

Clinical Research

The Effectiveness of Local Hypothermia and Peritoneal Lavage-Dialysis in the Treatment of Patients with Acute Destructive Pancreatitis

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Abstract

The aim of this study was to improve the principles of the pathogenetic therapy of acute pancreatitis and assess the effectiveness of local hypothermia of the pancreas, as well as peritoneal lavage-dialysis in the treatment of acute destructive pancreatitis. A total of 5889 patients with acute pancreatitis (AP) were examined. The leading role played by the lesions of the pancreatic lymphatic system in the development of destructive processes was noted. In experiments done on eight dogs, the first day of experimental acute pancreatitis showed necrosis of the lumbar retroperitoneal lymph nodes with a violation of lymph drainage from the pancreas before the retroperitoneal fat necrosis was initiated. The effectiveness of local hypothermia of the pancreas was experimentally demonstrated. In 32 patients with AP, the perioperative local hypothermia of the pancreas for 20-25 minutes was followed by the reduction of the alpha-amylase activity in the peripheral blood and in the portal system, as well as a significant reduction in the edema of the pancreas, that delayed the progression of the destructive lesions. An effective method of performing lavage-dialysis of the omental bursa, by using a transversely perforated tube with a pollution control device in the lumen, was developed.

Key words: *pancreas, lymphatic system, acute pancreatitis.*

Introduction

According to many studies, the percentage of acute pancreatitis (AP) in the structure of surgical diseases reaches up to 10% [1,2,3]. The growth rate of this disease is far ahead that of several other surgical processes of the abdominal cavity [4,5,6]. The destructive type of AP reaches to 15-20%. An infection in the foci of the tissue decay reaches to 70%, and this complication in 80% of destructive pancreatitis (DP) is the major cause of death [2,3,4,7].

It is extremely difficult to achieve effective solutions in the treatment of DP. Moreover, without suppressing the enzyme “storm” in the pancreas, the effectiveness of any treatment is not

possible [2,5,6]. Unfortunately, discovering an effective drug to reach this goal is still proving elusive, while achieving local hypothermia (LH) by using cooling machines is too inconvenient for clinical use [1,4,6,7, 8]. In light of this, optimization of the treatment of AP remains a major clinical problem.

The aim of this study was to improve the principles of the pathogenetic therapy of acute pancreatitis and assess the effectiveness of local hypothermia of the pancreas, as well as peritoneal lavage-dialysis in the treatment of acute destructive pancreatitis.

Material and Methods

To solve this problem, the technique of the local contact cooling of the pancreas developed earlier, “Method of hypothermia of the pancreas” (Patent of RF # 2110219 priority of May 10, 1998), has been used. The essence of the invention involves perioperative and postoperative visual 18-20 minute

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irrigations of the front and side surfaces of the pancreas with an intermittent stream of ethyl chloride allowing free evaporation into the atmosphere. This is accompanied by the formation of a layer of ice crystals on the entire surface of the irrigated tissue. This method allows the surface of the pancreas gland to cool to 0° - 4°, to a temperature at which there is a reduction in the destruction of the exocrine apparatus of the gland while maintaining the function of the islets of Langerhans [9]. All portions of the pancreas from head to tail can be easily irrigated; this method does not require a wide opening of the omental bursa and thus reduces the trauma of surgery.

Later on, this technique of local hypothermia of the pancreas was modified. Instead of using ethyl chloride during the operation, a sealed container with small pieces of melting ice weighing 1-2 kg with the ability to easily lie prone across the free surface of the pancreas was placed in the omental bursa for 20 - 25 minutes.

A median laparotomy was performed to apply the LH. The omental bursa was revealed by dissection of the gastrocolic ligament. The pancreas was isolated from the surrounding tissues with tampons. The peritoneum covering the gland surface was dissected, and then LH was performed. As described earlier, after cooling the pancreas, the omental bursa through the counter punctures in both the lumbar-hypochondriac areas, was drained in the transverse direction. This was done in the lumen using a perforated tube (diameter of 0.8 - 1.0 cm) carrying the pollution control device ("Device for draining purulent cavities", Patent of RF # 2066207 priority of September 10, 1996), which was a string of beads threaded on a fishing line.

