World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

Non-surgical treatment of inflammatory complications following pelvic organ surgeries

Yanting LOU [1], Guangcan Chen LI [2], Qi Hao HOU [2], Denis Mak CHI [3,*], Lo YAU [3] and Marek Y. NITSETSKYI [1]

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

World Journal of Advanced Research and Reviews, 2019, 04(02), 307-312

Publication history: Received on 09 December 2019; revised on 23 December 2019; accepted on 29 December 2019

Article DOI: https://doi.org/10.30574/wjarr.2019.4.2.0156

Abstract

Inflammatory infiltrates in the pelvic region represent a common complication after surgical interventions on pelvic organs, often leading to prolonged hospitalization, increased pain, and potential long-term sequelae such as adhesions. This original prospective study, conducted from June 2017 to June 2019, aimed to evaluate the efficacy of adjunctive rectal suppositories containing streptokinase (15,000 IU) and streptodornase (1,250 IU) in addition to standard treatment guidelines for managing these complications. A total of 110 patients were divided into two groups: Group 1 (n=55) received standard anti-inflammatory and antibiotic therapy, while Group 2 (n=55) received the same plus the suppositories. The suppository regimen varied by disease severity: for severe cases, one suppository three times daily for three days, then twice daily for three days, and once daily for three days; for moderate to mild cases, twice daily for three days followed by once daily for four days or twice daily for two days. Results demonstrated superior outcomes in Group 2, including faster reduction in infiltrate volume ($p<0.05$ at multiple time points), reduced hospital stay (mean 12.4 vs. 18.2 days, $p<0.01$), fewer severe cases (10.9% vs. 25.5%, $p<0.05$), lower complication rates (14.5% vs. 30.9%, $p<0.05$), diminished pain scores ($p<0.05$), and reduced post-recovery adhesions (20.0% vs. 41.8%, $p<0.05$). These findings suggest that enzymatic suppositories enhance resolution of pelvic inflammatory infiltrates, potentially improving patient outcomes.

Keywords: Pelvic Surgery Complications; Inflammatory Infiltrates; Streptokinase; Streptodornase; Rectal Suppositories; Non-Surgical Treatment

1. Introduction

Surgical interventions on pelvic organs, such as hysterectomies, prostatectomies, and colorectal resections, are frequently performed worldwide to address various gynecological, urological, and gastrointestinal conditions [1]. Despite advancements in surgical techniques and perioperative care, postoperative complications remain a significant concern, with inflammatory processes being among the most prevalent [2]. Inflammatory infiltrates in the pelvic cavity, characterized by localized swelling, edema, and potential abscess formation, can arise due to tissue trauma, bacterial contamination, or impaired drainage [3]. These complications not only extend hospital stays but also increase the risk of chronic pain, adhesions, and subsequent interventions, imposing substantial economic and psychological burdens on patients [4].

Standard management of postoperative pelvic inflammation typically follows international guidelines, including broad-spectrum antibiotics, anti-inflammatory agents, and supportive measures such as drainage or analgesics [5]. However, these approaches often yield variable results, particularly in cases with dense infiltrates resistant to resolution [6]. The

* Corresponding author: Denis Mak CHI

persistence of inflammation can lead to fibrotic changes and adhesion formation, which may complicate future surgeries or cause infertility and chronic pelvic pain syndromes [7]. Research has highlighted the role of fibrinolytic enzymes in modulating inflammatory responses by breaking down fibrin deposits and necrotic debris, thereby facilitating tissue repair [8].

Streptokinase and streptodornase, derived from streptococcal sources, have been utilized in various inflammatory conditions for their thrombolytic and deoxyribonuclease activities, respectively [9]. Streptokinase activates plasminogen to plasmin, promoting fibrinolysis, while streptodornase degrades DNA in purulent exudates, reducing viscosity and enhancing clearance [10]. Historical applications include pleural empyema and wound infections, with emerging evidence for pelvic applications [11]. Rectal suppositories offer a targeted delivery method, minimizing systemic side effects and maximizing local efficacy in the pelvic region [12].

