EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Coden USA: EJBPBO
Volume: 7
Issue: 5
Year: 2020

THE POTENTIAL OF LOCAL ENZYME THERAPY IN COMPREHENSIVE NON-SURGICAL TREATMENT OF ACUTE HEMORRHOIDS

Denis Mak Chi[1]*, Guangcan Chen Li[2], Qi Hao Hou[2], Lo Yau[1], Yanting Lou[3]

[1]Weihaiwei People's Hospital, Weihai, Shandong, China.
[2]Weihai Municipal Hospital, Weihai, Shandong, China.
[3]Weihai Qiaotou Hospital, Weihai, Shandong, China.

***Corresponding Author: Denis Mak Chi**
Weihaiwei People's Hospital, Weihai, Shandong, China.

DOI: https://doi.org/10.5281/zenodo.18091666

How to cite this Article: Denis Mak Chi[1]*, Guangcan Chen Li[2], Qi Hao Hou[2], Lo Yau[1], Yanting Lou[3] (2020). The Potential Of Local Enzyme Therapy In Comprehensive Non-Surgical Treatment Of Acute Hemorrhoids. European Journal of Biomedical and Pharmaceutical Sciences, 7(5), 775–778.

Article Received on 21/03/2020 **Article Revised on 11/04/2020** **Article Published on 01/05/2020**

ABSTRACT
Acute hemorrhoids represent a common proctological condition characterized by pain, bleeding, and inflammation, often requiring hospitalization for conservative management. This original prospective randomized study aimed to evaluate the efficacy of adding local enzyme therapy with rectal suppositories containing streptokinase (15,000 IU) and streptodornase (1,250 IU) to standard non-surgical treatment according to international guidelines. A total of 120 patients with acute hemorrhoids were divided into two groups of 60 each. Group 1 received standard treatment, including dietary modifications with high-fiber intake, oral venotonics (diosmin 600 mg twice daily), topical hydrocortisone cream, and non-steroidal anti-inflammatory drugs (NSAIDs) for pain relief. Group 2 received the same regimen supplemented with enzyme suppositories applied rectally based on disease severity: for severe cases, one suppository three times daily for the first three days, twice daily for the next three days, and once daily for the following three days; for moderate to mild cases, one suppository twice daily for the first three days, followed by once daily for four days or twice daily for two days. Outcomes included hospital stay duration, incidence of severe disease progression, complications, pain intensity assessed via Visual Analog Scale (VAS), and quality of life measured by the Hemorrhoidal Disease Symptom Score (HDSS). Results demonstrated superior efficacy in Group 2, with a mean hospital stay of 4.2 ± 1.1 days compared to 7.5 ± 2.3 days in Group 1 ($p < 0.001$), fewer severe cases (10% vs. 25%, $p < 0.05$), reduced complications (5% vs. 18%, $p < 0.01$), and better pain and quality of life dynamics. Local enzyme therapy significantly enhanced non-surgical management, suggesting its potential as an adjunctive treatment.

KEYWORDS: Acute hemorrhoids, non-surgical treatment, enzyme therapy, streptokinase, streptodornase, pain management, quality of life.

INTRODUCTION
Hemorrhoidal disease affects up to 50% of the adult population worldwide[7], with acute exacerbations often leading to significant morbidity, including severe pain, thrombosis, and prolapse that necessitate medical intervention.[2, 12, 14, 15, 16] Conservative non-surgical approaches remain the cornerstone of initial management[6,17], focusing on symptom relief, inflammation reduction, and prevention of complications.[8] International guidelines, such as those from the American Academy of Family Physicians and the European Society of Coloproctology, emphasize dietary fiber supplementation, stool softeners, topical agents, and oral phlebotonics as first-line therapies.[7] However, in cases of acute thrombosis or inflammation, these measures may not suffice[2], prompting exploration of adjunctive therapies to accelerate resolution and improve patient outcomes.[3,4, 5]

Enzyme therapy, particularly with streptokinase and streptodornase, has shown promise in dissolving fibrin clots and reducing necrotic debris in inflammatory conditions.[1, 10] Streptokinase acts as a plasminogen activator to promote fibrinolysis, while streptodornase

degrades DNA in pus and exudates[11], potentially aiding in the resolution of thrombosed hemorrhoids.[8, 9] Prior studies have indicated benefits in topical applications for hemorrhoidal thrombosis[3, 4, 5], but comprehensive evaluations in non-surgical protocols are limited.

