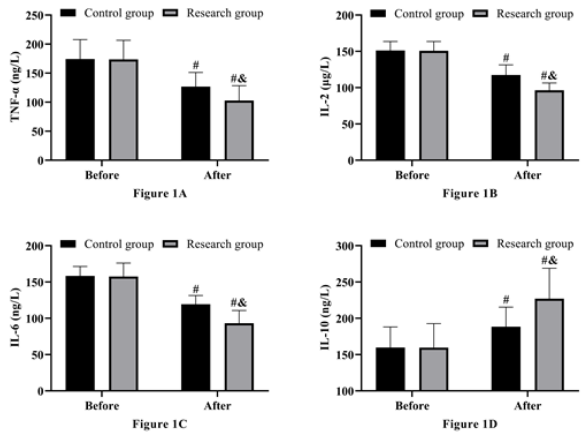


**Fig. 1. Comparison of inflammatory reaction.** (A) Comparison of TNF-α, (B) Comparison of IL-2, (C) Comparison of IL-6, (D) Comparison of IL-10. *vs.* control group, &P<0.05, *vs.* before treatment, #P<0.05.

### 3.5. Comparison of humoral immune function

The Ig test results did not differ significantly between groups prior to treatment (P>0.05). After treatment, IgM and IgA in both groups increased, with even higher levels in the research group; IgG and IgE decreased, with more marked reductions in the research group compared with the control group (P<0.05). Therefore, LDXGD combined with Huangbaiye Tuji has a better effect on improving hu-

moral immune function in AC patients (Figure 2).

### 3.6. Comparison of cellular immune function

The test results of T lymphocyte subsets revealed no evident inter-group difference before treatment (P>0.05). After treatment, $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ in both groups increased, with those in the research group being (73.91±6.34)%, (38.09±5.44)%, and (1.68±0.34), respectively, all of which were higher compared with the control group (P<0.05); while CD8+ decreased, with that in the research group being (23.03±2.99), which was even lower versus the control group (P<0.05). Therefore, LDXGD combined with Huangbaiye Tuji is also helpful in improving the cellular immune function of AC patients (Figure 3).

### 3.7. Comparison of oxidative stress

Similarly, SOD and MDA were not statistically different between the research and control groups before treatment (P>0.05). An elevation in SOD and a reduction in MDA were observed in both groups after treatment, with higher SOD and lower MDA in the research group compared with the control group (P<0.05), suggesting milder oxidative stress in the research group (Figure 4).

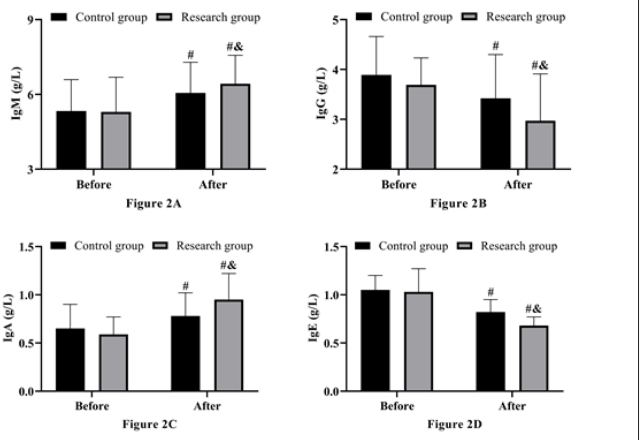


**Fig. 2. Comparison of humoral immune function.** (A) Comparison of IgM, (B) Comparison of IgG, (C) Comparison of IgA, (D) Comparison of IgE. *vs.* control group, &P<0.05, *vs.* before treatment, #P<0.05.

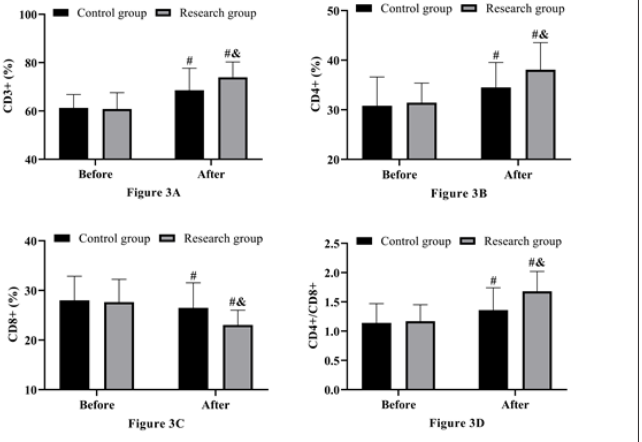


**Fig. 3. Comparison of cellular immune function.** (A) Comparison of CD3+, (B) Comparison of CD4+, (C) Comparison of CD8+, (D) Comparison of CD4+/CD8+. *vs.* control group, &P<0.05, *vs.* before treatment, #P<0.05.

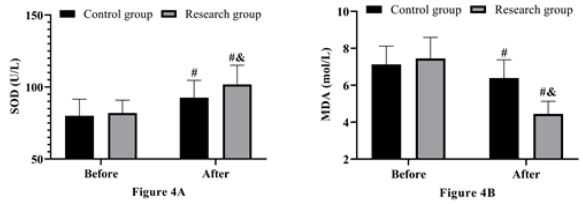


**Fig. 4. Comparison of oxidative stress.** (A) Comparison of SOD, (B) Comparison of MDA. *vs.* control group, &P<0.05, *vs.* before treatment, #P<0.05.

### 3.8. Comparison of prognostic recurrence

The prognostic follow-up successfully tracked all the subjects. The 1-year AC recurrence rate was 6.52% (3 cases) in the control group and 13.04% (6 cases) in the research group, with no significant difference (P>0.05).

