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Treatment of inflammatory infiltrates in the pelvic cavity: Opportunities and effectiveness of local therapy

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Abstract

Inflammatory infiltrates in the pelvic cavity represent a significant complication of pelvic inflammatory disease (PID), often leading to prolonged hospitalization, increased pain, and long-term sequelae such as adhesions. This original prospective study, conducted from January 2014 to December 2016, evaluated the efficacy of adding rectal suppositories containing streptokinase (15,000 IU) and streptodornase (1,250 IU) to standard international guideline-based treatment in 225 patients with confirmed pelvic inflammatory infiltrates. Patients provided informed consent and were randomized into two groups: Group 1 (n=110) received standard therapy, while Group 2 (n=115) received standard therapy plus the suppositories. The regimen for suppositories varied by disease severity: for severe cases, 1 suppository three times daily for 3 days, then twice daily for 3 days, then once daily for 3 days; for moderate to mild cases, twice daily for 3 days, then once daily for 4 days or twice daily for 2 days. Group 2 demonstrated superior outcomes, including faster reduction in infiltrate volume ($p<0.01$ at days 7 and 14), reduced hospital stay (mean 12.4 vs 15.8 days, $p<0.001$), fewer severe cases (8% vs 18%, $p<0.05$), fewer complications (6% vs 14%, $p<0.05$), and lower pain scores ($p<0.01$ at multiple timepoints). Adhesion formation was lower in Group 2 at 3, 6, and 12 months post-recovery ($p<0.05$). Mild local reactions occurred in 12 patients in Group 2, resolving spontaneously without intervention. These findings suggest that adjunctive local fibrinolytic therapy enhances treatment efficacy in pelvic inflammatory infiltrates.

Keywords: Pelvic Inflammatory Disease; Inflammatory Infiltrates; Streptokinase; Streptodornase; Local Therapy; Fibrinolysis

1. Introduction

Pelvic inflammatory disease (PID) is a polymicrobial infection of the upper female genital tract, encompassing endometritis, salpingitis, oophoritis, and peritonitis, often resulting from ascending spread of sexually transmitted pathogens such as Chlamydia trachomatis and Neisseria gonorrhoeae, or endogenous vaginal flora [1]. Globally, PID affects millions of women annually, with significant morbidity including chronic pelvic pain, infertility, and ectopic pregnancy [2]. In severe cases, inflammatory infiltrates form in the pelvic cavity, characterized by localized collections of exudate, fibrin, and inflammatory cells, leading to abscesses or parametritis [3]. These infiltrates exacerbate symptoms, prolong recovery, and increase the risk of adhesions, which can impair reproductive function [4].

Standard treatment follows international guidelines, emphasizing broad-spectrum antibiotics to cover aerobic, anaerobic, and atypical pathogens [5]. Regimens typically include cephalosporins, doxycycline, and metronidazole, administered parenterally for severe cases and orally for mild to moderate presentations [6]. However, antibiotics alone may not adequately address the fibrinous component of infiltrates, where persistent fibrin deposition hinders

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resolution and promotes scarring [7]. Fibrinolytic agents, such as streptokinase and streptodornase, have been explored for their ability to dissolve fibrin clots and degrade DNA in purulent exudates, respectively [8]. Streptokinase activates plasminogen to plasmin, promoting fibrinolysis, while streptodornase acts as a DNase, liquefying viscous material [9]. Early studies demonstrated their efficacy in thoracic empyema and hemothorax, where local application accelerated resolution [10, 11].

In gynecologic contexts, limited evidence supports fibrinolytic therapy for pelvic abscesses, with reports from the mid-20th century showing reduced abscess size and faster recovery when used vaginally or rectally [12]. Contemporary interest has revived due to the need for adjunctive therapies to mitigate long-term complications [13]. Animal models suggest that fibrinolysis reduces adhesion formation by clearing fibrin matrices that serve as scaffolds for fibroblast proliferation [14]. Clinical trials in abdominal surgery have similarly shown decreased postoperative adhesions with fibrinolytic agents [15]. Despite these insights, randomized studies on local fibrinolytic therapy in pelvic inflammatory infiltrates are scarce, particularly in modern cohorts adhering to current antibiotic guidelines [16].

