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THE USE OF RECTAL SUPPOSITORIES WITH STREPTOKINASE AND STREPTODORNASE IN THE TREATMENT OF ANAL FISTULAS WITH EXTENSIVE INFLAMMATORY INFILTRATION

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ABSTRACT

Background: Anal fistulas with extensive inflammatory infiltration pose significant challenges in treatment, often leading to prolonged hospital stays, complications, and reduced quality of life. This study evaluates the efficacy of rectal suppositories containing streptokinase (15,000 IU) and streptodornase (1,250 IU) as an adjunct to standard therapy. **Methods:** A prospective randomized controlled trial was conducted from January 2018 to December 2019 at Weihaiwei People's Hospital. One hundred and ten patients with anal fistulas and extensive inflammatory infiltration were divided into two groups: Group 1 (n=55) received standard treatment per international guidelines, while Group 2 (n=55) received the same plus rectal suppositories. Suppositories were administered based on disease severity: for severe cases, 1 suppository three times daily for 3 days, twice daily for 3 days, and once daily for 3 days; for moderate/mild cases, twice daily for 3 days, then once daily for 4 days or twice daily for 2 days. Outcomes included hospital stay duration, severe disease incidence, complications, pain syndrome (via Visual Analog Scale, VAS), and quality of life (QoLAF-Q). **Results:** Group 2 showed significantly shorter hospital stays (mean 12.4 ± 3.2 days vs. 18.7 ± 4.5 days, $p<0.001$), fewer severe cases (14% vs. 36%, $p<0.01$), fewer complications (9% vs. 25%, $p<0.05$), lower VAS scores, and improved QoLAF-Q scores compared to Group 1. **Conclusions:** Adjunctive use of streptokinase-streptodornase suppositories enhances treatment efficacy, reduces morbidity, and improves patient outcomes in anal fistulas with inflammatory infiltration.

KEYWORDS: Anal fistula, inflammatory infiltration, streptokinase, streptodornase, rectal suppositories, quality of life.

INTRODUCTION

Anal fistulas represent a common yet complex condition in coloproctology, characterized by an abnormal tract between the anal canal and perianal skin, often resulting from cryptoglandular infection.[1] When accompanied by extensive inflammatory infiltration, these fistulas can lead to significant morbidity, including recurrent abscesses, chronic pain, and impaired sphincter function, which collectively diminish patients' quality of life.[2] Traditional management strategies, as outlined in international guidelines, primarily involve surgical interventions such as fistulotomy or seton placement to eradicate sepsis and promote healing while preserving continence.[3] However, these approaches are associated with variable success rates, ranging from 70% to 95%, and risks of incontinence, particularly in complex transsphincteric fistulas.[4]

The pathophysiology of anal fistulas with inflammatory infiltration involves persistent infection, fibrin deposition, and necrotic debris accumulation, which hinder natural healing processes.[5] Enzymatic agents have been explored in wound management to facilitate debridement and reduce inflammation. Streptokinase, a

fibrinolytic enzyme, and streptodornase, a deoxyribonuclease, have demonstrated efficacy in liquefying pus and breaking down DNA in exudates, thereby promoting wound cleansing.[6] Their combined use in topical preparations, such as Varidase, has been documented in chronic wounds and leg ulcers, showing improved healing times and reduced bacterial burden.[7] Despite these benefits in general wound care, their application in anal fistulas remains underexplored, particularly in the form of rectal suppositories, which offer targeted delivery to the inflamed perianal region.[8]

Current literature highlights the limitations of standard treatments. For instance, fibrin glue injection, while sphincter-sparing, yields long-term success in only 30-60% of cases.[9] Similarly, collagen plugs and laser-based techniques provide alternatives but often require multiple procedures and carry recurrence risks.[10] In cases of extensive inflammation, adjunctive therapies are crucial to mitigate complications like sepsis or prolonged hospitalization.[11] Quality of life assessments, using validated tools like the Quality of Life in Patients with Anal Fistula Questionnaire (QoLAF-Q), reveal that untreated or poorly managed fistulas significantly impact physical, emotional, and social domains.[12] Studies indicate that patients with inflammatory fistulas experience higher pain levels and functional impairments compared to simple fistulas.[13]

This study addresses a gap in the evidence by investigating the adjunctive role of streptokinase-streptodornase suppositories in a randomized controlled setting. Drawing from enzymatic debridement principles in wound care[14], we hypothesize that these suppositories will enhance resolution of inflammation, reduce pain, and improve quality of life. Prior research on streptokinase in abscess management supports its safety and efficacy in dissolving clots without systemic effects when applied locally.[15] In coloproctology, limited trials suggest potential benefits in postoperative wound healing.[16] By integrating this with standard guidelines, our trial aims to provide a novel, non-invasive adjunct that could optimize outcomes in this challenging subset of patients.[17] The rationale is further supported by systematic reviews emphasizing the need for innovative therapies to reduce recurrence and morbidity in complex fistulas.[18] Ultimately, this research seeks to contribute to evidence-based practices, potentially shifting paradigms toward multimodal treatments that prioritize patient-centered outcomes.[5]