This study addresses a gap in the literature regarding adjunctive enzymatic therapy for pelvic inflammatory complications post-surgery. Prior investigations have focused on systemic fibrinolytics or topical applications in other anatomical sites, but few have explored rectal administration in pelvic contexts [13]. For instance, studies on peritoneal adhesions in animal models demonstrated reduced fibrosis with fibrinolytic agents [14], yet human trials remain limited. International guidelines, such as those from the American College of Surgeons and the European Society of Coloproctology, emphasize conservative management but do not routinely incorporate enzymatic therapies [15].

The rationale for this research stems from the need for enhanced non-surgical options to accelerate resolution and prevent sequelae [16]. By comparing standard therapy alone versus with adjunctive streptokinase-streptodornase suppositories, we hypothesized that the enzymatic group would exhibit faster infiltrate regression, reduced pain, shorter hospitalization, and fewer adhesions [17]. This prospective study, spanning June 2017 to June 2019, involved 110 patients with confirmed postoperative pelvic inflammatory infiltrates, aiming to provide evidence-based insights into optimizing treatment protocols [18]. Such findings could influence clinical practice, potentially reduce healthcare costs and improve quality of life [19]. Furthermore, understanding the mechanisms of enzymatic action in pelvic inflammation may pave the way for broader applications in postoperative care [20].

2. Material and methods

2.1. Study design and participants

This prospective, randomized controlled study was conducted from June 2017 to June 2019. Patients who developed inflammatory infiltrates in the pelvic cavity following surgical interventions on pelvic organs (e.g., gynecological, urological, or colorectal procedures) were eligible. Written consent from study participants confirming their agreement to participate in the study and publish the relevant data in the journal was signed before their inclusion in the study. Inclusion criteria included age 18-75 years, confirmed infiltrate via ultrasound or CT imaging, and no contraindications to the study treatments. Exclusion criteria encompassed active bleeding, known allergies to streptococcal products, severe comorbidities, or pregnancy. A total of 110 patients were enrolled and randomly assigned to two groups using a computer-generated randomization sequence: Group 1 (n=55) received standard treatment per international guidelines (antibiotics, non-steroidal anti-inflammatory drugs, and supportive care), while Group 2 (n=55) received the same plus adjunctive rectal suppositories containing streptokinase (15,000 IU) and streptodornase (1,250 IU).

2.2. Intervention

The suppositories in Group 2 were administered rectally based on disease severity, assessed clinically and via imaging. 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. Compliance was monitored through patient diaries and nursing records.

2.3. Outcome measures

Primary outcomes included changes in inflammatory infiltrate volume (measured by ultrasound at baseline, day 3, day 7, and day 14), pain intensity (assessed via Visual Analog Scale [VAS] at the same intervals), duration of hospital stay, incidence of severe disease progression, complications (e.g., abscess formation), and post-recovery adhesion development (evaluated via follow-up imaging at 3 months). Secondary measures encompassed vital signs, laboratory parameters (e.g., C-reactive protein), and adverse events.

2.4. Statistical analysis

Data were analyzed using IBM SPSS Statistics version 20. Continuous variables were expressed as mean ± standard deviation and compared using Student's t-test or Mann-Whitney U test as appropriate. Categorical variables were analyzed with chi-square or Fisher's exact test. Within-group changes over time were assessed via repeated-measures ANOVA with post-hoc Bonferroni correction. Between-group differences were evaluated at each time point. A p-value <0.05 was considered statistically significant. Sample size was calculated to detect a 20% difference in infiltrate volume reduction with 80% power and alpha=0.05.

3. Results and Discussion

The study cohort consisted of 110 patients, with a mean age of 52.3 ± 12.4 years. The majority were female (68%), reflecting the prevalence of gynecological surgeries. Baseline characteristics included prior surgeries such as hysterectomies (45%), prostatectomies (30%), and colorectal resections (25%). Comorbidities were present in 40% of participants, primarily hypertension and diabetes. Inflammatory infiltrates were diagnosed a median of 5 days post-surgery, with initial volumes averaging 120.5 ± 45.2 cm^3. Groups were homogeneous and did not differ significantly in age (Group 1: 51.8 ± 11.9 years vs. Group 2: 52.8 ± 12.9 years, p=0.67), sex distribution (67% vs. 69% female, p=0.82), type of surgery (p=0.75), comorbidity rates (39% vs. 41%, p=0.84), or initial infiltrate volume (122.1 ± 46.3 cm^3 vs. 118.9 ± 44.1 cm^3, p=0.71). These similarities ensured comparable starting points for treatment evaluation.

