Hasanova S.Y.k.**To the question of the treatment of pancreatic necrosis***Azerbaijan State Institute of Advanced Medical Training named after A. Aliyev
(Azerbaijan, Baku)*

doi 10.18411/gq-31-07-2021-06

Abstract

The results of surgical treatment of pancreatic necrosis using stem cells, the structure of mortality and complications for the period 2013-2019 were analyzed. It has been shown that the use of cordon blood stem cells after laparotomy in the treatment of pancreatic necrosis can reduce the mortality rate associated with complications of infected pancreatic necrosis and improve the overall results of treatment of acute pancreatitis.

Keywords: Acute pancreatitis, pancreatic necrosis, stem cells, laparotomy.

Аннотация

Проанализированы результаты хирургического лечения панкреонекроза, с использованием стволовых клеток, структура летальности и осложнений за период 2013-2019 годов. Показано, что применение после лапаротомии стволовых клеток кордоновой крови в лечении панкреонекроза может снизить уровень летальности, связанный с осложнениями инфицированного панкреонекроза и улучшить общие результаты лечения острого панкреатита.

Ключевые слова: Острый панкреатит, панкреонекроз, стволовые клетки, лапаротомия.

In 40-70% of cases of severe pancreatitis, infected pancreatic necrosis occurs. The development of infected necrosis in patients with ongoing organ failure is associated with an extremely high mortality rate (36-50%) [1]. To date, it has not been possible to reduce the mortality rate from purulent-septic complications, to reduce the duration of inpatient treatment, which is directly related to the peculiarities of the course of the disease [2]. Early recognition of severe acute pancreatitis and the choice of an adequate treatment method are the main tasks of successful treatment [3].

Currently, stem cell transplantation is widely used in the treatment of some surgical diseases. [4].

Objective: To study the effectiveness of treatment of patients with acute pancreatitis with stem cell transplantation after laparotomy.

Materials and methods. 82 patients with pancreatic necrosis were monitored from 2013 to 2019. Of these, 59 are women and 23 are men. Mostly patients are 20-65 years old. The treatment of patients was carried out in the surgical clinic of the Institute of Advanced Training of Doctors of the A. Aliyev Estate and in the 3rd city hospital. Cord blood stem cells were obtained by agreement from the International Center for Stem Cell Cultivation "Biostem" - Donetsk, Ukraine. The patients were treated in intensive care. The following groups of patients were identified who were diagnosed with pancreatic lesion. The main group, which included patients with pancreatic necrosis who received cell therapy after laparotomy. The number of patients in the group was 39 (47.6%). The control group consisted of patients with pancreatic necrosis who underwent only a laparotomy. The number of patients is 43 (52.7%).

After laparotomy, cord blood stem cells were injected intravenously slowly one time a day for 3-5 days in the patients of the main group starting from the second day. The total amount of injected cord blood was 50 ± 5 ml. Cord blood stem cells isolated from cord blood samples were selected in accordance with the blood group and Rh factor.

Patients of both groups were under control for about a year. For each treatment of patients, laboratory (general and biochemical blood analysis, determination of the level of

phosphatase and sugar in the blood) and instrumental (ultrasound, CT, MRI) research methods were used.

The results of the study and their discussion. The effectiveness of treatment of patients with necrotic pancreatitis using cellular technologies is on average twice as high as standard treatment. In the analysis of 82 patients, it was revealed that the frequency of complications of necrotic pancreatitis at admission in the control and main groups does not differ and is 94.3 and 95.9%, respectively. Frequent complications of necrotic pancreatitis in the control and main groups were: exudative pleurisy-66.9% and 64.4%, respectively, enzymatic peritonitis-46.2% and 79.4%, respectively, purulent omentobursitis-33% and 54.8%, respectively. The frequency of concomitant diseases in patients with necrotic pancreatitis in the control and in the main groups was the same and amounted to 48.7% and 49.5%, respectively. Surgical interventions for necrotic pancreatitis in the control and main groups of patients did not differ and were performed according to generally accepted methods. Frequent surgical interventions were: necrosectomy of the pancreas with omentobursostomy, lumbotomy, cholecystectomy with external drainage of the choledochus and drainage of the omentum sac, opening, drainage of the omentum sac abscess and retroperitoneal abscess. Upon admission to the hospital, all patients were prescribed intensive conservative therapy in the amount that depended on the severity of the disease. When using intravenous administration of cord blood stem cells, no allergic reactions were detected in patients. Of the 39 patients, 11 (69.8%) had an increase in body temperature to 39 ° C within 3-5 days. After the end of cell therapy, the temperature returned to normal. A serious complication of destructive forms of pancreatitis is the formation of acute fluid accumulations. Acute pancreatitis is complicated by the formation of a cyst in 1.18-19.4%. More often, pseudocysts occur in necrotic pancreatitis - from 30 to 50% of cases. According to a retrospective analysis, in 46.6% of cases, necrotic pancreatitis was complicated by the formation of a pancreatic cyst. 23 patients were under observation for one year. They were examined every 3, 6, 12 months. After 3 months, the patients were examined as follows: they performed a clinical examination, did a general blood test, determined the level of blood glucose, alkaline phosphatase in the blood, and performed an ultrasound examination. After 6 months of observation, a clinical examination of the patient, a general blood test, blood glucose, the level of alkaline phosphatase in the blood, ultrasound examination, computed tomography of the abdominal organs were performed. After 12 months, patients underwent a clinical examination, a general blood test, the level of alkaline phosphatase in the blood was determined, and an ultrasound examination was performed. Such indicators as the levels of red blood cells, hemoglobin, leukocytes, glucose and blood amylase did not change significantly and corresponded to the control values. The activity of alkaline phosphatase increased in the first 3 and 6 months by 1.43 and 2.06 times, respectively, and after 1 year it gradually decreased, but remained increased by 25.6%. This fact indicates some activity of cord blood stem cells. In 2 out of 39 patients, a pancreatic cyst was detected during the year, which is 6.1%. According to ultrasound and computed tomography, 21 (53.8%) patients had signs of chronic pancreatitis without signs of calcification. Thus, it can be argued that stem cell transplantation in patients with necrotic pancreatitis leads to inhibition of cystic genesis in the pancreas compared to the data of a retrospective analysis (46.6%) and literature data, where the percentage of cysts formation is from 30 to 50%.

