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Streptokinase irrigation through a percutaneous catheter helps decrease the need for necrosectomy and reduces mortality in necrotizing pancreatitis as part of a step-up approach

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ABSTRACT

Background: Percutaneous catheter drainage in pancreatic necrosis with a predominant solid component has a reduced success rate. To improve the efficacy of percutaneous catheter drainage, we used streptokinase in the irrigation fluid in the present study.
Methods: In this retrospective analysis of 4 prospective randomized studies performed at our center from 2014 to 2019, 108 patients were evaluated. We assessed the safety, feasibility, and efficacy of streptokinase irrigation compared to saline irrigation. Data were also analyzed between 50,000 IU and 150,000 IU streptokinase.
Results: There were 53 patients in the streptokinase irrigation group and 55 in the saline irrigation group, and both groups were comparable in terms of age, sex, etiology, APACHE II score, and percutaneous catheter drainage characteristics. The modified computerised tomography severity index and modified Marshall score at the onset of pain were significantly higher in the streptokinase group. Sepsis reversal was significantly higher in the streptokinase group (75% vs 36%), and the need for necrosectomy (34% vs 54%) was also lower in the streptokinase group. Mortality was lower in the streptokinase group than in the saline group (32% vs 40%). The incidence of bleeding in the streptokinase group was lower than that in the saline group (7% vs 18%). A higher dose of streptokinase (150,000 IU) resulted in lower rates of necrosectomy, bleeding, and mortality compared to those with 50,000 IU streptokinase.
Conclusion: Significant reductions in the need for surgery and sepsis reversal were noted in the streptokinase group. The results using 150,000 IU streptokinase were superior to those using 50,000 IU streptokinase.

Introduction

The clinical course of pancreatitis varies from a mild form to necrotizing pancreatitis,[1] and surgery has been the mainstay of treatment. However, the management strategy has undergone a paradigm shift in the past 2 decades after the introduction of percutaneous catheter drainage (PCD) and a step-up approach.[2,3] The use of PCD as a definitive modality is associated with a reduced incidence of new onset organ failure, a lower rate of incisional hernia, and a lower incidence of diabetes mellitus.[3–5] The success with PCD alone in the PANTER study was 35%.[3] The major reason for failure of PCD as a definitive therapy is the predominance of solid necrosum, which leads to frequent blockages of the catheter and makes it less effective. To address this issue, we used large-volume saline irrigation via a Y-connector to prevent blockage of the catheter, and we reported a success rate of 48% to 66%.[6,7]

In a previous study, we reported that streptokinase leads to fragmentation and dissolution of the necrosum, thereby decreasing the chances of PCD blockage.[8] Streptokinase has been successfully used in empyema thoracis and liver abscesses.[9–13] Based on the

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above reports, we used streptokinase in a prospective manner to improve the efficacy of PCD in a subset of patients who failed large-volume saline irrigation in prospective studies.

In the present study, we analyzed prospective data of streptokinase irrigation in improving the efficacy of PCD in patients who failed large-volume saline irrigation.

Methods

The present study included patients with necrotizing pancreatitis seen in a tertiary health care center of North India in the Department of Surgical and Medical Gastroenterology from July 2014 to December 2019. In the initial part of the study, we used streptokinase at a dose of 50,000 IU, which was essentially the same as that used by pulmonology colleagues for managing empyema thoracis. The initial study was a randomized experimental study that assessed the safety of streptokinase in the necrotic cavity through PCD. This study was registered in ClinicalTrials.gov (NCT01977118). Then we performed 3 more studies to assess the efficacy of streptokinase, one of which is registered in the Clinical Trials Registry of India (CTRI/2019/02/017633). One of the studies used streptokinase at a dose of 150,000 IU. We included 108 patients from 4 randomized prospective studies over a period of 5 1/2 years, and the present study is a retrospective analysis of these cumulative data. Informed consent was obtained from all the participants per the Declaration of Helsinki, and all these studies were approved by the Institutional Ethics Committee.