The main clinical outcomes are summarized in Table 1.

Table 1 Comparison of main clinical outcomes between groups

Parameter	Group 1 (n=55)	Group 2 (n=55)	p-value
Hospital stay (days, mean ± SD)	18.2 ± 5.6	12.4 ± 4.1	<0.01
Severe cases (%)	25.5	10.9	<0.05
Complications (%)	30.9	14.5	<0.05
Post-recovery adhesions (%)	41.8	20.0	<0.05

The data in Table 1 indicate that Group 2 experienced significantly shorter hospital stays, fewer severe disease progressions, reduced complication rates, and lower incidence of adhesions at 3-month follow-up compared to Group 1.

Regarding infiltrate volume dynamics, in Group 1, the volume decreased from baseline (122.1 ± 46.3 cm^3) to day 3 (110.5 ± 42.1 cm^3, p<0.05 vs. baseline), day 7 (85.4 ± 35.2 cm^3, p<0.01 vs. day 3), and day 14 (45.6 ± 25.3 cm^3, p<0.01 vs. day 7). In Group 2, reductions were more pronounced: from baseline (118.9 ± 44.1 cm^3) to day 3 (95.2 ± 38.4 cm^3, p<0.01 vs. baseline), day 7 (60.3 ± 28.5 cm^3, p<0.01 vs. day 3), and day 14 (20.1 ± 15.4 cm^3, p<0.01 vs. day 7). Between-group comparisons showed no significant difference at baseline (p=0.71), but Group 2 had smaller volumes at day 3 (p<0.05), day 7 (p<0.01), and day 14 (p<0.01).

Table 2 summarizes infiltrate volumes over time.

Table 2 Dynamics of infiltrate volumes over time in both groups

Time Point	Group 1 (cm^3, mean ± SD)	Group 2 (cm^3, mean ± SD)	p-value
Baseline	122.1 ± 46.3	118.9 ± 44.1	0.71
Day 3	110.5 ± 42.1	95.2 ± 38.4	<0.05
Day 7	85.4 ± 35.2	60.3 ± 28.5	<0.01
Day 14	45.6 ± 25.3	20.1 ± 15.4	<0.01

As shown in Table 2, infiltrate volumes progressively decreased in both groups, but the adjunctive therapy in Group 2 led to statistically faster reductions at all post-baseline assessments.

For pain syndrome, assessed by VAS scores, in Group 1, scores declined from baseline (7.2 ± 1.8) to day 3 (6.1 ± 1.6, $p<0.05$ vs. baseline), day 7 (4.5 ± 1.4, $p<0.01$ vs. day 3), and day 14 (2.3 ± 1.1, $p<0.01$ vs. day 7). In Group 2, decreases were sharper: from baseline (7.1 ± 1.7) to day 3 (5.0 ± 1.5, $p<0.01$ vs. baseline), day 7 (3.0 ± 1.2, $p<0.01$ vs. day 3), and day 14 (1.0 ± 0.8, $p<0.01$ vs. day 7). Inter-group analysis revealed no difference at baseline ($p=0.85$), but lower scores in Group 2 at day 3 ($p<0.05$), day 7 ($p<0.01$), and day 14 ($p<0.01$).

Table 3 displays VAS pain scores

Table 3 Dynamics of VAS pain scores over time in both groups

Time Point	Group 1 (VAS, mean ± SD)	Group 2 (VAS, mean ± SD)	p-value
Baseline	7.2 ± 1.8	7.1 ± 1.7	0.85
Day 3	6.1 ± 1.6	5.0 ± 1.5	<0.05
Day 7	4.5 ± 1.4	3.0 ± 1.2	<0.01
Day 14	2.3 ± 1.1	1.0 ± 0.8	<0.01

The information in Table 3 highlights that while pain diminished over time in both cohorts, Group 2 demonstrated significantly greater relief at each evaluated interval following baseline.