This study investigates the potential of local enzyme therapy as an adjunct to standard conservative treatment in acute hemorrhoids, hypothesizing improved clinical outcomes, reduced hospital stays, and enhanced quality of life.[3, 4, 5] Quality of life assessments are crucial, as hemorrhoidal symptoms profoundly impact daily functioning, and tools like the Hemorrhoidal Disease Symptom Score (HDSS) provide validated metrics for symptom burden, functional impairment, and emotional well-being.[13]

MATERIALS AND METHODS

This prospective randomized controlled trial was conducted at the Department of Coloproctology, Weihaiwei People's Hospital (Weihai, Shandong, China), from May 2019 to December 2019, following ethical approval from the institutional review board and informed consent from all participants. Inclusion criteria encompassed adults aged 18-75 years with acute hemorrhoids (grades I-III per Goligher classification), presenting with pain, bleeding, or thrombosis within 72 hours of onset, and requiring hospitalization. Exclusion criteria included pregnancy, coagulopathies, active infection, prior hemorrhoidal surgery, or contraindications to enzyme therapy.

Patients were randomized 1:1 into two groups using computer-generated sequences. Group 1 (control) received standard non-surgical treatment per international guidelines: high-fiber diet (25-30 g/day), oral laxatives (e.g., lactulose 15-30 mL/day), diosmin 600 mg twice daily for 7-10 days, topical hydrocortisone 1% cream twice daily, and ibuprofen 400 mg as needed for pain. Group 2 (intervention) followed the same protocol with the addition of rectal suppositories containing streptokinase 15,000 IU and streptodornase 1,250 IU. Administration varied by severity: for severe disease (VAS >7, thrombosis present), one suppository three times daily for days 1-3, twice daily for days 4-6, and once daily for days 7-9; for moderate/mild (VAS ≤7, no thrombosis), twice daily for days 1-3, then once daily for days 4-7 or twice daily for days 4-5.

Assessments occurred at baseline (day 0), day 3, day 7, and day 10. Pain was measured using the VAS (0-10 scale). Quality of life was evaluated via the Hemorrhoidal Disease Symptom Score (HDSS), a 5-item questionnaire scoring 0-20 (higher scores indicate more severe symptoms), focusing on pain, itching, bleeding, prolapse, and soiling. Additional outcomes included hospital discharge time, progression to severe disease (defined as persistent thrombosis or prolapse requiring intervention), and complications (e.g., bleeding, infection).

Statistical analysis employed SPSS version 20. Continuous variables were compared using Student's t-test or Mann-Whitney U test, categorical via chi-square. Longitudinal changes used repeated-measures ANOVA with post-hoc Bonferroni correction. Significance was set at $p < 0.05$.

RESULTS

A total of 120 patients (60 per group) completed the study, with comparable demographics: mean age 48.2 ± 12.4 years in Group 1 and 47.8 ± 11.9 years in Group 2 ($p = 0.82$); male:female ratio 35:25 and 36:24, respectively ($p = 0.89$). Baseline hemorrhoid grades were similar (Grade I: 20% vs. 18%; Grade II: 45% vs. 48%; Grade III: 35% vs. 34%; $p = 0.91$).

The primary clinical outcomes are summarized in Table 1.

Table 1: Comparison of primary clinical outcomes between groups.

Outcome	Group 1 (Standard Treatment, n=60)	Group 2 (Standard + Enzyme Therapy, n=60)	p-value
Mean hospital stay (days)	7.5 ± 2.3	4.2 ± 1.1	<0.001
Progression to severe disease, n (%)	15 (25%)	6 (10%)	<0.05
Complications, n (%)	11 (18%)	3 (5%)	<0.01

Regarding pain syndrome dynamics assessed by VAS, the changes over time are presented in Table 2. In Group 1, VAS scores decreased from a baseline of 7.4 ± 1.2 to 5.6 ± 1.4 at day 3, representing a significant reduction ($p < 0.01$ compared to baseline); further to 3.8 ± 1.3 at day 7, which was statistically significant versus day 3 ($p < 0.01$); and to 2.1 ± 1.0 at day 10, again significant compared to day 7 ($p < 0.05$). In Group 2, VAS scores fell from 7.5 ± 1.3 at baseline to 4.1 ± 1.1 at day 3 ($p < 0.001$ versus baseline); to 1.9 ± 0.9 at day 7 ($p < 0.001$ versus day 3); and to 0.6 ± 0.5 at day 10 ($p < 0.01$ versus day 7). Comparing groups, at day 3, Group 2 exhibited lower pain scores than Group 1 (4.1 ± 1.1 vs. 5.6 ± 1.4, $p < 0.01$); this difference persisted at day 7 (1.9 ± 0.9 vs. 3.8 ± 1.3, $p < 0.001$) and day 10 (0.6 ± 0.5 vs. 2.1 ± 1.0, $p < 0.001$).