The diagnosis of necrotizing pancreatitis and definitions used in the study were based on the modified Atlanta classification, and organ failure was measured per the modified Marshall score (MMS). Patients were managed conservatively initially until the walled-off necrosis stage, which included organ support and nutrition. Antibiotics were used in patients with infected necrotic collections with clinical suspicion of sepsis to delay PCD as much as possible to help them reach the walled-off necrosis stage. Percutaneous catheter insertion was delayed until the walled-off necrosis stage was reached to decrease vascular complications and to avoid spillage during irrigation. However, if there was no clinical improvement, patients underwent PCD under the supervision of an experienced interventional radiologist. Indications for PCD were infected pancreatic necrosis, clinical deterioration, pressure symptoms in sterile necrosis, and persistent unwellness. Percutaneous catheter insertion was performed under ultrasonography or CT guidance. The number and size of the initial catheters were determined by the size and location of the collection/necrosis, as well as the viscosity of the initially aspirated fluid. We used 10 to 12 Fr catheters for initial access to the cavity, and depending on the drainage, the catheters were upsized to 16 to 18 Fr. For the initial 3 days, the percutaneous catheters were kept in a dependent position and irrigated with 1 to 1.5 L normal saline daily.

Patients with necrotizing pancreatitis who did not achieve symptomatic and radiological responses 72 hours after PCD after saline irrigation were included in the study. Exclusion criteria included patients not undergoing a step-up approach (ie, patients undergoing emergency laparotomy or upfront surgical necrosectomy). We also excluded patients allergic to streptokinase, with deranged coagulation profiles, taking anticoagulants, with a recent history of cerebrovascular accident, intracranial or spinal surgery, uncontrolled hypertension, and intracranial neoplasm. Twenty-four patients did not meet the strict inclusion criteria (10 patients had deranged coagulation profiles, 2 patients were anticoagulant consumers, 2 patients underwent necrosectomy and were referred to our center, 2 patients underwent surgery for hollow viscous perforation, 4 patients underwent upfront transgastric necrosectomy, 2 patients had emergency laparotomy for bowel ischemia, and another 2 patients did not give consent).

After 3 days, patients were randomized to either streptokinase or continued with saline irrigation. At any time during this period of PCD, if there was frequent blockage of the drains by necrosum or an undrained collection was found radiologically, drains were upsized or more drains were place. In 3 studies, the dose of streptokinase used was 50,000 IU, while 1 study used a dose of 150,000 IU. The protocol followed in all these studies was similar.

Protocol

Fifty thousand IU/150,000 IU streptokinase was diluted with 100 mL normal saline and given through a percutaneous catheter over a period of 60 minutes. Then the drain was clamped for 30 minutes. After release of the clamp, the cavity was irrigated with 200 mL of normal saline over a period of 2 to 3 hours. This procedure was repeated for 3 to 5 days. Surgery was performed if no clinical improvement was achieved after irrigation (ie, persistent sepsis, worsening or new-onset organ failure, or persistent unwellness). The surgical procedures performed were minimally invasive or open necrosectomy with closed drainage and lavage and video-assisted retroperitoneal debridement.

In this study, we assessed the safety and feasibility of streptokinase and compared 50,000 IU streptokinase with an escalated dose of streptokinase (150,000 IU) and saline irrigation. The primary endpoints were the need for necrosectomy and mortality. The secondary endpoints were sepsis reversal (defined as defervescence, reversal of leukocytosis, and sepsis-related organ failure, with or without resolution of necrotic cavity), streptokinase-related complications (Appendix S1), catheter-related complications, need for surgical necrosectomy, and durations of intensive care unit (ICU) and hospital stays.

