Official Title	**The use of cell and tissue grafts in the complex treatment of patients with pancreatic necrosis**
Study Start Date	2008
Estimated Primary Completion Date	2010
Brief Summary	Acute pancreatitis is a severe disease which resulting in necrosis of part of the pancreas or the whole organ and causing a high mortality rate among patients. The severity of the disease, the reduction of general and local reparative processes and immune reactivity in patients with necrotic pancreatitis, the low effectiveness of conventional treatment methods, including surgery, became the background for developing a new method for treating pancreatic necrosis using allogeneic cryopreserved umbilical cord blood stem cells (UCB-SCs) and allogeneic cryopreserved umbilical cord tissue (UCT). UCBSCs secrete a large number of bioactive molecules which have possible anti-inflammatory, antifibrotic and wound-healing effects and can slow the progress of the disease.
Study aim	The purpose of the clinical study was to increase the effectiveness of complex treatment of patients with pancreatic necrosis through systemic and local stimulation of reparative regeneration processes using intravenous administration of the cryopreserved allogeneic umbilical cord blood total nucleated cells (UCB-TNCs) and local transplantation of cryopreserved allogeneic UCT.
Study Type	Interventional
Phase	1-2
Study Design	Allocation: Non-Randomized Intervention Model: Parallel Assignment Masking: None (Open Label) Primary Purpose: Treatment
Endpoint Classification	Safety and Efficacy Study
Condition or disease	Pancreonecrosis
Intervention/treatment	Biological: Stem Cells, systemic administration; umbilical cord tissue (UCT) transplantation
Cells type	Cryopreserved allogeneic Umbilical cord blood total nucleated cells (UCB-TNCs) allogeneic cryopreserved umbilical cord tissue (UCT)
Study Arms	Experimental Group A. Patients with pancreatic necrosis and peripancreatic necrosis who received cellular* and tissue** therapy (n = 32); control group - patients with pancreatic necrosis and peripancreatic necrosis who received standard treatment without cell therapy (n=47). Experimental Group B: Patients with isolated pancreatic necrosis who received cellular* and tissue** therapy (n = 22); control group - patients with isolated pancreatic necrosis who received standard treatment without cell therapy (n = 32). Experimental Group C. Patients with isolated peripancreatic necrosis who received cellular* and tissue** therapy (n = 19); control group - patients with isolated peripancreatic necrosis who received standard treatment (n = 27) without cellular therapy. *Cell therapy - Intravenous injection of $0,45 \cdot 10^9$ UCB-TNCs once a day for 5 days ($CD34^+$ cells – no less $1,0 \pm 0,01 \cdot 10^3$/ml) in 200 ml of normal saline solution. **Tissue therapy - Patients with direct indications for an open surgery were transplanted cryopreserved allogeneic UCT. TPK was used as surgical grafts to close pancreatic fistulas and improve healing. Transplantation of TPK was performed on residual pancreatic tissue from all sides by surgical procedure. The graft was removed on 2-3 days after surgery and a course of cell therapy has been conducted. No HLA matching or immunosuppression required.
Recruitment Information	**Completed status**

Recruitment Status	Not Recruiting
Estimated Enrollment	73
Sexes Eligible for Study	All
Ages Eligible for Study	From 20 Years to 80 Years (Adult, Senior)
Accepts Healthy Volunteers	No

Eligibility Criteria

Inclusion Criteria:

1. Aseptic pancreatic necrosis;
2. Infected pancreatic necrosis;
3. Pancreatogenic abscess;
4. Age of 20-80 years;
5. Written informed consent.

Exclusion Criteria:

1. Age less than 20 or more than 80 years old;
2. Participation in other clinical trials;
3. Pregnancy, breastfeeding;
4. Decompensated diseases;
5. Cognitive or language barriers that prohibit obtaining informed consent or any study elements.

Original Primary

Safety of systemic stem cell application and umbilical cord tissue transplantation.

