THE USE OF CELLULAR TECHNOLOGIES IN THE COMPLEX TREATMENT OF PURULENT-SEPTIC WOUNDS

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Abstract

Treatment of complicated forms of purulent wounds is an actual problem of modern medicine. A serious problem of the preoperative period is purulent complications that develop in 15-35% of cases, mortality reaches 25-60%. It is known that the predominant pathological syndrome in complicated forms of purulent sepsis is the syndrome of endogenous intoxication (SEI).

Objective. *In this regard, the desire of many researchers to study new methods of intensive care for the syndrome of endogenous intoxication is understandable [1,2,3,4,5,5,6,7,8]. The authors analyzed the effectiveness of the use of mediators (surfactant) of fetal hepatocytes in the complex treatment of purulent-septic wounds.*

Material and methods. *A prospective study method was carried out for the main group, which consisted of patients with purulent-septic wounds (PSW) - 50 people, in the complex treatment of which cellular mediators (CM) were used; control group - 50 patients with PSW treated according to the traditional scheme.*

Results. *The results of treatment with cellular mediators were evaluated in 50 patients who received this drug at a dose of 0.15 ml/kg. The control group consisted of 50 patients who received saline at a dose of 0.15 ml/kg as a placebo. Men 27, women 23. The study was conducted in accordance with the Clinical Protocol for Surgical and Diagnostic Intervention of Transplantation of Fetal Cell Mediators Recommended by the Expert Council of the RSE on REM «Republican Center for Health Development» of the Ministry of Health and Social Development of the Republic of Kazakhstan dated September 30, 2015 (Protocol №. 10).*

Conclusion. *The results of the study have been implemented in the practice of the PKP on the REM of the Nur-Sultan MCH №2 and the Nur-Sultan MCH №1 ; highlighted in the work of the poster session of the VII Congress of Surgeons of Kazakhstan with international participation in Almaty from 30.09.-01.10.2021. Received AC No. 18079 of the Republic of Kazakhstan dated May 27, 2021 (www. kazpatent.kz)*

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Conflict of interest
The authors declare that they have no conflicts of interest

Keywords
cellular mediators, fetal hepatocytes, purulent-septic wounds

Применение клеточных технологий в комплексном лечении гнойно-септических ран

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Аннотация

Лечение осложненных форм гнойных ран - актуальная проблема современной медицины. Серьезной проблемой предоперационного периода являются гнойные осложнения, которые развиваются в 15-35% случаев. У таких пациентов летальность достигает 25-60%. Известно, что преобладающим патологическим синдромом при осложненных формах гнойного сепсиса является синдром эндогенной интоксикации (СЭИ).

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Конфликт интересов
Авторы заявляют об отсутствии конфликта интересов

Цель. *В связи с этим понятно стремление многих исследователей к изучению новых методов интенсивной терапии синдрома эндогенной интоксикации [1,2,3,4,5,6,7,8]. Авторами проведен анализ эффективности применения медиаторов (сурфактанта) фетальных гепатоцитов в комплексном лечении гнойно-септических ран. Представлены результаты применения клеточных медиаторов фетальных гепатоцитов у данной категории больных.*

Материал и методы. *Проведен проспективный метод исследования основной группы, которую составили больные с гнойно-септическими ранами (далее ГСР) – 50человек, в комплексном лечении которых применяли клеточные медиаторы (далее КМ); контрольной группы – 50 больных ГСР, пролеченных по традиционной схеме.*

Результаты. *Результаты лечения клеточными медиаторами оценены у 50 пациентов, получавших этот препарат в дозе 0,15 мл/кг. Контрольную группу составили 50 пациентов, получавших физиологический раствор в дозе 0,15 мл/кг в качестве плацебо. Мужчин 27, женщин 23. Исследование проводилось в соответствии Клиническим Протоколом оперативного и диагностического вмешательства трансплантации медиаторов фетальных клеток Рекомендованным Экспертным советом РГП на ПХВ «Республиканский центр развития здравоохранения» Министерства Здравоохранения и социального развития РК от 30.09.2015 г. (Протокол № 10).*

Заключение. *Результаты исследования внедрены в практическую деятельность ГКП на ПХВ МГБ №2, ГКП на ПХВ ГБ №1 г. Нур-Султан; освещены в работе постерной сессии YII Конгресса Хирургов Казахстана с международным участием г. Алматы от 30.09.- 01.10.2021г. Получено АС № 18079 РК от 27. 05.2021г. (www. kazpatent.kz)*

Ключевые слова
клеточные медиаторы, фетальные гепатоциты, гнойно-септические раны.