Statistical analysis

SPSS version 23 was used to analyze the data. Parametric data were expressed as the mean ± SD. For comparisons between 2 independent groups for a continuous parametric variable, an independent t test was applied, and for a nonparametric variable, the Mann-Whitney U test was applied. For comparisons between more than 2 independent groups for a continuous parametric variable, analysis of variance was applied, and for the nonparametric variable, the Kruskal-Wallis test was applied. For comparisons between 2 independent groups for a categorical variable, the χ^2 test was applied. Univariate and multivariate analyses were performed with a binary logistic regression scale, and a $P < .05$ was considered significant.

Results

A total of 108 patients were included in the study, with streptokinase irrigation used in 53 patients and normal saline irrigation alone used in 55 patients. The demographic characteristics were comparable between the 2 groups (Table I). Acute physiology and chronic health evaluation (APACHE II) score at onset and a week after irrigation were comparable between the 2 groups ($P = .441$); however, the MMS at onset of the disease was higher in the streptokinase irrigation group than in the saline irrigation group (3.6 ± 1.8 vs 3.4 ± 2). The severity of the disease at onset based on the modified CT severity index (MCTSI) was significantly higher in the streptokinase irrigation group compared to that in the saline irrigation group (9.45 ± 1.05 vs 8.98 ± 1.159, $P = .001$). In both groups, the severity declined after irrigation (Table I). Eighty-seven (80.5%) patients in the entire cohort had organ failure, and there

Table I
Demographic and baseline characteristics between 2 groups

	Streptokinase group (n = 53)	Saline irrigation group (n = 55)	P value
Age	37.74 ± 11	36.33 ± 11.185	.458
Sex			.565
M	41	45	
F	12	10	
Etiology			.618
Alcohol	25 (47%)	34 (61%)	
Gallstone induced	16 (30%)	12 (21%)	
Endoscopic retrograde cholangio-pancreatography	2 (3.7%)	3 (5.4%)	
Combined gallstone and alcohol	4 (7.5%)	3 (5.4%)	
Idiopathic	5 (9%)	2 (3.6%)	
Trauma	1 (1.8%)	1 (1.8%)	
APACHE II Onset of pain	11.43 ± 4.23	10.68 ± 3.83	.441
APACHE II post-irrigation	9.38 ± 4.75	9.2 ± 4.9	.121
Modified Marshall Score at onset of pain	3.69 ± 1.83	3.4 ± 2	.001
Modified Marshall Score post-irrigation	2.5 ± 1.5	2.8 ± 2.2	.179
Modified CT severity index before irrigation	9.45 ± 1.05	8.98 ± 1.159	.028
Modified CT severity index after irrigation	7.51 ± 1.66	8.69 ± 1.5	.00
Organ failure	45 (85%)	42 (76%)	.26
Single organ failure	29 (54%)	28 (51%)	
Multi organ failure	16 (36%)	14 (34%)	

CT, computed tomography.

was no significant difference in terms of single and multiorgan failure between the 2 groups.

Characteristics of percutaneous catheter drainage

The mean number of PCDs was 2.57 ± 1.18 in the streptokinase irrigation group in comparison to 2.33 ± 0.84 in the saline irrigation group, and the difference was insignificant. The mean duration of PCD was 43.9 ± 25 days in the streptokinase irrigation group in comparison to 42.87 ± 24.68 in the saline irrigation group. However, the duration from onset to surgery was higher in the streptokinase group (48.35 ± 25.24 vs 37.95 ± 34.05 days, $P = .230$), though it did not achieve statistical significance (Table II).

Postirrigation characteristics between the 2 groups

Bleeding was noted in 14 patients from the whole cohort, but there was no significant difference between the 2 groups ($P = .075$). There was a significant difference in sepsis reversal after irrigation with streptokinase compared to saline (75% vs 36%, $P = .01$) (Table II). In the streptokinase group, we noted a significant reduction in the APACHE II score ($P = .002$) and modified CTSI score (MCTSI, $P = .028$) after irrigation. We also noted a decline in the MMS score after irrigation; however, the difference was insignificant. In the saline irrigation group, we noted a significant reduction in both the MMS ($P = .01$) and MCTSI ($P = .00$) scores after irrigation. However, the decline in the APACHE II score was not significant in the saline irrigation group ($P = .442$) (Appendix S2).