This study aimed to investigate the opportunities and effectiveness of adjunctive rectal suppositories containing streptokinase and streptodornase in treating pelvic inflammatory infiltrates. By comparing standard therapy alone versus combined with local fibrinolysis, we hypothesized improved clinical outcomes, including faster infiltrate resolution, reduced pain, shorter hospitalization, fewer complications, and diminished adhesion formation. Conducted over three years (2014-2016), this research addresses a gap in evidence-based local therapies for PID complications, potentially offering a safe, targeted approach to enhance recovery and prevent sequelae [17]. The rationale stems from the pathophysiology of infiltrates, where fibrin and DNA-rich exudates resist antibiotic penetration, necessitating enzymatic degradation for optimal healing [18]. With informed consent from all participants, this trial provides robust data on the integration of historical fibrinolytic strategies into contemporary PID management [19].

2. Material and methods

2.1. Study design and participants

This prospective, randomized, controlled study was conducted at a tertiary care hospital from January 2014 to December 2016. Eligible patients were women aged 18-45 years with confirmed inflammatory infiltrates in the pelvic cavity, diagnosed via clinical symptoms (lower abdominal pain, fever, cervical motion tenderness), laboratory findings (elevated white blood cell count, C-reactive protein), and ultrasound evidence of pelvic masses or fluid collections. Exclusion criteria included pregnancy, immunodeficiency, allergy to study drugs, or concurrent malignancies. All participants provided written informed consent. The study was approved by the institutional ethics committee and registered accordingly.

Patients were randomized into two groups: Group 1 (n=110) received standard treatment per international guidelines (e.g., intravenous ceftriaxone 1 g daily plus doxycycline 100 mg twice daily plus metronidazole 500 mg three times daily, transitioned to oral after clinical improvement); Group 2 (n=115) received the same plus rectal suppositories containing streptokinase (15,000 IU) and streptodornase (1,250 IU).

2.2. Intervention

Suppository administration depended on disease severity: for severe cases (high fever, large infiltrates >5 cm), 1 suppository three times daily for 3 days, then twice daily for 3 days, then 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.

2.3. Assessments

Infiltrate volume was measured by transvaginal ultrasound at baseline, days 3, 7, 14, and discharge. Pain was assessed using the Visual Analog Scale (VAS, 0-10) at the same intervals. Hospital stay, disease severity (mild/moderate/severe based on clinical scoring), complications (e.g., abscess rupture, sepsis), and adhesion formation (assessed by hysterosalpingography or laparoscopy at 3, 6, and 12 months post-recovery) were recorded. Adverse events were monitored daily.

2.4. Statistical analysis

Data were analyzed using IBM SPSS Statistics version 20. Continuous variables were compared with Student's t-test or Mann-Whitney U test; categorical variables with chi-square test. Changes over time were evaluated with repeated-measures ANOVA. P-values <0.05 indicated statistical significance.

3. Results and Discussion

The study included 225 patients: Group 1 (n=110, mean age 32.5 ± 6.2 years) and Group 2 (n=115, mean age 32.8 ± 5.9 years). Baseline characteristics were homogeneous, with no significant differences in age, parity (1.4 ± 1.1 vs 1.5 ± 1.0, p=0.62), prior PID history (22% vs 24%, p=0.74), infiltrate size (48.2 ± 12.4 cm^3 vs 47.9 ± 11.8 cm^3, p=0.88), VAS score (7.2 ± 1.5 vs 7.1 ± 1.4, p=0.71), or disease severity (severe: 25% vs 23%, p=0.78). Laboratory parameters, including WBC (14.2 ± 3.1 x10^9/L vs 14.0 ± 3.0 x10^9/L, p=0.65) and CRP (85.4 ± 20.1 mg/L vs 84.9 ± 19.8 mg/L, p=0.82), were comparable.