Depending on the severity of the necrobiotic process, the operation was finished by suturing the median wound or by creating a broad omentoburso-pancreatic stoma in patients with contaminated DP to eliminate intra-abdominal hypertension and provide free abruption of necrotic tissue with purulent detritus. In the presence of widespread peritonitis, the drainage of the pelvic cavity, including the right and left areas of the abdominal cavity were performed. For postoperative peritoneal lavage-dialysis, perforated tubes (of diameter 0.8-1.0 cm) were applied [10]. To determine the efficacy and safety of both the methods of LH, experiments were conducted on 8 mongrel dogs weighing 20 ± 2 kg. One day prior to the application of LH, under general anesthesia, the canalicular-hypertensive model of DP described in the monograph by VS Saveliev et al. [11], was modeled on 6 dogs. This model involves the development of PD due to the direct perioperative injection of the auto-bile (0.5 ml / kg) in the pancreatic duct. The next day, under general anesthesia, a blood

sample was taken from the animal limb. Then relaparotomy with revision of the abdominal cavity was done. Then DP in varying degrees with infiltration of the retroperitoneal fat, and widespread hemorrhagic enzymatic peritonitis was diagnosed in all the animals. After revision, the blood samples from the portal system were collected and the thickness of the pancreas in middle section was measured. It ranged from 4 cm to 5 cm. Next, hypothermia of the pancreas with chloroethyl (in 3 dogs) or melting ice (in 3 dogs) was performed. After cooling in the same place the thickness of the gland was measured again and its decrease by 0.5-0.8 cm was detected. After completion of the cooling, the surface temperature of the pancreas was immediately measured and then the temperature in its depth. Needle thermometers were dipped into the gland tissue along the entire gland length, at a distance of 3.0 - 3.5 cm from each other. After measuring the temperature of the pancreas, the animal was put down. The pancreas and the retroperitoneal adipose tissue from the lymph nodes were taken for pathomorphological study.

The activity of the serum alpha-amylase and the trypsin inhibitory activity in the peripheral and portal blood were studied before and after performing LH in all the eight animals. Before the experiment and during relaparotomy, the effective concentration of the albumin was also measured. This study was performed on the AKL-01 (Russia) using the Probe-Albumin set of reagents. The level of the cationic proteins of the neutrophils in the portal system was evaluated before the destructive effects on the pancreatic tissue (under laparotomy), after one day of DP development and after 45-60 minutes of the LH of the pancreas. The cationic protein level of the neutrophils was assessed using a cytochemical reaction with amido black 10B. The results of the reaction were evaluated with a computer image analysis of the cells by using the cytochemical index (CCI).

The clinical study included 5889 patients with AP between 2005 and 2010. Table 1 presents the data on the clinical forms of AP and the mortality in each of them. Among the 940 patients with DP, 681 (72.5%) were males. Patients varied in age from 25 to 86 years (mean age 46.9 ± 2.2 years). In all, 802 (85.3%) patients had a history of 1 to 6 episodes of AP. During the initial chest x-ray an effusion in the left side of the pleural cavity was observed in only 25 (2.6%) patients, and later it was seen to develop in 284 (30.2%) cases. During examination, the alpha-amylase activity in the systemic circulation and in the abdominal cavity effusion was determined. All patients had a laparoscopy performed.

Table 1
Clinical forms of acute pancreatitis

Clinical forms of AP	Number of patients	Mortality
Edematous pancreatitis	4898 (83.17%)	45 (0.92%)
Hemorrhagic pancreonecrosis	51 (0.86%)	6 (11.7%)
Destructive infected pancreonecrosis	940 (15.97%)	173 (13.82%)
Total	5889 (100%)	224 (3.8%)

The data obtained was processed by statistical variation methods. Calculation of the numerical characteristics was made using the IBM PC Intel Celeron 1400. The sequential probability ratio was calculated.