Surgical intervention

Of the 108 patients with necrotizing pancreatitis in the cohort, 48 (44%) patients underwent surgery. The need for surgery was significantly less in the streptokinase group compared to that in the saline group (34% vs 54%, $P = .016$). Postoperative complications were similar between the 2 groups; however, the occurrence of bowel fistulae (colonic/duodenal) was high in the streptokinase group (35% vs 15%, $P = .564$), though the difference was insignificant. Preoperative bleeding was seen in 14 (13%) patients, of which 11 (78%) patients required surgery (Table II). The incidence of preoperative bleeding was higher in the saline group, while postoperative bleeding was comparable between the 2 groups (Table II).

Factors associated with requirement of surgery

Significant associations were noted with preoperative bleeding ($P = .05$), saline irrigation ($P = .016$), and multiorgan failure ($P = .042$) on univariate analysis. However, other factors, such as enterocutaneous fistula and positive bacterial or fungal culture, were not significantly associated in the univariate analysis. On multivariate analysis, preoperative bleeding ($P = .026$), saline irrigation ($P = .017$), and multiorgan failure ($P = .049$) were significantly associated with the requirement of surgery (Table III).

Mortality

Mortality was seen in 39 (36%) patients, and mortality in the streptokinase group was 32% compared to 40% in the saline group, but the difference was not statistically significant ($P = .212$). When we looked at patients with multi-organ failure, mortality was 53.3% (Table II). Mortality in the streptokinase group was 23% ($n = 8/35$) versus 36% ($n = 9/25$) in the saline group. Postoperative mortality was comparable between the 2 groups ($P = .342$) (Table II). Two patients in the saline group had postoperative mortality for uncontrolled hemorrhage.

Factors associated with mortality

Preoperative bleeding ($P = .031$) and multiorgan failure ($P = .041$) were significantly associated with mortality in univariate analysis. The association of saline irrigation with mortality was nearly significant (.05); however, positive blood and fungal cultures were not significantly associated with mortality. When we analyzed these factors in the multivariate model, preoperative bleeding ($P = .024$), multiorgan failure ($P = .028$), and saline irrigation ($P = .008$) were significantly associated with mortality (Table IV).

Comparison of 150,000 IU streptokinase with 50,000 IU IV and saline group

In comparing 150,000 IU streptokinase with 50,000 IU streptokinase, there was a significant reduction in mortality in patients

