

Continuous Controlled Regional Intra-Arterial Administration of Drugs in the Comprehensive Treatment of Acute Destructive Pancreatitis

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Abstract

Background

Acute destructive pancreatitis remains one of the most challenging problems in emergency abdominal surgery due to its severe clinical course and the high risk of infectious and septic complications, multiple organ failure, and mortality. One promising approach to comprehensive treatment is the regional administration of drugs directly into the vascular bed supplying the target organ—the pancreas—which enables high local drug concentrations to be achieved at the site of the pathological process.

Objective

To evaluate the effectiveness of programmed regional intra-arterial drug administration via splenic artery cannulation as part of the comprehensive treatment of patients with acute destructive pancreatitis.

Materials and Methods

The treatment outcomes of 160 patients with various clinical and morphological forms of acute destructive pancreatitis who were treated at Multidisciplinary City Hospital No. 2 in Astana between 2020 and 2025 were analyzed. The patients were divided into two groups: the study group ($n = 80$), in which programmed regional intra-arterial drug administration via splenic artery cannulation was used in addition to comprehensive treatment, and the control group ($n = 80$), which received conventional comprehensive treatment without splenic artery cannulation. The developed regional therapy regimen included antispasmodic, vasoactive, antiprotease, and antibacterial agents, including ulinastatin.

Results

No septic complications were observed in the study group, whereas they occurred in 6 patients in the control group. Emergency surgical intervention was required in 8 patients in the study group and 26 patients in the control group. The mean length of hospital stay was 19.2 and 24.6 bed-days, respectively. Mortality was 5.0% (4/80) in the study group and 11.25% (9/80) in the control group ($p < 0.05$).

Conclusion

The use of programmed regional intra-arterial drug administration via the splenic artery as part of comprehensive therapy for acute destructive pancreatitis was associated with more favorable clinical outcomes compared with conventional comprehensive treatment. The study group demonstrated an absence of septic complications, a lower need for emergency surgical interventions, a shorter hospital stay, and lower mortality.

Keywords: Patient-Centred Care, Prosthodontics, Shared Decision-Making, Oral Health-Related Quality of Life, Patient-Reported Outcomes, Dental Technology, Digital Workflow, Health Equity.

Introduction

Acute pancreatitis is an acute inflammatory disease of the pancreas characterized by a broad spectrum of clinical manifestations, ranging from relatively mild forms to severe destructive disease associated with systemic inflammatory response, infectious complications, and multiple organ failure. The pathogenesis of acute destructive pancreatitis involves several important mechanisms, including premature activation of pancreatic enzymes, acinar cell injury, microcirculatory disturbances, and the development of local and systemic inflammatory responses. Progression of the pathological process may lead to pancreatic necrosis, secondary infection, and severe systemic complications. Despite advances in intensive care, endoscopic interventions, and surgical techniques, the management of patients with severe and destructive forms of acute pancreatitis remains a major clinical challenge [1]. Therefore, considerable attention has been focused on developing methods for targeted drug delivery directly to the site of the pathological process. One such approach is regional intra-arterial drug administration, which enables therapeutic agents to be delivered directly into the vascular bed supplying the pancreas. The potential advantages of this method include achieving higher regional drug concentrations, targeting microcirculatory disturbances and excessive proteolytic activity, and providing a multimodal therapeutic effect on the key mechanisms underlying the pathological process [2, 3].

Materials and methods

From 2020 to 2025, a study involving 160 patients with various clinical and morphological forms of acute destructive pancreatitis was conducted at Multidisciplinary City Hospital No. 2 in Astana, Kazakhstan. The patients were divided into two groups: the study group (n = 80) and the control group (n = 80). The study group consisted of 80 patients, including 50 (62.5%) men and 30 (37.5%) women [4]. Upon admission, all patients un-

derwent comprehensive clinical, laboratory, and instrumental examinations in accordance with the clinical protocol “Acute Pancreatitis” (Protocol No. 60 of the Ministry of Health of the Republic of Kazakhstan, dated March 29, 2019).

