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Research Article

Stem Cell Therapies on Acute Pancreatitis

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Abstract

Acute pancreatitis (AP) is one of the most common gastrointestinal causes for hospitalization. In 2015, AP accounted for 390940 hospitalizations making it one of the most frequent causes of gastrointestinal hospitalizations in the nation with the annual incidence only expected to increase over time [1-3]. Despite recent advances in gastroenterology, AP continues to be associated with substantial mortality, morbidity and healthcare resource utilization [7,14,20].

Keywords: Acute Pancreatitis (AP); Stem Cell; American Gastroenterological Association (AGA)

The last two decades have seen the emergence of significant evidence that has altered certain aspects of the management of acute pancreatitis. While most cases of acute pancreatitis are mild, the challenge remains in managing the severe cases and the complications associated with acute pancreatitis. Gallstones are still the most common cause with epidemiological trends indicating a rising incidence. The surgical management of acute gallstone pancreatitis has evolved. In 40-70% of cases of severe pancreatitis, infected pancreatic necrosis occurs [5,17,20]. The development of infected necrosis in patients with ongoing organ failure is associated with an extremely high mortality rate (36-50%).

The type of disease severity has had a major influence on mortality. Patients with severe acute pancreatitis had a more increased mortality rate than patients with mild acute pancreatitis (45.63% vs. 2.22%). Moreover, the recent Japanese study showed similar values in terms of increased mortality in patients with severe acute pancreatitis.

To date, It has not been possible to reduce the mortality rate from purulent-septic complications, to reduce the duration of in-patient treatment, peculiarities which is directly related to the peculiarities of the course of the disease.

AP is the inflammation of the pancreas that is often associated with systemic inflammatory response syndrome (SIRS) that may impair the function of other organs. The etiology of AP can be readily identified in 75% to 85% of cases [8]. The American Gastroenterological Association (AGA) provides a comprehensive guide to determine the etiology of pancreatitis [4,16].

Mastery of the management of acute pancreatitis is an art that can challenge experienced clinicians at the best of times. One facet to the art of managing acute pancreatitis is classification of the disease severity so that one can recognize, anticipate, and treat accordingly complications of the disease. The revised 2012 Atlanta criteria for classification of the severity of acute pancreatitis are widely accepted [13]. This revised classification defines transient organ failure as organ failure which resolves completely within 48 hours, whereas failure of resolution of organ failure is defined as persistent. The presence of persistent organ failure, usually with one or more local complications, indicates severe acute pancre-

atitis. On the other hand, the absence of organ failure without any local or systemic complications indicates mild acute pancreatitis. "Moderately severe acute pancreatitis", indicated by transient organ failure and/or local or systemic complications in the absence of persistent organ failure, is the new grade of severity between mild and severe that was introduced in the revised classification [13]. Multiple scoring systems for the prediction of the disease severity and prognostic implications exist [12,14]. The prognostic features aid the clinician in predicting complications of acute pancreatitis [8].

The evaluation should begin with a detailed history focusing on symptoms and presentation. The investigation should focus on evaluation of any previous documented gallstones, alcohol use, history of hypertriglyceridemia or hypercalcemia, family history of pancreatic diseases, prescription/non-prescription drug history, history of trauma, and presence of autoimmune disease [7,14,18]. On presentation to the hospital, patients should have a serum amylase or lipase level checked along with liver chemistries (bilirubin, aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase), and abdominal ultrasound assessing for cholelithiasis or choledocholithiasis. Early recognition of severe acute pancreatitis and the choice of an adequate treatment method are the main tasks of successful treatment [17,22,29].

The Acute Physiology and Chronic Health Evaluation (APACHE) II scoring system has demonstrated the highest accuracy for predicting severe acute pancreatitis when compared with other scoring systems [15]. Other markers of severe acute pancreatitis based on evidence from the literature have been outlined in. The APACHE II score can be repeated daily and its trends correlate well with clinical progress or deterioration. However, there is no significant difference in the prognostic accuracy between the APACHE II and multiple factor scoring systems such as Ranson, computed tomography severity index (CTSI) [15,16], and the bedside index for severity in acute pancreatitis [17].

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

Objective

To study the effectiveness of treatment of patients with acute pancreatitis with stem cell transplantation after laporotomy.

Materials and Methods

82patients with pancretic necrosis were monitored from 2013 to 2019.Of these,59 are women and 23 are men. Mostly patients are20-65 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". The patients were treated in intensive care. The following groups of 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 50ml. 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 phospotase 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 group 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% respectively, enzymatic peritonitis-46,2% and 79% respectively, purulent omentobursitis-33% and 54% respectively. The frequency of concomitant diseases in patients with necrotic pancreatitis in the control and int the main groups was the same and amounted to 48% and 49% 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: necrosequestrectomy of the pancreas with pmentobursostomy, 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 cells, no allergic reactions were detected in patients. Of the 39, 11 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 1-19%. More often, pseudocysts occur in necrotic pancreatitis - from 30 to 50% of cases. According to a retrospective analysis in 46% 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 month. 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. Such indicators as the levels of red blood cells, hemoglobin, leukocytes, glucose and blood amylase did not change significantly and corresponds to the control values. 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 indicators, pregnancy and lactation. The mechanism of action of cord blood stem cells should be considerer the result of humoral stimulation of reparative processes which is caused by the unique property on 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

- With laparotomy performed only, the mortality rate of patients with necrotic pancreatitis is on average 19% and with complex treatment using stem cells 9%. That’s the mortality rate has decreased by 2 times.
- 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
- Observations have shown that the transplantation of cord blood cells in patients with necrotic pancreatitis leads to the suppression of cystogenesis in occurs in 6% and in patients of the control group in 46%
- 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.
- Results showed that serum amylase activity was decreased and pulmonary edema and the expression of TNF-α was significantly diminished in SC transplanted group. It has been suggested that steam cell has a role in pancreatic tissue repair by contribute to the pancreatic stellate cell population. In the absence of preneoplastic lesions, these cells contribute at a very low level to the ductal epithelium of the chronically inflamed pancreas. Steam cells alleviate pancreatic edema and inflammatory infiltration by regenerating pancreatic cells. Steam cells alleviate AP through specific accumulation in injured pancreatic tissue rather than through cell regeneration. In this study, inflammation was inhibited by promoting apoptosis of CD4+ T cells. Steam cells reduced expression of inflammation mediators and cytokines with mild and severe AP. Steam cells suppressed the mixed lymphocyte reaction and increased expression of Foxp3(+) (a marker of regulatory T cells) in lymph node cells. Steam cells might alleviate pancreatitis by regulating immune function rather than by regeneration of pancreatic tissue.

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