Key clinical outcomes are summarized in Table 1.

Table 1 Comparison of key clinical outcomes between groups

Outcome	Group 1 (n=110)	Group 2 (n=115)	p-value
Hospital stay (days, mean ± SD)	15.8 ± 4.1	12.4 ± 3.2	<0.001
Severe cases during treatment (%)	18.2	8.0	0.02
Complications (%)	16.3	6.0	0.04
Intestinal manifestations (flatulence, diarrhea, constipation)	13.6	14.8	0.95
Adhesions at 3 months (%)	28.2	9.3	0.003
Adhesions at 6 months (%)	23.6	8.0	0.005
Adhesions at 12 months (%)	20.0	6.0	0.009

Group 2 exhibited shorter hospital stays (12.4 ± 3.2 days vs 15.8 ± 4.1 days, p<0.001), fewer severe cases during treatment (8.0% vs 18.2%, p=0.02), and fewer complications (6.0% vs 16.3%, p=0.04). Adhesion rates were lower in Group 2 at follow-up: 3 months (9.3% vs 28.2%, p=0.003), 6 months (8.0% vs 23.6%, p=0.005), and 12 months (6.0% vs 20.0%, p=0.009).

Intestinal manifestations such as flatulence, diarrhea, and constipation occurred with equal frequency in both groups (14.8% vs 13.6%, p=0.95), which appears to be related to the antibiotic therapy used.

Table 1 presents the main clinical results, highlighting the superior efficacy in Group 2 across multiple parameters, with statistically significant reductions in hospitalization duration, disease progression to severe forms, acute complications, and long-term adhesion development.

Infiltrate volume dynamics are shown in Table 2.

Table 2 Infiltrate volume dynamics over time in both groups

Timepoint	Group 1 (cm^3, mean ± SD)	Group 2 (cm^3, mean ± SD)	p-value
Baseline	48.2 ± 12.4	47.9 ± 11.8	0.88
Day 3	42.1 ± 11.2	38.5 ± 10.1	0.03
Day 7	32.5 ± 9.8	24.6 ± 8.3	<0.01
Day 14	18.4 ± 7.2	10.2 ± 5.4	<0.001
Discharge	8.2 ± 4.1	4.1 ± 2.8	<0.001

In Group 1, volume decreased from baseline (48.2 ± 12.4 cm^3) to day 3 (42.1 ± 11.2 cm^3, p=0.04 vs baseline), day 7 (32.5 ± 9.8 cm^3, p<0.01 vs day 3), day 14 (18.4 ± 7.2 cm^3, p<0.001 vs day 7), and discharge (8.2 ± 4.1 cm^3, p<0.001 vs day 14). In Group 2, reductions were more pronounced: baseline (47.9 ± 11.8 cm^3) to day 3 (38.5 ± 10.1 cm^3, p<0.01 vs baseline), day 7 (24.6 ± 8.3 cm^3, p<0.001 vs day 3), day 14 (10.2 ± 5.4 cm^3, p<0.001 vs day 7), and discharge (4.1 ± 2.8 cm^3, p<0.001 vs day 14). Intergroup comparisons revealed no difference at baseline (p=0.88), but significant differences at day 3 (p=0.03), day 7 (p<0.01), day 14 (p<0.001), and discharge (p<0.001).

Table 2 illustrates the progressive reduction in infiltrate volume, with Group 2 showing accelerated resolution at all post-baseline assessments, underscoring the additive benefit of local fibrinolysis.

Pain syndrome dynamics are detailed in Table 3.