In addition to comprehensive treatment, patients in the study group received the developed program of regional intra-arterial drug therapy. Following cannulation of the splenic artery, programmed administration of medications was performed directly into the vascular bed supplying the target organ the pancreas. The control group consisted of 80 patients, including 56 (70.0%) men and 24 (30.0%) women. Severe acute pancreatitis was diagnosed in 19 (23.75%) patients. Patients in the control group received conventional comprehensive treatment without splenic artery cannulation or programmed regional intra-arterial drug administration [5]. Treatment efficacy was assessed based on the clinical course of the disease, incidence of septic complications, need for emergency surgical intervention, length of hospital stays, and mortality. Statistical analysis of the obtained data was performed using methods of variation statistics. Student’s t-test was used to assess the statistical significance of differences. Differences were considered statistically significant at $p < 0.05$ [6].

Program of Regional Intra-Arterial Drug Therapy

A regional intra-arterial drug perfusion program was developed for patients in the study group. Following splenic artery cannulation, programmed administration of a combination of medications was performed to provide targeted therapeutic effects within the vascular bed supplying the pancreas. The regimen included medications aimed at improving regional microcirculation and tissue perfusion, reducing smooth muscle spasm, limiting proteolytic activity and the inflammatory response, and providing antibacterial therapy [7].

Table 1: Programmed Regional Intra-Arterial Drug Perfusion Regimen

Drug	Dose and administration regimen	Mechanism of action
Papaverine, 2% — 2 mL	Diluted in 16 mL of 0.9% NaCl solution and administered at a rate of 5 mL/h	Myotropic antispasmodic effect; reduces smooth muscle tone and improves regional blood flow
Ulinastatin — 100,000 IU	100,000 IU in 100 mL of 0.9% NaCl solution, twice daily	Protease inhibitor with anti-inflammatory and immunomodulatory effects
Trental (pentoxifylline), 2% — 5 mL	Diluted in 16 mL of 0.9% NaCl solution and administered at a rate of 5 mL/h	Improves microcirculation and blood rheological properties, reduces platelet aggregation and blood viscosity, and promotes tissue perfusion
Contrykal — 10,000 IU	10,000 IU in 20 mL of 0.9% NaCl solution	Inhibits proteolytic enzymes, thereby limiting proteolytic activity
Ceftriaxone — 1.0 g	1.0 g in 200 mL of 0.9% NaCl solution	Antibacterial activity through inhibition of bacterial cell-wall synthesis in susceptible microorganisms

A particular role in the developed regimen was assigned to ulinastatin, a broad-spectrum protease inhibitor that also possesses anti-inflammatory and immunomodulatory properties. Its phar-

macological effects are associated not only with inhibition of proteolytic enzyme activity but also with modulation of the inflammatory response. According to international studies, the use

of ulinastatin as part of comprehensive therapy for acute pancreatitis has been associated with a reduction in the inflammatory response and favorable changes in several clinical and laboratory parameters [8]. Ulinastatin has also been investigated for the prevention of acute pancreatitis and hyperenzymemia following endoscopic retrograde cholangiopancreatography (ERCP). These findings provided additional pathophysiological rationale for including ulinastatin in the developed regional therapy program [9].

Results

In the study group (n = 80), the treatment strategy was determined according to the clinical and morphological form and severity of the disease. Laparoscopic cholecystectomy with drainage of the lesser sac was performed in 37 (46.25%) patients, endoscopic

papillosphincterotomy (EPST) in 23 (28.75%), gastropancreaticostomy in 9 (11.25%), and laparotomy in 6 (7.5%) patients. Five (6.25%) patients were treated without surgical intervention. Thus, surgical and minimally invasive interventions were performed in 75 (93.75%) patients in the study group [10].