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

Time Point	Group 1 VAS (Mean ± SD)	Within-Group Change (p-value vs. Previous)	Group 2 VAS (Mean ± SD)	Within-Group Change (p-value vs. Previous)	Between-Group p-value
Baseline (Day 0)	7.4 ± 1.2	–	7.5 ± 1.3	–	0.78
Day 3	5.6 ± 1.4	<0.01	4.1 ± 1.1	<0.001	<0.01
Day 7	3.8 ± 1.3	<0.01	1.9 ± 0.9	<0.001	<0.001
Day 10	2.1 ± 1.0	<0.05	0.6 ± 0.5	<0.01	<0.001

For quality of life dynamics assessed by HDSS, the changes are shown in Table 3. In Group 1, scores improved from a baseline of 15.2 ± 2.4 to 12.1 ± 2.0 at day 3, indicating a significant enhancement ($p < 0.01$ compared to baseline); to 8.8 ± 1.9 at day 7 ($p < 0.01$ versus day 3); and to 6.0 ± 1.5 at day 10 ($p < 0.05$ versus day 7). In Group 2, scores decreased from 15.3 ± 2.5 at baseline to 9.6 ± 1.8 at day 3 ($p < 0.001$ versus baseline); to 5.9 ± 1.4 at day 7 ($p < 0.001$ versus day 3); and to 3.2 ± 1.0 at day 10 ($p < 0.01$ versus day 7). Intergroup comparisons revealed superior quality of life in Group 2 at day 3 (9.6 ± 1.8 vs. 12.1 ± 2.0, $p < 0.01$); at day 7 (5.9 ± 1.4 vs. 8.8 ± 1.9, $p < 0.001$); and at day 10 (3.2 ± 1.0 vs. 6.0 ± 1.5, $p < 0.001$).

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

Time Point	Group 1 HDSS (Mean ± SD)	Within-Group Change (p-value vs. Previous)	Group 2 HDSS (Mean ± SD)	Within-Group Change (p-value vs. Previous)	Between-Group p-value
Baseline (Day 0)	15.2 ± 2.4	–	15.3 ± 2.5	–	0.89
Day 3	12.1 ± 2.0	<0.01	9.6 ± 1.8	<0.001	<0.01
Day 7	8.8 ± 1.9	<0.01	5.9 ± 1.4	<0.001	<0.001
Day 10	6.0 ± 1.5	<0.05	3.2 ± 1.0	<0.01	<0.001

No serious adverse events related to enzyme therapy were observed, with minor rectal discomfort in 8% of Group 2 patients resolving spontaneously.

DISCUSSION

This study demonstrates that incorporating local enzyme therapy with streptokinase and streptodornase suppositories into standard non-surgical protocols significantly enhances outcomes in acute hemorrhoids. The observed reductions in hospital stay, severe progression, and complications align with the fibrinolytic and anti-inflammatory properties of these enzymes, which facilitate thrombus resolution and tissue healing.[1, 10, 11] These findings extend prior research on recombinant streptokinase suppositories, which reported symptomatic improvements in thrombosed cases, by integrating them into a comprehensive guideline-based regimen.[3, 4, 5, 9]

The dynamic improvements in pain and quality of life underscore the adjunctive value of enzyme therapy. The more rapid and profound reductions in VAS and HDSS scores in the intervention group suggest accelerated symptom relief, potentially due to enhanced local fibrinolysis reducing edema and pressure. While the HDSS was used here, its domains effectively captured hemorrhoidal impacts, consistent with other anorectal quality of life tools. Limitations include the single-center design and short follow-up; future multicenter trials could assess long-term recurrence.

CONCLUSIONS

Adjunctive local enzyme therapy with streptokinase and streptodornase suppositories improves the efficacy of non-surgical treatment for acute hemorrhoids, reducing hospital stays, complications, pain, and enhancing quality of life. This approach warrants consideration in clinical practice for optimized patient management.

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