Results and Discussion

Experimental studies have shown that both the local hypothermia methods reduced the temperature in the center of the affected pancreas up to $+ 19^{\circ} - + 22^{\circ}$; however, on the surface of the pancreas the temperature was $0^{\circ} - +4^{\circ}$. At this temperature, a significant inhibition of the exocrine apparatus was noted, without any structural collapse and without affecting the function of the islets of Langerhans. This was confirmed by biochemical study.

Thus, immediately after perioperative local hypothermia of the healthy gland in two dogs, the alpha - amylase activity in the portal blood was reduced up to 10 - 16% and maintained at this level for one hour. These animals were studied to determine the role of hypothermia in reducing the effects of acute post-traumatic pancreatitis that develops post surgery in the gastroduodenal area. After 4-6 hours of the traumatic impact on the pancreas during the resection of the stomach in two dogs, an increase was observed in the amylase activity in the portal circulation by 3.45 times compared with the original value. After a 20-minute cooling time of the pancreas, the amylase activity fell by 46% in the peripheral blood and by 63% in the portal system.

The histological study of the pancreatic tissue taken immediately after local hypothermia, revealed the displacement of the cationic protein from the apical to the basal regions of the pancreatic cells. This was indicative of a suppression of their functions.

After local hypothermia in 75% of animals with destructive pancreatitis, there was a decrease in the amylase activity by 15-20% (from the initial value) in the blood of the portal system, while the inhibitory activity of trypsin increased by 20 - 28%. However, the alpha-amylase activity increased by 14 -15% and the trypsin inhibitory activity decreased by 39 - 40% in 25% of the dogs; in all these animals, total pancreonecrosis was observed.

All the animals revealed a higher (at 14 - 16% more) trypsin inhibitory activity in the portal system blood than in the peripheral blood. Consequently, local hypothermia was effective only in animals where a total destruction of the pancreatic tissue had not occurred.

A significant reduction in the effective concentration of albumin (up to 13.8 ± 1.81 g / l) was revealed in the animals with destructive pancreatitis, whereas it was 19.9 ± 0.96 g/L ($p < 0.001$) in the dogs used as control. These data indicate the pronounced transformation of the albumin in patients with destructive pancreatitis.

The activity of the neutrophil leukocytes also revealed the severity of condition of the animal. The CCI value was 0.7 ± 0.08 RU in healthy animals. On the day after destructive pancreatitis modeling, the CCI increased up to 2.49 ± 0.09 RU, whereas after applying local hypothermia, the CCI fell to 1.58 ± 0.03 RU.

The development of acute pancreatitis, therefore, was associated with an increase in the cationic proteins in 3.4 times ($P < 0.01$); after local hypothermia application, while the cationic

protein level decreased 1.6 times (fell to 1.58 ± 0.03 RU).

In brief, these experiments revealed that a single application of local hypothermia in the animals during the first day of the modulated destructive pancreatitis was accompanied by a significant reduction in the pancreatic edema and that of the surrounding tissues. The α -amylase activity dropped up to 46% in the peripheral blood and up to 63% in the portal system. However, in dogs, during this time, necrosis of the retroperitoneal lymph nodes (at Th12-L2 level) developed, although retroperitoneal fat necrosis did not happen yet.

Based on the segmental structure of the lymphatic system, under the action of the pancreatic enzymes, the destructive pathological process was triggered by a lesion of the amyous intervalve segments of the lymphatic post capillaries that control passive lymph flow. The energy deficit of the extravasal factors activates the involvement the muscular intervalve segments of the lymphangions in the pathological process. Their contraction pushed the lymph into the veins. The lymphoid lymphangions regulated the volume and structure of lymph in the lymph nodes [9]. The pathomorphological examination of the dead animals revealed the development of a purulent-destructive process first of all, in the lymphatic system of the pancreas (LSP) and retroperitoneal space, thus causing a decay of the regional lymph nodes. In our opinion, this lesion of the LSP is accompanied by a progressive edema of the pancreas that leads to tissue ischemia and the compression of the ducts. Therefore, the destruction of the parenchyma with the subsequent release of the enzymes into the surrounding fat, omental bursa and free abdominal cavity is noted. As a result, the pathological process causes a snowballing destructive effect.