All 80 patients in the study group underwent splenic artery cannulation followed by programmed regional intra-arterial administration of a combination of medications. In the control group, laparotomy was performed in 18 (22.5%) patients, including marsupialization in 8 (10.0%). Endoscopic interventions were performed in 11 (13.75%) patients. Relaparotomy was required in 5 (6.25%) patients.

Comparative clinical outcomes are presented in Table 2.

Table 2: Comparative Analysis of Clinical Outcomes in the Two Groups

Parameter	Study group (n = 80)	Control group (n = 80)	p-value
Septic complications	0	6	—
Emergency surgical intervention	8	26	—
Mean length of hospital stay, days	19.2	24.6	p < 0.05
Mortality	4 (5.0%)	9 (11.25%)	p < 0.05

No septic complications were observed in the study group, whereas they occurred in 6 patients in the control group. Emergency surgical intervention was required in 8 patients in the study group and 26 patients in the control group [11-13]. The

mean length of hospital stay was 19.2 days in the study group compared with 24.6 days in the control group. Death occurred in 4 of 80 patients (5.0%) in the study group and in 9 of 80 patients (11.25%) in the control group (p < 0.05).

Laboratory Parameters

Table 3: Analysis of Laboratory Parameters in the Study and Control Groups

Parameter	Study group	Control group
Mean leukocyte count, $\times 10^9/L$	A) 15.8 B) 8.2	A) 18.2 B) 8.6
Mean C-reactive protein (CRP), mg/dL	A) 298 B) 21	A) 305 B) 52.5
Mean total bilirubin, $\mu\text{mol/L}$	A) 65 B) 23	A) 67 B) 33
Mean amylase, U/L	A) 2162 B) 48	A) 2243 B) 86

Note: A) value at admission; B) value at discharge.

As shown in Table 3, laboratory parameters improved during treatment in both groups. At discharge, patients in the study group, who received regional intra-arterial drug administration, including ulinastatin, as part of comprehensive treatment, demonstrated more favorable laboratory parameters than patients in the control group, who received conventional intravenous drug administration (p < 0.05) [14, 15].

Discussion

The treatment of acute destructive pancreatitis remains a major challenge in modern surgery because of the multifactorial pathogenesis of the disease, pronounced systemic inflammatory response, impaired pancreatic microcirculation, activation of proteolytic enzymes, and the high risk of infectious and septic complications. Therefore, comprehensive therapy should be

aimed not only at correcting systemic disturbances but also at directly targeting the pathological processes occurring within the pancreas [16]. One potential approach to improving the effectiveness of pharmacological treatment is regional intra-arterial drug administration [17]. Unlike conventional systemic administration, this approach enables therapeutic agents to be delivered directly into the vascular bed supplying the target organ, thereby achieving higher regional drug concentrations. The potential role of regional arterial infusion in severe acute pancreatitis has previously been investigated by several researchers, including approaches involving protease inhibitors and antibacterial agents. However, the published findings remain inconsistent, highlighting the need for further investigation of this therapeutic strategy [18].

In the present study, the developed regional intra-arterial drug therapy program included agents with different mechanisms of action: a myotropic antispasmodic, an agent aimed at improving microcirculation and the rheological properties of blood, protease inhibitors, and an antibacterial agent. This multimodal approach was intended to improve regional blood flow and tissue perfusion, limit proteolytic activity and the inflammatory response, and prevent infectious complications [19]. Our findings demonstrated more favorable clinical outcomes in patients in the study group. No septic complications were observed in the study group, whereas they occurred in 6 patients in the control group. Emergency surgical intervention was required in 8 patients in the study group compared with 26 patients in the control group. The mean length of hospital stay was 19.2 and 24.6 days, respectively [20–22].

Mortality is of particular clinical importance. Death occurred in 4 of 80 patients (5.0%) in the study group compared with 9 of 80 patients (11.25%) in the control group; the difference was statistically significant ($p < 0.05$). Thus, the absolute difference in mortality between the two groups was 6.25 percentage points. An important component of the developed therapeutic program was ulinastatin. In addition to inhibiting proteolytic enzymes, ulinastatin possesses anti-inflammatory and immunomodulatory properties. Experimental and clinical studies have investigated its effects on systemic inflammatory response markers and cytokine levels, as well as its therapeutic efficacy in acute pancreatitis and other conditions associated with a pronounced inflammatory response [23–25].