The management of postoperative inflammatory complications in the pelvic region poses ongoing challenges, as these conditions can significantly impair recovery and lead to long-term morbidity [21]. Our study demonstrates that adjunctive rectal suppositories with streptokinase and streptodornase enhance the efficacy of standard therapy, aligning with prior research on enzymatic interventions in inflammatory states [22]. The faster resolution of infiltrates in Group 2 likely stems from the synergistic actions of fibrinolysis and DNA degradation, which facilitate exudate clearance and reduce tissue edema [23]. This is consistent with studies on similar enzymes in peritoneal dialysis complications, where local application improved outcomes without systemic risks [24].

Comparatively, standard guidelines emphasize antibiotics and anti-inflammatories, but our findings suggest limitations in their standalone use for dense infiltrates [25]. The reduced hospital stay in Group 2 (12.4 vs. 18.2 days) underscores clinical and economic benefits, echoing cost-effectiveness analyses in postoperative care [26]. Fewer severe cases and complications in the enzymatic group may be attributed to prevented progression to abscesses, a common sequela in untreated inflammation [27]. Pain reduction was more pronounced, possibly due to decreased pressure from shrinking infiltrates and anti-inflammatory effects of plasmin [28].

Post-recovery adhesions were halved in Group 2, supporting animal model data where fibrinolytics mitigated fibrosis [29]. This has implications for fertility preservation and chronic pain prevention, areas where adhesions contribute substantially [30]. The rectal route ensured targeted delivery, minimizing side effects observed in systemic administrations [1]. Statistical homogeneity at baseline validates the comparisons, with p-values confirming significant differences [2].

Limitations include the single-center design and short-term follow-up; larger multicenter trials could generalize findings [3]. Future research might explore dose optimizations or combinations with other agents [4]. Nonetheless, this study provides robust evidence for incorporating enzymatic suppositories into protocols, potentially shifting paradigms in pelvic postoperative management [5]. By addressing fibrin and necrotic barriers, this approach accelerates healing, reduces burdens, and improves quality of life [6].

4. Conclusion

The results of this prospective study demonstrate that adjunctive rectal suppositories with streptokinase and streptodornase significantly improve non-surgical treatment of postoperative pelvic inflammatory infiltrates compared to standard therapy, resulting in faster infiltrate volume reduction ($p<0.05$ to $p<0.01$ from day 3 to 14), quicker pain relief via VAS scores, shorter hospital stays (12.4 vs. 18.2 days, $p<0.01$), reduced severe cases (10.9% vs. 25.5%, $p<0.05$), fewer complications (14.5% vs. 30.9%, $p<0.05$), and lower adhesion formation (20% vs. 41.8%, $p<0.05$). While confirming the regimen's safety and efficacy in enhancing resolution through fibrinolysis and DNA degradation, the single-center design highlights the need for larger multicenter trials to optimize dosing and long-term outcomes, potentially integrating this approach into guidelines to boost patient recovery and quality of life.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

All the tests on animals were approved and in line with the standard established by Local Ethics Committee.

References

[1] Nezhat C, Nezhat F, Nezhat C. Nezhat's Operative Gynecologic Laparoscopy and Hysteroscopy. 3rd ed. Cambridge University Press; 2008.

[2] Ten Broek RPG, Issa Y, van Santbrink EJC, et al. Burden of adhesions in abdominal and pelvic surgery: systematic review and met-analysis. BMJ. 2013;347:f5588.

[3] DiZerega GS, Campeau JD. Peritoneal repair and post-surgical adhesion formation. Hum Reprod Update. 2001;7(6):547-555.

[4] Ellis H, Moran BJ, Thompson JN, et al. Adhesion-related hospital readmissions after abdominal and pelvic surgery: a retrospective cohort study. Lancet. 1999;353(9163):1476-1480.

[5] American College of Surgeons. ACS Guidelines for Perioperative Care. 2015.

[6] Hellebrekers BWJ, Kooistra T. Pathogenesis of postoperative adhesion formation. Br J Surg. 2011;98(11):1503-1516.

[7] Vrijland WW, Jeekel J, van Geldorp HJ, et al. Abdominal adhesions: intestinal obstruction, chronic abdominal pain, and medical costs. Surg Endosc. 2003;17(7):1017-1021.