MATERIALS AND METHODS

This prospective randomized controlled trial was conducted at the Department of Coloproctology, Weihaiwei People's Hospital, from January 2018 to December 2019. Ethical approval was obtained from the hospital's institutional review board, and all participants provided written informed consent. Inclusion criteria were patients aged 18-70 years with confirmed anal fistulas and extensive inflammatory infiltration (defined as perianal swelling >5 cm, elevated CRP >20 mg/L, and MRI evidence of diffuse edema). Exclusion criteria included Crohn's disease, immunodeficiency, pregnancy, or prior fistula surgery within 6 months.

Patients were randomized 1:1 into two groups using computer-generated codes. Group 1 (control, n=55) received standard treatment per international guidelines[3], including abscess drainage, antibiotics (e.g., metronidazole and ciprofloxacin), and fistulotomy or seton placement as indicated.[1] Group 2 (intervention, n=55) received the same plus rectal suppositories containing streptokinase (15,000 IU) and streptodornase (1,250 IU). Suppository administration varied by severity: for severe cases (VAS >7, fever >38°C), 1 suppository thrice daily for 3 days, twice daily for 3 days, once daily for 3 days; for moderate/mild (VAS 4-7 or <4), twice daily for 3 days, then once daily for 4 days or twice daily for 2 days.

Outcomes were assessed at baseline, days 3, 6, 9, and discharge. Primary endpoints: hospital stay duration, incidence of severe disease (persistent fever/sepsis), complications (recurrence, incontinence). Secondary: pain via VAS (0-10), quality of life via QoLAF-Q (17-85, higher scores indicate worse QoL).[12] Statistical analysis used SPSS software: t-tests for continuous variables, chi-square for categorical, repeated-measures ANOVA for dynamics, with $p<0.05$ significant.

RESULTS

Demographics were comparable: mean age 45.2 ± 10.1 years in Group 1 vs. 44.8 ± 9.7 in Group 2; 60% male in both.

The primary clinical outcomes are summarized in Table 1.

Table 1: Comparison of primary clinical outcomes between groups.

Outcome	Group 1 (Standard Treatment, n=55)	Group 2 (Standard + Enzyme Therapy, n=55)	p-value
Mean hospital stay (days)	18.7 ± 4.5	12.4 ± 3.2	<0.001
Severe disease	20/55 (36%)	8/55 (14%)	<0.01
Complications	14/55 (25%) (7 recurrences, 5 incontinence, 2 sepsis)	5/55 (9%) (3 recurrences, 2 incontinence)	<0.05

Group 2 demonstrated superior outcomes. Mean hospital stay was 18.7 ± 4.5 days in Group 1 vs. 12.4 ± 3.2 days in Group 2 ($p<0.001$). Severe disease occurred in 20/55 (36%) in Group 1 vs. 8/55 (14%) in Group 2 ($p<0.01$).

Complications: 14/55 (25%) in Group 1 (7 recurrences, 5 incontinence, 2 sepsis) vs. 5/55 (9%) in Group 2 (3 recurrences, 2 incontinence) ($p<0.05$).

The dynamics of pain syndrome (VAS scores) over time in both groups is summarized in Table 2.

Table 2: Dynamics of pain syndrome (VAS scores) over time in both groups.

Time Point	Group 1 VAS (Mean ± SD)	Group 2 VAS (Mean ± SD)	p-value (Between Groups)
Baseline	7.8 ± 1.2	7.9 ± 1.1	0.72
Day 3	6.5 ± 1.3	5.2 ± 1.0	<0.001
Day 6	5.1 ± 1.4	3.4 ± 0.9	<0.001
Day 9	4.0 ± 1.2	2.1 ± 0.8	<0.001
Discharge	2.5 ± 1.0	1.2 ± 0.7	<0.001

In Group 1, VAS decreased from baseline to day 3 (7.8 to 6.5, $p<0.01$), day 3 to 6 (6.5 to 5.1, $p<0.05$), day 6 to 9 (5.1 to 4.0, $p<0.05$), and day 9 to discharge (4.0 to 2.5, $p<0.01$). All changes were statistically significant. In Group 2, VAS reduced from baseline to day 3 (7.9 to 5.2, $p<0.001$), day 3 to 6 (5.2 to 3.4, $p<0.001$), day 6 to 9 (3.4 to 2.1, $p<0.001$), and day 9 to discharge (2.1 to 1.2, $p<0.01$), with all differences highly significant. Between-group comparisons showed no difference at baseline ($p=0.72$), but Group 2 had significantly lower scores at day 3 ($p<0.001$), day 6 ($p<0.001$), day 9 ($p<0.001$), and discharge ($p<0.001$).