Outcome Measures

Safety of systemic UCB-TNCs application and UCT transplantation were evaluated by reviewing the clinical outcomes and adverse events in the postoperative period and every six months after inpatient treatment during a three year period.
Major adverse events were adjudicated:
- hospitalization;
- gastrointestinal bleeding;
- multiple organ failure;
- death.

Original Secondary

Efficacy of systemic UCB-TNCs application and UCT transplantation were evaluated by reviewing the clinical outcomes and adverse events in the postoperative period and every six months after inpatient treatment during a three year period.
Outcome criteria:
- changes in the intensity of pain syndrome;
- changes in the duration of the illness;
- pancreas anatomical and functional integrity preservation;
- reduction of the number of early (bleeding, gastrointestinal fistula, sepsis) and late complications (cysts, pancreatic fistulas).

Results

The use of minimally invasive surgery under ultrasound guidance, followed by the infusion of UCB-TNCs, led to a 1.65 fold ($p<0.05$) increase in cured patients who were able to avoid open surgery. 2. The duration of their hospital stay was shortened 1.47-fold ($p<0.05$) compared with control group.3. The UCB-TNCs-treated patients who went to the second stage of open surgery were able to postpone needed surgery, which contributed to improved outcome. 4. The overall mortality of UCB-TNCs-treated patients was 2.06-fold ($p<0.05$) lower compared with control group, and their duration of post-operative hospital stay was 1.83-fold lower ($p<0.05$). 5. Among patients with necrotic pancreatitis, who received UCB-TNCs infusions and cord tissue grafts showed 4.71-fold ($p<0.001$) lower incidence of gastrointestinal bleeding from the abdominal cavity compared with control group. 6. During the five days of UCB-TNCs infusions, the early mortality of study patients from enzymatic toxemia was decreased 1.98-fold ($p<0.05$). 7. The development of disseminated intravascular coagulation syndrome in patients treated with UCB-TNCs occurred 3.48-fold ($p<0.001$) less often compared with

control group. 8. The frequency of postoperative complications in the control group of patients associated with infection, impaired microcirculation, and the direct effect of pancreatic enzymes that fell in the abdominal cavity was 48.1 % versus 24.7 % in UCB-TNCs - treated group.

Publication

1. Kebkalo A.B. Surgery and cellular technologies in the complex treatment of patients with pancreatic necrosis. Klin Khir. 2012; (10):53-6. [Article in Russian]
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3. Kebkalo A.B., Lobintseva G.S., Seminog V.I., Shabliy V.A. The cord blood and umbilical cord use in the complex treatment of patients with pancreatic necrosis. UkrJEmergMed named after G. O. Mozhaev. 2012; 13(1):77-85. [Article in Russian]
4. Kebkalo A.B., Mamchych V.I., Lobyntseva G.S., Shabliy V.A. The effect of cord blood stem cells on the system of haemostasis in patients with different stages of necrotic pancreatitis. Ukr J Clin Lab Med. 2011, 6 (1): 67-73. [Article in Ukrainian]
5. Kebkalo A.B., Lobintseva G.S., Shabliy V.A. Cord blood and umbilicum in the complex treatment of patients with pancreatic necrosis. Ukr J Emergency Med named after G.O. Mozhaev, 2011, 12 (1):54-61. [Article in Ukrainian]
6. Kebkalo A.B. Evaluation of clinical efficcacy of complex treatment for necrotic pancreatitis using cord blood stem cell transplantation and cryopreserved cord tissue. Ukr J Surg. 2013, 21 (2): 47-53. [Article in Ukrainian]
7. Kebkalo A.B., Salyutin R.V., Lobintseva G.S. Biochemical changes in the blood plasma of patients with pancreatitis necrotizing transplantation of stem cells cord blood. Med Today and Tomorrow. 2011, 1–2: 50–51. [Article in Ukrainian]

Administrative Information

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