Іріңді-септикалық жараларды кешенді емдеуде жасушалық технологияларды қолдану

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Аңдатпа

Мүдделер қақтығысы
Авторлар мүдделер қақтығысының жоқтығын мәлімдейді

Іріңді жаралардың асқынған түрлерін емдеу қазіргі заманғы медицинаның өзекті мәселесі болып табылады. Операция алдындағы кезеңнің маңызды мәселесі 15-35% жағдайда дамитын іріңді асқынулар болып табылады. Мұндай науқастарда өлім 25-60% жетеді. Іріңді сепсистің асқынған түрлерінде басым болатын патологиялық синдром эндогендік интоксикация синдромы (ЭИС) екені белгілі.

Мақсаты. *Осыған байланысты көптеген зерттеушілердің эндогендік интоксикация синдромын интенсивті терапияның жаңа әдістерін зерттеуге деген ұмтылысы түсінікті. Авторлар іріңді-септикалық жараларды кешенді емдеуде ұрық гепатоциттерінің медиаторларын (беттік белсенді зат) қолданудың тиімділігін талдады,. Науқастардың осы санатындағы ұрық гепатоциттерінің жасушалық медиаторларын қолдану нәтижелері берілген.*

Материал және әдістер. *Негізгі топты зерттеудің перспективалық әдісі жүргізілді, ол іріңді-септикалық жаралары бар науқастардан (бұдан әрі – ІСЖ) – 50 адам, кешенді емдеуде жасушалық медиаторлар (бұдан әрі – ЖМ) қолданылды; бақылау тобы – дәстүрлі схема бойынша емделген ІСЖ бар 50 науқас.*

Нәтижелер. *Жасушалық медиаторлармен емдеу нәтижелері осы препаратты 0,15 мл/кг дозада қабылдаған 50 пациентте бағаланды. Бақылау тобына физиологиялық еріткішті плацебо ретінде 0,15 мл/кг дозада қабылдаған 50 пациент кірді. Ерлер 27, әйелдер 23. Зерттеу Қазақстан Республикасы Денсаулық сақтау және әлеуметтік даму министрлігінің «Республикалық денсаулық сақтауды дамыту орталығы» ШЖҚ РМК Сараптамалық кеңесі ұсынған ұрық жасушасының медиаторларын трансплантациялаудың хирургиялық және диагностикалық араласуының клиникалық хаттамасына сәйкес жүргізілді. Қазақстан 2015 жылғы 30 қыркүйектегі (No10 хаттама).*

Қорытынды. *Зерттеу нәтижелері №2 қалалық ауруханасы ШЖҚ МКК, Нұр-Сұлтан қаласының № 1 қалалық ауруханасы ШЖҚ МКК тәжірибесіне енгізілді; 30.09.-01.10.2021 ж. аралығында Алматыда халықаралық қатысумен Қазақстан хирургтарының VII Конгресінің постер сессиясының жұмысында атап өтілді. Қазақстан Республикасының 2021 жылғы 27 мамырдағы № 18079 АК (www.kazpatent.kz) алынды.*

Түйін сөздер
жасушалық медиаторлар, ұрықтың гепатоциттері, іріңді-септикалық жаралар.

Relevance:

Despite the results achieved in the complex treatment of purulent wounds, this problem continues to be relevant and needs to be further developed. The clinical diversity of manifestations of purulent infection of soft tissues determines the need to search for an algorithm for diagnosing the severity of the course of a purulent wound process, clarifying indications for use and optimizing the components of complex treatment. Treatment of complicated forms of purulent wounds is an urgent problem in practical public health. A serious problem of the preoperative period is purulent complications that develop in 15-35% of cases. In such patients, mortality reaches 25-60%. It is known that the predominant pathological syndrome in complicated forms of purulent sepsis is the syndrome of endogenous intoxication (SEI). At the same time, the traditional intensive therapy of SEI in complicated forms of PSW does not always give an effect. Patients have long-term fever, encephalopathy, and intoxication. Therefore, the desire of many researchers to study new methods of intensive care for the syndrome of endogenous intoxication is understandable. [1,2,3,4,5,6,7,8]. The use of cellular technologies in the treatment of sepsis and HSR is primarily due to: the wide positive properties of fetal stem cells (hereinafter referred to as FH) and cell mediators (hereinafter referred to as CM), as well as their increasing use in transplantation in general. The relevance of this work is substantiated by the need to further improve the biotechnology of preservation and the methods of introducing FH and CM, as well as to increase the effectiveness of the complex treatment of patients with purulent-septic wounds.