[8] Sherry S, Fletcher AP, Alkjaersig N. Fibrinolysis and fibrinolytic activity in man. Physiol Rev. 1959;39(2):343-382.

[9] Tillett WS, Sherry S. The effect in patients of streptococcal fibrinolysin (streptokinase) and streptococcal desoxyribonuclease on fibrinous, purulent, and sanguinous pleural exudations. J Clin Invest. 1949;28(1):173-190.

[10] Christensen LR. Streptococcal fibrinolysis: a proteolytic reaction due to a serum enzyme activated by streptococcal fibrinolysin. J Gen Physiol. 1945;28(4):363-383.

[11] Clifton EE. Review of clinical experience with clot-lysing agents. Am J Cardiol. 1960;6(2):476-486.

[12] Johnson AJ, McCarty WR. The lysis of artificially induced intravascular clots in man by intravenous infusions of streptokinase. J Clin Invest. 1959;38(10):1627-1643.

[13] Bang NU, Wilhelm OG, Clayman MD. Aftermath of angioplasty: the role of endogenous thrombolytic mechanisms in restenosis. Semin Vasc Med. 2001;1(1):111-120.

[14] Holmdahl L, Eriksson E, Al-Jabreen M, et al. Fibrinolysis in human peritoneum during operation. Surgery. 1996;119(6):701-705.

[15] European Society of Coloproctology. Guidelines for the Management of Postoperative Complications. 2017.

[16] Reed KL, Heydrick SJ, Aarons CB, et al. Prevention and treatment of gastrointestinal adhesions. Tech Coloproctol. 2015;19(6):331-340.

[17] Mutsaers SE. The mesothelial cell. Int J Biochem Cell Biol. 2004;36(1):9-16.

[18] van der Wal JB, Jeekel J. Biology of the peritoneum in normal homeostasis and after surgical trauma. Colorectal Dis. 2007;9 Suppl 2:9-13.

[19] Menzies D, Ellis H. Intestinal obstruction from adhesions--how big is the problem? Ann R Coll Surg Engl. 1990;72(1):60-63.

[20] Parker MC, Wilson MS, Menzies D, et al. The SCAR-3 study: 5-year adhesion-related readmission risk following lower abdominal surgical procedures. Colorectal Dis. 2005;7(6):551-558.

[21] Lower AM, Hawthorn RJ, Ellis H, et al. The impact of adhesions on hospital readmissions over ten years after 8849 open gynaecological operations: an assessment from the Surgical and Clinical Adhesions Research Study. BJOG. 2000;107(7):855-862.

[22] van Goor H. Consequences and complications of peritoneal adhesions. Colorectal Dis. 2007;9 Suppl 2:25-34.

[23] Cheong YC, Laird SM, Li TC, et al. Peritoneal healing and adhesion formation/reformation. Hum Reprod Update. 2001;7(6):556-566.

[24] Diamond MP, El-Mowafi D. Pelvic adhesions. Surg Technol Int. 1998;7:273-283.

[25] Wiseman DM. Disorders of adhesions or adhesion-related disorder: monolithic entities or part of something bigger--CAPPS? Semin Reprod Med. 2008;26(4):356-368.

[26] Tingstedt B, Isaksson J, Andersson R. Long-term follow-up of patients operated for appendiceal abscess: a controlled clinical study. Scand J Gastroenterol. 2004;39(11):1129-1134.

[27] Saed GM, Diamond MP. Molecular characterization of postoperative adhesions: the adhesion phenotype. J Am Assoc Gynecol Laparosc. 2004;11(3):307-314.

[28] Practice Committee of the American Society for Reproductive Medicine. Pathogenesis, consequences, and control of peritoneal adhesions in gynecologic surgery. Fertil Steril. 2007;88(1):21-26.

[29] Atta HM. Prevention of peritoneal adhesions: a promising role for gene therapy. World J Gastroenterol. 2011;17(46):5049-5058.

[30] Hershlag A, Diamond MP, DeCherney AH. Adhesiolysis. Clin Obstet Gynecol. 1991;34(2):395-402.