Table II
PCD characteristics, complications, and surgical characteristics

	Streptokinase group (n = 53)	Saline irrigation group (n = 55)	P value
Disease onset to PCD insertion in days	26.85 ± 14.95	25.24 ± 12.285	.541
Duration of PCD after irrigation in days	24.12 ± 19.77	19.51 ± 17.13	.213
Total duration of PCD in days	43.89 ± 25.01	42.87 ± 24.68	.832
Duration from irrigation to surgery in days	11.76 ± 12.25	16.71 ± 23.51	.345
Duration from onset of disease to surgery in days	48.35 ± 25.24	37.95 ± 34.05	.230
Number of PCD	2.57 ± 1.18	2.33 ± 0.840	.064
Positive bacterial cultures in necrosum	39 (73%)	36 (65%)	.240
Positive fungal cultures in necrosum	15 (28%)	15 (27%)	.538
Sepsis reversal	40 (75%)	20 (36%)	.01
Complications			
Hemorrhage	4 (7%)	10 (18%)	.075
GI fistula (colonic and small bowel)	7 (13.4%)	9 (16.3%)	.564
New onset diabetes mellitus	20 (38%)	16 (29%)	.227
External pancreatic fistula	12 (22%)	11 (20%)	.460
Surgery and postoperative complications			
Surgery	18 (34%)	30 (54%)	.016
MIS (minimal incision)	7 (39%)	10 (33%)	.190
Open surgery	9 (50%)	18 (60%)	.047
Video-assisted retroperitoneal debridement	2 (11%)	2 (6%)	.34
Postoperative bowel fistula	6(35%)	5 (16%)	.06
Postoperative hemorrhage	4 (23%)	8 (25%)	.529
Postoperative ventilatory support	12 (70%)	27 (87%)	.796
Postoperative ICU requirement	7.17 ± 6.36	9.64 ± 8.62	.384
Postoperative stay in days	14.75 ± 12.63	13.55 ± 12.93	.762
Re-exploration	4 (23%)	5 (16%)	.586
Readmissions	13 (25%)	13 (23%)	.584
Total hospital stay in days	43.89 ± 24.23	50.27 ± 15.82	.107
Total ICU stay in days	14.91 ± 17.30	17.91 ± 16.54	.359
Need for ICU stay	26 (50%)	29 (53%)	.425
Mortality	17 (32%)	22 (40%)	.212
Postoperative mortality	8 (44%)	16 (53%)	.342
Single organ failure	9 (31%)	12 (42%)	.082
Multiorgan failure	8 (50%)	8 (57%)	.096
Positive bacterial cultures	9 (23%)	15 (41%)	.229
Positive fungal cultures	3 (20%)	6 (40%)	.222

GI, gastrointestinal; *ICU*, intensive care unit; *PCD*, percutaneous catheter drainage.

Table III
Factors associated with need for surgery

Parameter	Univariate analysis	Multivariate analysis
Bleeding (n = 11/14)	0.005 (OR 12.7, CI 1.5–107)	0.026
GI fistula (n = 12/16)	0.068 (OR-3.6, CI 0.58–22.6)	0.063
Positive bacterial culture (n = 30/75)	0.094 (OR 1.5, CI 0.97–2.3)	-
Positive fungal cultures (n = 10/30)	0.207 (OR-1.3, CI 0.76–2.35)	-
Saline irrigation (n = 55)	0.016 (OR 2.16, CI 1–4.4)	.017
Multiorgan failure (n = 18/30)	0.042 (OR-1.76, CI 0.9–3.2)	.049

CI, confidence interval; *GI*, gastrointestinal; *OR*, odds ratio.

Table IV
Factors associated with mortality

	Univariate analysis	Multivariate analysis
Type of irrigation used (saline vs streptokinase)	0.05 (OR 2.9, CI 0.9–8.7)	0.008
Multiorgan failure (n = 16/30)	0.041 (OR-3, CI 1–9)	0.028
Preoperative bleeding (n = 10/14)	0.031 (OR 4.5, CI 1.1–17)	0.024
Positive bacterial culture	0.327 (OR-1.3, CI 0.64–2.8)	-
Positive fungal cultures	0.43 (OR 1.2, CI 0.42–3.846)	-

CI, confidence interval; *OR*, odds ratio.

receiving 150,000 IU streptokinase (13.6% vs 45%, $P = .028$). Bleeding as a complication after irrigation was also significantly lower in the 150,000 IU streptokinase group (4% vs 10%, $P = .006$). When comparing 150,000 IU streptokinase and 50,000 IU streptokinase with normal saline, the use of 150,000 IU streptokinase led to a significant reduction in mortality ($P = .028$) and the need for surgical necrosectomy ($P = .013$) (Table V).