Research objective:

To improve the results of treatment of purulent-septic wounds through the use of cellular mediators of fetal hepatocytes. To solve the problem: an algorithm for complex intensive care of patients with PSW, including the use of cellular mediators of fetal hepatocytes, was developed and implemented in practice at the departments of surgical infection of the Nur-Sultan MCH №2 and the Nur-Sultan MCH №1 (Acts of implementation from 2021).

Materials and methods of research:

The results of treated patients with PSW were studied retrospectively and prospectively in the conditions of the departments of surgical infection of the Nur-Sultan MCH №2 and the Nur-Sultan MCH №1. The control group of 50 people - patients treated in the traditional way; the main one - 50 people - complex treatment of HSR included the use of CM according to the developed algorithm.

- Clinical and anamnestic data of patients with purulent-septic wounds;

- Analysis of the results of biochemical and instrumental studies,

- Immunological studies: study of IL, TNFα, MCM, determination of the cytokinin spectrum

- Hematological studies: LII (leukocyte index of intoxication), HII hematological index of intoxication), CBC(detailed complete blood count - 12 indicators); biochemical blood tests.

- Microbiological studies: results of the tank. sowing from wound surfaces (CFU / 1g of tissue) on a dense nutrient medium (agar-agar), with the determination of the sensitivity of microflora to antibiotics.

- Planimetry of a purulent wound: the change in the area of the wound and the rate of healing were assessed at 3s, 5s, 7s, 15 days.

A) The percentage of reduction in the area of wounds (WAP) from the initial size (calculated by the formula: WAP = (So–S) / Sox 100%, where So is the initial average level of the area at the beginning of treatment, mm^2, S is the average wound area at the time of measurement, mm^2.

B) Wound healing rate (WHR), i.e. % decrease in the area of the wound per day was calculated by the formula WHR =(WAP 1– WAP o)/ T, where WAP1 is the percentage of reduction in the area of wounds from the original at the time of measurement; WAP0 - the percentage of reduction in the area of wounds during the previous measurement; T- is the number of days between study measurements.

- Statistical processing of the obtained results (data analysis and processing of the results). Statistical processing of the material was performed using the computer program Statistica 6.0 from StatSoft (USA). Data processing was carried out by the nonparametric Wilcoxon-Mann-Whitney method. The purpose of processing was to identify a statistically significant difference between the indicators at different stages of treatment. The tables reflect the average values, standard deviations, p-criterion for the significance of differences. The results were considered significant at $p<0.05$.

Research results and discussion:

The results of treatment with cellular mediators were evaluated in 50 patients who received this drug at a dose of 0.15 ml/kg. The control group consisted of 50 patients who received saline at a dose of 0.15 ml/kg as a placebo. Age of patients from 17 to 75, 27 men, 23 women. The study was conducted in accordance with the Clinical Protocol for the surgical and diagnostic intervention of transplantation of fetal cell mediators Recommended by the Expert Council of the RSE on REM «Republican Center for Health Development» of the Ministry of Health and Social Development of the Republic of Kazakhstan dated September 30, 2015 (Protocol No. 10). In the course of the work, medical records were examined and detailed information on the results of clinical and laboratory studies of the medical history. Weighted sampling was used in data analysis throughout the study. Prior to enrollment in the study, all patients received a patient information leaflet and signed an informed consent form for participation in the study.

Characteristics of the object of study:

Patients of the main group were injected with cellular mediators. Cellular mediators are an extracellular fraction of cryopreserved fetal tissues of a human fetus at 17-20 weeks of gestation. Fetal material is tested by PCR for the following pathogens: *Chlamydia trachomatis, Chlamydia pnevmonica, Ureaplasma*

surelyticum, Ureaplasma sparvum, Mycoplasma hominis, Mycoplasma genitalium, Neisseria gonorrhoeae v.1, Neisseria gonorrhoeae v.2, Trichomonas vaginalis, Cytomegalovirus, Gardnerella vaginalis, HSV 1, HPV 18 (Human papillomavirus), HSV 6 (Human herpesvirus), Candida albicans, Treponema pallidum, Toxoplasma gondii, Mycobacterium tuberculosis, Hepatitis A virus, Hepatitis B virus, Hepatitis C virus, Hepatitis D virus, Hepatitis G virus, Brucella species, Epshtein-Barr virus, Salmonella. Fetal material was tested for Human immunodeficiency virus (HIV) by enzyme immunoassay (ELISA).