Analysis of the clinical data suggests that the edematous form of acute pancreatitis is accompanied by the release of the pancreatic enzyme into the retroperitoneal space and free abdominal cavity only in 10%, and into the blood and lymphatic systems in 90%. In destructive pancreatitis, 90% the pancreatic enzymes are released into the retroperitoneal space and free abdominal cavity. These enzyme levels gradually reduce in the peritoneal exudate during convalescence. A sharp fall was observed in patients 2-4 days before death. The enzymatic activity of the exudate in patients with destructive pancreatitis reached up to 16,000 U/L and higher, while the activity of alpha-amylase in the blood was normal. The enzymatic activity of the exudate in patients with the edematous form of acute pancreatitis was 00.00-270.00 U/L, although the level of this enzyme in the blood reached up to 960.00 U/L and more.

The treatment of destructive pancreatitis was usually begun with a minimally invasive drainage of the omental bursa and the pelvic cavity under laparoscopic control or using the ultrasound.

The increase in the intoxication and growth of the phlegmon were revealed in 442 (47%) patients after 12-38 days. This necessitated a laparotomy with removal of the decaying pancreatic tissue and retroperitoneal fat; it should be noted that the necrotic zone reached up to pelvic cavity in some patients. The tissue thus removed weighed 1 kg or more. It is quite obvious that the decay of the adipose tissue occurred by the uncontrolled steady flow of the enzymes from the residual pancreatic parenchyma into the surrounding tissue. Given the area damaged and the progression of the purulent-destructive processes in the retroperitoneal fat, the decision to apply

peritoneal lavage-dialysis was taken. This method was used in 52 patients, of whom 12 (23.1%) patients died.

Intraoperative local hypothermia was performed in 32 patients aged 19 to 67 years. During surgery, the edematous form of the acute pancreatitis was seen in 4 (12.5%) patients, the hemorrhagic form in 8 (25%), and DP in 20 (62.5%).

Local hypothermia was performed only once in 26 (81.2%) patients (including 6 patients with the remnants of the pancreas after necrosectomy), repeatedly in 6 (18.8%) patients (initially 7-10 days after surgery, at 12-14 and 16-18 days after surgery). Tissue edema was significantly reduced in all the patients post local hypothermia.

The drainage of the omental bursa with the cross-perforated drainage tube carrying the pollution control device was performed in all the 32 patients during the postoperative period (4 -14 days).

All the patients also received comprehensive medical therapy. All patients with the edematous and hemorrhagic forms of acute pancreatitis, where local hypothermia had been applied, showed no complications; the mean length of the hospital stay was 24-34 days. Mean length of hospital stay was 35 to 79 days in 20 patients with destructive pancreatitis; 3 of whom (15%) died: 1 patient within 7 hours after the operation, of toxemia and 2 patients between 56 and 64 days after multiple surgeries because of septic complications.

Conclusion

The development of the purulent-necrotic process in the retroperitoneal space in acute pancreatitis was associated with a violation of the functional state of the regional lymphatic system. The development of the purulent-necrotic process in the retroperitoneal space is associated with a violation of the functional state of the regional lymphatic system in patients with acute pancreatitis. It was observed that local hypothermia slows the development of destructive lesions by reducing the enzymatic activity of the pancreas and the edema of the pancreas and surrounding tissues.

Active usage of the perforated drainage tube with the pollution control device and peritoneal lavage-dialysis allowed

complete clean up of the omental bursa from the enzymes, fibrin and tissue detritus.

Also, local hypothermia was found to reduce the risk of developing of destructive pancreatitis and the other purulent-necrotic complications of acute pancreatitis.

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