The dynamics of quality of life (HDSS scores) over time in both groups is summarized in Table 3.

Table 3: Dynamics of quality of life (HDSS scores) over time in both groups.

Time Point	Group 1 QoLAF-Q (Mean ± SD)	Group 2 QoLAF-Q (Mean ± SD)	p-value (Between Groups)
Baseline	62.4 ± 8.5	63.1 ± 8.2	0.68
Day 3	58.2 ± 7.9	52.6 ± 7.0	<0.01
Day 6	52.7 ± 7.4	44.3 ± 6.1	<0.001
Day 9	47.1 ± 6.8	36.8 ± 5.4	<0.001
Discharge	40.5 ± 6.2	30.2 ± 4.9	<0.001

In Group 1, QoLAF-Q scores improved from baseline to day 3 (62.4 to 58.2, $p<0.05$), day 3 to 6 (58.2 to 52.7, $p<0.05$), day 6 to 9 (52.7 to 47.1, $p<0.01$), and day 9 to discharge (47.1 to 40.5, $p<0.01$), with all changes significant. In Group 2, scores decreased from baseline to day 3 (63.1 to 52.6, $p<0.001$), day 3 to 6 (52.6 to 44.3, $p<0.001$), day 6 to 9 (44.3 to 36.8, $p<0.001$), and day 9 to discharge (36.8 to 30.2, $p<0.001$), indicating highly significant improvements. Intergroup analysis revealed no baseline difference ($p=0.68$), but Group 2 exhibited better scores at day 3 ($p<0.01$), day 6 ($p<0.001$), day 9 ($p<0.001$), and discharge ($p<0.001$).

No serious adverse events related to enzyme therapy were observed.

DISCUSSION

The findings of this study underscore the therapeutic potential of rectal suppositories containing streptokinase and streptodornase as an adjunct to standard treatment for anal fistulas with extensive inflammatory infiltration. By facilitating enzymatic debridement, these agents appear to accelerate resolution of inflammation, leading to shorter hospital stays, reduced severe disease incidence, fewer complications, alleviated pain, and enhanced quality of life.[6] This aligns with prior wound care research where streptokinase-streptodornase combinations have been shown to effectively liquefy necrotic tissue and reduce bacterial load in chronic ulcers.[7] In the context of anal fistulas, where persistent exudates and fibrin contribute to tract patency[5], the targeted rectal delivery likely enhances local efficacy without systemic risks, as evidenced by the absence of adverse events in our cohort.[15]

Compared to traditional approaches, such as fistulotomy, which carries a 10-30% incontinence risk[4], our adjunctive therapy preserved sphincter integrity while improving outcomes. This is particularly relevant for complex fistulas, where sphincter-sparing techniques like fibrin glue or plugs yield inconsistent results.[9, 10] Our data indicate a 64% reduction in severe cases and 64% fewer complications in the intervention group, suggesting that enzymatic action mitigates inflammatory escalation.[11] The shorter hospital stay (33% reduction) not only implies cost savings but also reflects faster clinical improvement, consistent with studies on enzymatic agents in abscess management.[14]

Pain dynamics revealed progressive reductions in both groups, attributable to standard interventions like drainage and antibiotics.[1] However, the intervention group's more rapid and significant declines ($p<0.001$ at most points) highlight the anti-inflammatory benefits of streptodornase in breaking down DNA-rich pus, reducing tissue pressure and nociception.[8] Similarly, QoLAF-Q improvements were more pronounced in Group 2, corroborating literature on the instrument's sensitivity to

treatment effects.[12] The greater intergroup differences over time suggest that adjunctive therapy addresses not only physical symptoms but also emotional and social burdens, as seen in prior fistula QoL assessments.[13]

Limitations include the single-center design and lack of long-term follow-up beyond discharge, though recurrence rates were low in both groups. Future multicenter trials could validate these findings and explore dose optimizations.[16] Nonetheless, this study advances the field by integrating enzymatic principles from wound care.[17] into coloproctology, potentially broadening options for inflammatory fistulas where guidelines emphasize multimodal strategies.[3] Compared to emerging techniques like laser fistulotomy[5], our approach is non-invasive and accessible, offering a bridge between conservative and surgical management.[18] Overall, streptokinase-streptodornase suppositories represent a promising adjunct, warranting inclusion in updated protocols to optimize patient-centered care.[2]

CONCLUSIONS

Adjunctive rectal suppositories with streptokinase and streptodornase significantly enhance the treatment of anal fistulas with extensive inflammatory infiltration, reducing hospital stays, complications, pain, and improving quality of life compared to standard therapy alone. This enzymatic approach offers a safe, effective addition to current guidelines.

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