In the main group of patients with PSW treated according to the developed algorithm [9], starting from the 3rd day of the postoperative period, there was a positive trend in the course of the endogenous intoxication syndrome (hereinafter referred to as SEI). This was expressed with the normalization of body temperature, a decrease in tachycardia to 76-64 bpm, improving appetite, reducing the effects of intoxication and encephalopathy. In laboratory parameters, there was a decrease in LII to 0.41 units, HII to 0.7 units, a decrease in plasma osmolarity to 291.03 mosmol/l. The severity of SEI decreased to 1 degree. The number of points on the SAPS scale reached 16, which corresponded to a 2.3% probability of death. For example: Patient K., 42 years old with PSW , operated on September 27, 2004, received CM at a dose of 10.0 ml IM x 1 time per day for 5 days in complex treatment; already on the 4th day after the operation, he was transferred to the specialized surgical department due to the stabilization of his condition. After 7-9 days, patients of the main group were discharged in a satisfactory condition. Total stay in the hospital 10+-0.52 bed-days, including 3-4 bed-days in the intensive care unit (department of anesthesiology and resuscitation).

These results demonstrate the possibility of successful correction of SEI in patients with PSW through the introduction of cellular mediators in complex intensive care. In order to study the effect of therapy with cellular mediators on the dynamics of changes in SEI markers, the leukocyte index of intoxication, the hematological index of intoxication (HII), the level of medium molecules (LMM), plasma osmolarity, urea, creatinine, bilirubin, ALT, AST, interleukin 2 (IL-2), interleukin 6 (IL-6), interleukin - 10 (IL-10), tumor necrosis factor (TNFα) in patients of the main and control groups. The diagrams below clearly reflect the dynamics of the inflammatory process against the background of ongoing therapy in the main and control groups.

Figure 1.
LMM-level of medium molecules

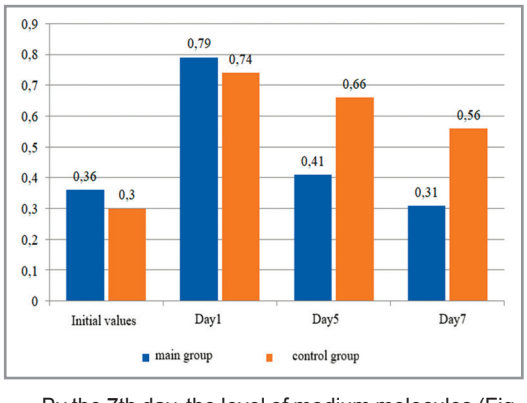
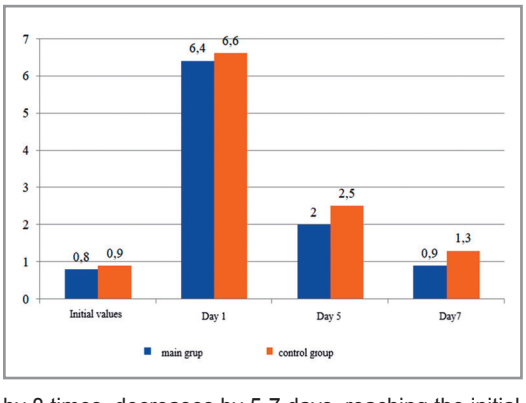


Figure 2.
HII-hematological index of intoxication



By the 7th day, the level of medium molecules (Fig. 1) in the main group was lower by 0.25 c.u. (1.8 times) than in the control group ($p < 0.05$).

The leukocyte intoxication index (LII) increases statistically significantly on the first day after surgery by 8 times, decreases by 5-7 days, reaching the initial level. In the main group, compared with the control group, on the 7th day LII (Fig. 2) was 1.4 times lower ($p < 0.05$).