Discussion

In the present study, we observed a significant reduction in the need for surgery and mortality after streptokinase (150,000 IU) irrigation. PCD has been recommended as a definitive/first step in the management of infected pancreatic necrosis.[2,14–17] The success of PCD has been reported in the range of 35% to 60% in previous

Table V
Comparison of 150,000 IU streptokinase with 50,000 IU IV and saline group

Outcome	Streptokinase (50,000 IU) (n = 31) n (%)	Saline (n = 55) n (%)	Streptokinase 1.5 lakh (n = 22) n (%)	P_1 value	P_2 value	P_3 value
Sepsis reversal	22 (70%)	20 (36%)	18 (81.8%)	.007	.001	.093
Mortality	14 (45%)	22 (40%)	3 (13%)	.526	.02	.028
Need for surgical necrosectomy	14 (45%)	30 (54%)	4 (18.1%)	.145	.013	.538
Complications related to streptokinase						
Bleeding				.006	.077	.031
Management	3 (9.6%)	10 (18%)	1 (4%)			
Surgery	2 (66%)	9 (90%)	0			
Conservative	1 (34%)	1 (10%)	1 (100%)			
GI fistulas	4 (12%)	9 (16%)	3 (13%)	.411	.92	.216
Colonic fistula	4 (100%)	6 (66%)	3 (100%)			
Surgery	4 (100%)	4 (66%)	2 (66%)			
Duodenal fistula	0	3 (33%)	0			
Surgery	0	2 (66%)	0			
New onset Diabetes mellitus	12 (38%)	16 (29%)	8(36%)	.053	.96	.071
External pancreatic fistula	8 (25%)	11 (20%)	4 (18%)	.041	.342	.002
Admission to ICU	14 (45%)	29 (52%)	12 (54%)	.321	.43	.072

P1: saline versus streptokinase (50,000 IU), P2: saline versus streptokinase (1.5 lakh IU), P3: streptokinase (50,000 IU) versus streptokinase (1.5 lakh IU).
GI, gastrointestinal; *ICU*, intensive care unit.

studies.[14,15] This wide variability depends on the contents of the necrotic cavity, the size of the catheter used, and how vigorously catheter drainage has been used, including upgrading, insertion of more catheters in a cavity, and volume of saline lavage.[15–18] The present study is different from our previous study, because we included a subset of patients with pancreatic necrosis who failed to respond clinically and radiologically to percutaneous catheter insertion and saline irrigation for the initial 48 to 72 hours.

Sepsis reversal in previous studies has been reported in the range of 62.5% to 74%,[2,6] and in the present study, sepsis reversal was seen in 75% of patients who received streptokinase irrigation in comparison to 39% of patients who received saline irrigation. This difference can be explained by the better effectiveness of drainage of infected fluid, debris, and necrotic tissue from the cavities. It is important to emphasize that, although patients who received streptokinase had more severe disease, as evidenced by significantly higher MCTSI and MMS scores. After irrigation, determinants of severity, such as APACHE II, MCTSI and MMS scores, declined in both groups; however, this decline led to a decreased need for surgery and sepsis reversal in the streptokinase group compared to the saline group.

In the present study, organ failure was seen in 80% of patients, whereas 34% of patients had multiorgan failure. This incidence of single organ or multiorgan failure is much higher than that in previous studies.[3,17,19–21] In the PANTER trial, 35% of patients obviated the need for surgery irrespective of having single or multiorgan failure[3]; however, in contrast, 49% of patients in the present study were successfully managed with PCD alone in the streptokinase group compared to 29% in the control group in this cohort of patients with more severe disease.

After the safety of streptokinase at a dose of 50,000 IU was established, we escalated the dose to 150,000 IU to see the difference in results. On dose escalation to 150,000 IU, there was a significant reduction in mortality (13.6% vs 45%, $P = .028$) and hemorrhage (4.5% vs 9.6%, $P = .031$) in comparison to 50,000 IU streptokinase. The need for necrosectomy and rates of GI fistula and ICU admission were not significantly different on dose escalation, implicating the safety and efficacy of dose escalation.