Table 3 Pain syndrome dynamics over time in both groups

Timepoint	Group 1 (VAS, mean ± SD)	Group 2 (VAS, mean ± SD)	p-value
Baseline	7.2 ± 1.5	7.1 ± 1.4	0.71
Day 3	5.8 ± 1.3	4.9 ± 1.2	0.01
Day 7	4.1 ± 1.1	2.8 ± 0.9	<0.01
Day 14	2.2 ± 0.9	1.1 ± 0.6	<0.001
Discharge	0.8 ± 0.5	0.4 ± 0.3	0.02

In Group 1, VAS decreased from baseline (7.2 ± 1.5) to day 3 (5.8 ± 1.3, p=0.02 vs baseline), day 7 (4.1 ± 1.1, p<0.01 vs day 3), day 14 (2.2 ± 0.9, p<0.001 vs day 7), and discharge (0.8 ± 0.5, p<0.001 vs day 14). In Group 2, declines were steeper: baseline (7.1 ± 1.4) to day 3 (4.9 ± 1.2, p<0.01 vs baseline), day 7 (2.8 ± 0.9, p<0.001 vs day 3), day 14 (1.1 ± 0.6, p<0.001 vs day 7), and discharge (0.4 ± 0.3, p<0.001 vs day 14). Between groups, differences emerged at day 3 (p=0.01), day 7 (p<0.01), day 14 (p<0.001), and discharge (p=0.02).

Table 3 depicts the temporal improvement in pain, with Group 2 achieving faster and more substantial relief, reflecting enhanced symptomatic control through adjunctive therapy.

In Group 2, 12 patients (10.4%) experienced mild local reactions (irritation, minor pain, edema at insertion site), which did not worsen overall condition, required no intervention, and resolved post-treatment. All affected patients continued therapy.

This study demonstrates that adjunctive rectal suppositories with streptokinase and streptodornase significantly enhance the treatment of pelvic inflammatory infiltrates compared to standard antibiotic therapy alone. The accelerated reduction in infiltrate volume in Group 2 aligns with the fibrinolytic and DNase activities of these enzymes, which facilitate exudate liquefaction and absorption [8]. Intragroup analyses showed progressive, statistically significant decreases at each interval, but intergroup differences emerged early (day 3), suggesting rapid onset of local effects [20]. Similarly, pain relief was more pronounced in Group 2, likely due to decreased inflammation and pressure from resolving infiltrates [21]. These findings corroborate earlier reports where streptokinase-streptodornase improved outcomes in purulent collections, such as empyema, by enhancing drainage without surgery [10, 11].

The shorter hospital stays and reduced complications in Group 2 highlight clinical efficiency, potentially reducing healthcare burdens [22]. Fewer severe progressions may stem from better pathogen clearance in fibrin-rich environments, where antibiotics penetrate poorly [7]. Long-term, lower adhesion rates at 3-12 months support the anti-fibrotic role of fibrinolysis, preventing peritoneal scarring [14, 15]. Animal studies have shown that plasminogen activators like streptokinase inhibit adhesion formation by degrading fibrin bands [23]. In human trials, similar agents reduced postoperative adhesions in abdominal surgery [24], extending relevance to PID [25].

Baseline homogeneity ensured comparable groups, minimizing bias. The polymicrobial nature of PID necessitates broad antibiotics [5, 6], but our addition targeted the pathophysiological sequela of infiltrates [3]. Mild reactions in Group 2 were self-limiting, consistent with historical safety profiles [12, 26]. No serious adverse events occurred, affirming tolerability [9].

Limitations include single-center design and ultrasound-based volume measurement, though reliable in PID [27]. Future multicenter trials could validate generalizability. Compared to guidelines emphasizing antibiotics [16], our approach offers a novel adjunct for refractory cases [13]. Emerging data on Mycoplasma genitalium in PID [28] suggest potential synergies, but our focus was on infiltrates. Cost-effectiveness analyses could further advocate integration [29].

Overall, this regimen addresses a therapeutic gap, improving acute and chronic outcomes [4, 18]. By reviving fibrinolytic strategies [19], it provides a targeted, low-risk enhancement to PID management [2, 17].

4. Conclusion

Adjunctive local therapy with rectal streptokinase-streptodornase suppositories proves more effective than standard treatment alone for pelvic inflammatory infiltrates, yielding faster resolution, reduced pain, shorter hospitalization, fewer complications, and decreased adhesion formation.

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.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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