The level of interleukins in dynamics

Figure 3.
Interleukin 6

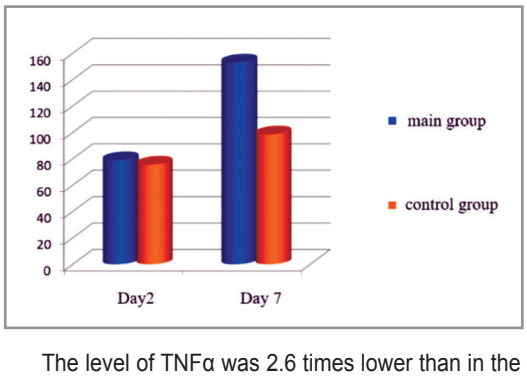
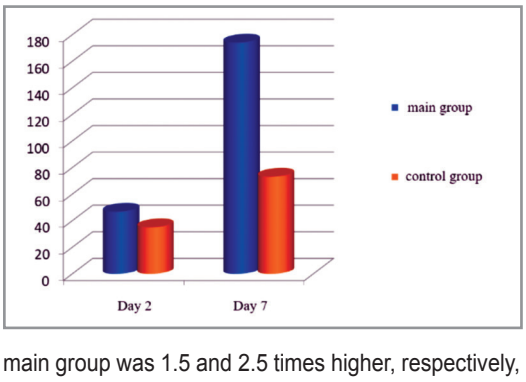


Figure 4.
Interleukin 2



The level of TNFα was 2.6 times lower than in the control group ($p < 0.05$).

The concentration of IL-6 and IL-2 (Fig. 3, 4) in the main group was 1.5 and 2.5 times higher, respectively, than in the control group. The results of planimetric methods for studying the rate of wound healing in the

main (Fig. 6) and control (Fig. 7) groups correlated with the results of the dynamics of changes in SEI markers: leukocyte index of intoxication (LII), hematological index of intoxication (HII), level of medium molecules (LMM), interleukin 2(IL-2), interleukin 6 (IL-6), interleukin - 10 (IL-10), tumor necrosis factor (TNFα) in patients of the main and control groups. In the main group of patients, the healing rate was consistently high throughout the entire observation period, which indicates a pronounced CM activity: the regeneration phases are significantly accelerated ($p < 0.05$).

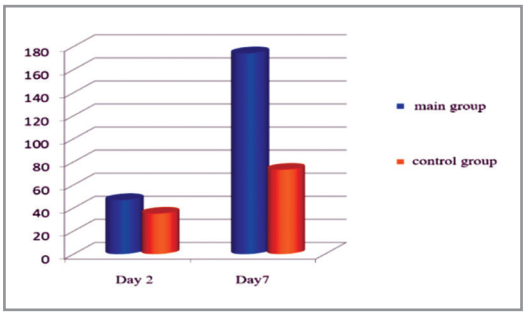
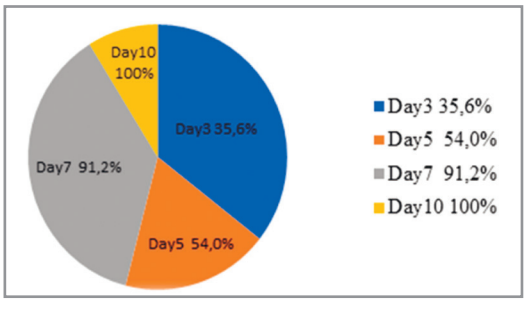


Figure 5.
TNFα in dynamics



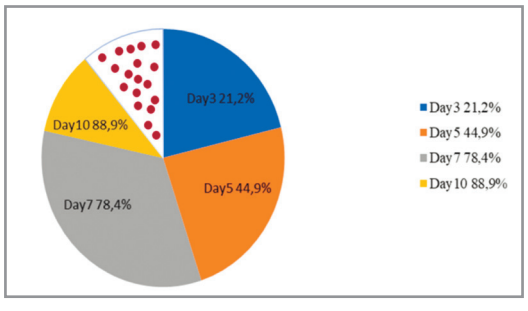


Figure 6.
Wound healing rate of the main group

Figure 7.
Wound healing rate of the control group

Conclusions:

1. For the first time, an optimal algorithm for the complex treatment of patients with purulent-septic wounds using cellular mediators of fetal hepatocytes has been developed and proposed.

2. The clinical efficacy of cellular mediators of fetal hepatocytes in the complex intensive care of patients with purulent-septic wounds is substantiated.

3. Author's certificate № 18079 RK dated 27.05.2021 received.

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