A comparative analysis revealed that the frequency of postoperative complications in the main group was 1.95 times less than in the control group. Pancreatic fistula in patients of the main group was 3.12 times less common than in patients of the control group. Gastrointestinal bleeding in patients of the main group was 2.77 times less than in patients of the control group. Such severe complications as erosive bleeding from the omentum were observed 4.71 times less in patients of the main group than in the control group. The development of DIC syndrome in patients of the main group was detected 3.48 times less than in patients of the control group.

In the main group of 39 patients, 6 died, the mortality rate was 15.7%. The mortality rate among 43 patients of the control group was 25.4% (11 died). The use of stem cells allowed to reduce the mortality rate by 2 times. The average bed-day stay of patients of the control group was 30.2 ± 2.9 days, and patients of the main group 24.5 ± 3.5 days.

Thus, the results obtained indicate a high efficiency of the introduction of stem cells to stimulate the connective tissue processes of proliferative repair in necrotic pancreatitis. Taking into account the above, the indication for the transplantation of cord blood stem cells in patients with severe pancreatitis is the suppression of the processes of proliferative repair in areas of the pancreas and a decrease in immunity in necrotic pancreatitis. The frequency of transplantation was determined individually by the nature of the disease, its stage, the presence of concomitant diseases, as well as the degree of compensation of laboratory and clinical indicators characterizing the level of the pathological process. Contraindications to cell transplantation are the presence of concomitant decompensated diseases, diagnosed acquired human immunodeficiency syndrome, detection of concomitant cancer pathology in the patient according to clinical and / or laboratory indicators, pregnancy and lactation. The mechanism of action of cord blood stem cells should be considered the result of humoral stimulation of reparative processes, which is caused by the unique property of neonatal cells, cytokines and growth factors that are in the drug. However, the most important thing in the problem of acute necrotic pancreatitis is that stem cells, adapting to the microenvironment conditions and responding to local organ and tissue-specific regulatory signals, can act as a producer of autocrine stem regulatory mediators. At the same time, stem precursors can realize the potential of a "plastic building" material capable of restoring the structures of damaged areas of organs and tissues. The high probability that stem cells stimulate the obliteration of the pancreatic ducts prevents the formation of post-necrotic pancreatic fistulas and cysts.

Conclusions:

1. With laparotomy performed only, the mortality rate of patients with necrotic pancreatitis is on average 19.8%, and with complex treatment using stem cells 9.6%. That is, the mortality rate has decreased by 2 times.
2. When comparing the postoperative periods of both groups, it was determined that the frequency of complications in the main group was 2 times less than in patients in the control group.
3. Observations have shown that the transplantation of cord blood stem cells in patients with necrotic pancreatitis leads to the suppression of cystogenesis in the pancreas. The occurrence of pancreatic cysts in patients of the main group occurs in 6.1%, and in patients of the control group in 46.6%.
4. The activity of cord blood stem cells persists for a year after transplantation. This is evidenced by the increased level of alkaline phosphatase in patients who were treated with stem cells.

1. Biology of stem cells and cell technologies / ed. by M. A. Paltsev. M.: Medicine, Chicot, 2009. Vol. 2. pp. 75-96.
2. Egorov V. V., Ivanov A. A., Fingers M. A. Human stem cells. // Molecular Medicine. 2003. No. 2. pp. 3-14.
3. Revision of the Atlanta classification of acute pancreatitis. Acute Pancreatitis Classification Working Group, April 9, 2008 [Электрон. ресурс]. Режим доступа: <http://pancreasclub.com/resources/AtlantaClassification.pdf>.
4. Bakker O.J., van Santvoort H.C., Besselink M.G. [et al.] Prevention detection and management of infected necrosis in severe acute pancreatitis // Curr. Gastroenterol. Rep. - 2009. - Vol. 11, № 2. - P. 104-110.