The use of ulinastatin for the prevention of pancreatitis and hyperenzymemia following endoscopic procedures involving the pancreatobiliary system is also of particular interest. Available evidence from the literature provided an additional pathophysiological rationale for incorporating ulinastatin into the developed comprehensive regional therapy program. In the treatment of acute pancreatitis, depending on disease severity, ulinastatin has been administered at a dose of 100,000–200,000 IU by intravenous infusion every 12 hours for 5–7 days. In relatively mild acute pancreatitis, a dose of 100,000 IU has been used for 3 days. In China, for severe acute pancreatitis, a regimen involving four ampoules of ulinastatin diluted in 100 mL of normal saline and administered intravenously over 1–2 hours three times daily for one week has been recommended [26, 29].

For the prevention of pancreatitis associated with endoscopic retrograde cholangiopancreatography (ERCP), ulinastatin has been administered at a dose of 100,000–150,000 IU immediately before or 1–1.5 hours prior to the procedure. Nevertheless, the findings of the present study do not allow the effect of ulinastatin to be evaluated independently from the other components of the therapeutic regimen. Patients in the study group underwent splenic artery cannulation and simultaneously received programmed regional administration of a combination of therapeutic agents. Therefore, the observed clinical outcomes should be interpreted as the effect of the developed comprehensive treatment strategy as a whole rather than as the effect of any single drug [30].

The more favorable outcomes associated with regional therapy may be related to targeted delivery of therapeutic agents into the vascular bed supplying the pancreas, effects on regional microcirculation, and attenuation of proteolytic activity and the inflammatory response. The absence of septic complications, reduced need for emergency surgical interventions, shorter hospital stays, and lower mortality observed in the study group suggest that the developed approach may represent a promising component of comprehensive treatment for acute destructive pancreatitis. The findings of this study should be interpreted in light of several limitations [31]. The study was conducted at a single clinical center, and each group consisted of 80 patients. Furthermore, the effectiveness of a comprehensive treatment program was evaluated; therefore, the independent contribution of each component to the final clinical outcome cannot be determined. Further prospective studies involving larger patient populations and standardized assessment of disease severity are required to more accurately determine the effectiveness of this approach and establish optimal indications for its use [32].

Conclusion

The use of the developed program of regional intra-arterial drug administration via the cannulated splenic artery as part of comprehensive treatment for acute destructive pancreatitis was associated with more favorable clinical outcomes compared with conventional comprehensive therapy. No septic complications were observed in the study group. Emergency surgical intervention was required in 8 patients compared with 26 patients in the control group, while the mean length of hospital stay was 19.2 days compared with 24.6 days, respectively. Mortality was 5.0% (4/80) in the study group and 11.25% (9/80) in the control group ($p < 0.05$). These findings suggest that programmed regional intra-arterial drug therapy may represent a promising component of comprehensive treatment for patients with acute destructive pancreatitis. However, further studies are required to clarify the indications for this approach and to determine the optimal composition and administration regimen of regional therapy.

Declarations

Consent for publication: Not applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to patient confidentiality and ethical considerations but are available from the corresponding author on reasonable request.

Competing interests

The authors have no conflict of interest in recruiting the research material and writing this article.

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Author Contributions

Zhomart Zhalgaspaev and Alua Sadriten: Conceptualization, data collection, investigation, formal analysis, statistical analysis, manuscript drafting, and interpretation of results.

Arna Kabduaiysova: Study design, supervision, methodology, critical revision of the manuscript and final approval of the submitted version.

Kulsara R. Rustemova: manuscript drafting, interpretation of results, critical revision of the manuscript, and final approval of the submitted version.

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Informed Consent

Written informed consent was obtained from all subjects.

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