## 4. Discussion

The incidence of AC has shown a trend of increasing in recent years, which seriously affects people's normal life [12]. This study found that the combination of LDXGD and Huangbaiye Tuji was highly effective in the treatment of AC, which can improve the humoral immunity and cellular state of patients and inhibit inflammation more effectively, demonstrating the great application potential of this combination therapy in the future clinical treatment of AC.

First of all, the inter-group comparison of clinical efficacy showed a markedly higher total effective rate in the research group compared with the control group, confirming the excellent therapeutic effect of Huangbaiye Tuji combined with LDXGD. In addition, the absence of statistical difference in adverse reactions between groups suggests that the use of LDXGD will not increase any toxic and side effects, with high clinical applicability, which is also due to the fact that the traditional Chinese medicine prescriptions are all composed of natural compounds or plants with reliable safety [13]. In traditional Chinese medicine, AC is considered to belong to the category of "perianal abscess" and "mixed hemorrhoids and perianal abscess", mostly due to improper diet, excessively spicy, pungent, fatty, and greasy food, intense dampness-heat stagnation of the anus, long-term stagnation of qi and blood, and obstruction of collaterals, with the syndrome of interior dampness-heat found in the majority [14]. Therefore, according to the characteristics of chronic AC, traditional Chinese medicine usually adopts the methods of heat-clearing and detoxicating, invigorating the spleen to eliminate dampness, and inducing diuresis to alleviate edema [15]. Relevant pharmacological research on LDXGD shows that Sophora flavescens contained in LDXGD has the effect of clearing heat and drying dampness, which in combination with Cortex Phellodendri can enter the kidneys and bladder, clearing away heat, drying dampness, clearing deficient heat, removing hectic fever due to yin-deficiency, detoxifying, and treating sores; Radix Gentianae can reach the liver and gallbladder to clear heat and dry dampness, and Sophora flavescens, Cortex Phellodendri, Radix Gentianae, and Scutellaria baicalensis jointly dissipate dampness-heat in the lower energizer; Alisma orientalis can promote bladder smooth; Radix Angelicae Sinensis mois-

tens the intestines to relieve constipation and relieve pain; Radix Angelicae Sinensis and Rehmannia glutinosa work together to nourish and replenish blood; Hedyotis diffusa has the functions of clearing away heat and toxic materials, invigorating blood circulation and alleviating pain; Houttuynia cordata can heat and detoxify, reduce swelling, treat sores, strengthen stomach, and promote digestion; Pueraria lobata resolves the flesh, help produce saliva, and slake thirst, and; Licorice pieces can tonify the spleen and stomach and regulate various medicines [16]. The combination of various medicines enables LDXGD to play an excellent role in clearing away heat, drying dampness, reducing swelling, and detoxifying [17]. Because of this, the research group achieved better treatment outcomes. Similarly, in previous studies, we also observed that the use of LDXGD can promote the recovery of cervicitis [18], which can also support the results of this study.

On the other hand, the occurrence of AC is known to be a chronic inflammatory progression caused by bacterial infection, in which inflammation and oxidative stress, both regulated by immune function, are the most important pathological injury processes [19]. Therefore, we further observed changes in inflammatory reaction, oxidative stress reaction, and immune function. The pro-inflammatory factors TNF-α, PCT, IL-2, and IL-6 in the research group all decreased, the anti-inflammatory factor IL-10 increased, and the oxidative stress damage was significantly reduced, further confirming the excellent pathological improvement effect of Huangbaiye Tuji combined with LDXGD in the treatment of AC, which was mainly due to the excellent immunomodulatory ability of this combination therapy. Immune function refers to the body's resistance to diseases, and its strength directly reflects the body's ability to resist the invasion of germs [20]. T lymphocyte subsets mainly include helper T lymphocytes $CD3^+$, $CD4^+$, and inhibitory or cytotoxic T lymphocytes $CD8^+$ [21]. Igs are antigen receptors on the B cell membrane, which can specifically recognize antigen molecules with a conditioning and antibody-dependent cell-mediated cytotoxicity [22]. T lymphocyte subsets and Igs are the major components of the human immune system, and their immune dysfunction is the key mechanism leading to the aggravation of AC and organ function damage [23]. After treatment, IgM, IgA, $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ increased in the research group, while IgG, IgE, and $CD8^+$ decreased, which fully confirms the excellent immunomodulatory effect of Huangbaiye Tuji combined with LDXGD. Similarly, Tao LL et al. observed a more significant improvement in the immune function of patients with polycystic ovary syndrome after treatment with Huangbaiye Tuji [17], which is consistent with our view.

Finally, in the prognostic follow-up, we found no significant difference in the one-year AC recurrence rate between the two groups, suggesting that both treatment schemes have relatively stable prognostic effects. It may also be due to the small number of cases included in this paper, resulting in no significant difference in recurrence rates. Therefore, further confirmation will be made by increasing the number of cases and extending the follow-up period. Besides, further in vitro tests are needed to confirm the therapeutic mechanism of Huangbaiye Tuji combined with LDXGD on AC, so as to provide a more reliable reference for clinical practice.

## 5. Conclusion

Huangbaiye Tuji combined with LDXGD has a remarkable effect in treating AC, which can effectively inhibit inflammation and oxidative stress and improve cellular immune function, with an excellent recurrence control effect. This combination therapy is recommended in the future clinical treatment of AC, which can further improve the rehabilitation of patients on the premise of ensuring patient safety.

## Conflict of Interests

The author has no conflicts with any step of the article preparation.

## Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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