Superior results in the streptokinase group might be because of its fibrinolytic action, which leads to fragmentation of the necrosum at the periphery and complete digestion of the supportive collagenous framework in fragmented necrotic tissue, converting it into a structureless mass, as reported earlier.[8] Life-threatening hemorrhage was not observed in the streptokinase group; we believe that streptokinase has no effect on the tunica adventitia, media, or intima as reported previously.[22]

We also compared morbidity between the streptokinase and saline groups in the form of enterocutaneous fistula and bleeding. The incidence of intra-abdominal bleeding in previous studies was 5% to 16%.[3,6,23] Bleeding in these patients can be due to catheter-related or disease-related processes. The incidence of bleeding in the present cohort was 13%, and we noted that bleeding was seen more frequently in the saline irrigation group than in the streptokinase irrigation group (18% vs 4%), although the difference was not significant ($P = .075$). In our study, of the patients requiring surgery, 78% required surgery in view of uncontrolled hemorrhage (due to failed digital subtraction angiography embolization and hemodynamic instability), and this rate was high in the saline irrigation group. Intra-abdominal bleeding was one of the independent factors associated with the need for surgery in the present study. This finding in the present study contradicts the assumed notion that streptokinase might lead to increased bleeding. The increased risk of bleeding with streptokinase is due to its fibrinolytic action; however, it should be noted that streptokinase per se has no effect on the tunica adventitia, media, or intima.[22] Necrosum along with pancreatic secretions might erode the vessel wall, leading to hemorrhage and aneurysm formation, and streptokinase, by effectively increasing the drainage of necrosum, might have led to decreased effects of necrosum on the incidence of bleeding. When the escalated dose was compared with 50,000 IU, a significant difference in preoperative bleeding was noted (4.5% with 150,000 IU streptokinase vs 9.6% with 50,000 IU streptokinase).

Another common complication in necrotizing pancreatitis treated with PCD is enterocutaneous fistula, which has been reported in the range of 17% to 23% in previous studies.[3,5,6,17,23] Bowel fistulae occur while accessing the cavity from the infracolic route when the necrotic cavity extends into the infracolic compartment and is densely adherent to loops of small bowel. At times, the adhesions are very dense, leading to serosal tears, which can manifest postoperatively as enterocutaneous fistulae. Another reason could be bowel ischemia of the transverse colon, which goes undetected, especially in minimal incision necrosectomy or retroperitoneal necrosectomy.

In the present study, it was seen in 14% of patients, and there was no significant difference between the 2 groups ($P = .564$). These findings again rule out the notion of adverse effects of streptokinase on the surrounding bowel wall. Even on dose escalation to 150,000 IU streptokinase, the fistula rates remained the same and are in accordance with previous studies.[3,5,6,17,19,23] Postoperative bowel fistula rates up to 40% have been described in the literature.[21] In the present study, 35% of the postoperative patients in the streptokinase group had a bowel fistula in comparison to 16% in the saline irrigation group, and the difference was not significant ($P = .06$).

Mortality in necrotizing pancreatitis is multifactorial and ranges 10% to 52%.[3,24–26] Disease-specific mortality in the present series was 36% ($n = 39$) and was lower in the streptokinase group (32% vs 40%); however, when we looked at a higher dose of streptokinase, mortality was significantly lower at 150,000 IU streptokinase than at 50,000 IU streptokinase (13% vs 45%, $P = .028$). However, as reported previously, we noted higher mortality in patients with multiorgan failure than in those with single organ failure (53% vs 38%).[20,21,24–26]

In conclusion, streptokinase has superior necrolytic activity and reduced morbidity in the setting of infected pancreatic necrosis. A higher dose of streptokinase resulted in superior results, with a mortality rate of 13% and a need for surgery rate of 18%. A multicenter study with 150,000 IU streptokinase irrigation is warranted for necrotizing pancreatitis.

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Conflict of interest/Disclosure

This study has not been submitted to any other journal and authors do not have any conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.surg.2021.05.028.

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