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TREATMENT OF LATE STRICTURE OF HEPATICOJEJUNAL ANASTOMOSIS AFTER POST-CHOLECYSTECTOMY BILE DUCT INJURIES

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

Abstract

Hepaticojejunostomy stricture is the disastrous complication of biliary surgery, if untreated can lead to intrahepatic stones, recurrent cholangitis, biliary cirrhosis and hepatic failure. Here, we report a case with the one-more year history of recurrent cholangitis, caused by late stricture of hepaticojejunal anastomosis after iatrogenic bile duct injury.

Case: *46-year old female patient underwent Roux-en Y hepaticojejunostomy (RYHJ) with transhepatic drain following iatrogenic bile duct injury during open cholecystectomy in rural hospital. After 11 year she represent re-stricture of hepatico-jejunal anastomosis with acute recurrent cholangitis attacks and intrahepatic lithiasis. Before admitting to our center it was tried to cross the stricture radiologically with the percutaneous transhepatic dilatation. As the multiple attempt of interventional radiology failed revision surgery required. Despite technical challenge we successfully managed the patient with the revision surgery by performing hepatic resection and creating double–barrel Roux-en Y hepaticojejunostomy with transhepatic transanastomotic stent placement.*

Conclusion. *Hepatico-jejunal anastomotic stricture is one of the challenging and serious complication of biliary surgery resulting multiple hospital readmissions and procedure. Recently, in many referral centers treatment of the re-strictures of hepatico-jejunal anastomosis can be achieved by nonsurgical methods such as stenting with endoscopic retrograde cholangiopancreatography and percutaneous transhepatic balloon dilatation. In cases of failure these methods, surgical treatment is considered. Nowadays in the surgical management of bilio-enteric anastomotic strictures the trend is not to drain anymore still in a number of situations this procedure cannot be avoided. In our case, double-barell hepaticojejunostomy on a transhepatic transanastomotic drain was the best choice of treatment.*

Keywords:
iatrogenic biliary injuries, anastomotic strictures, recurrent cholangitis, Roux-en Y hepaticojejunostomy, double-barrel hepaticojejunostomy

Лечение поздней стриктуры гепатикоеюнального анастомоза после постхолецистэктомического повреждения желчного протока

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Аннотация

Стриктура гепатикоеюностомии является катастрофическим осложнением гепатобилиарной хирургии и если ее не лечить может привести к внутрипеченочным холангиолитиазу, рецидивирующему холангиту, билиарному циррозу и нарушению функции печени. Мы докладываем о случае с более чем годовой историей рецидивирующего холангита, вызванного поздними стриктурами гепатикоеюнального анастомоза после ятрогенного повреждения желчного протока.

Случай. *Пациентке было выполнена гепатикоеюностомия по Ру с чреспеченочным дренажом после ятрогенного повреждения желчного протока во время открытой холецистоэктомии в сельской больнице. Через 11 лет появилась клиника стриктуры гепатикоеюнаанастомоза с приступами острого рецидивирующего холангита и внутрипеченочным холангиолитиазом. Перед поступлением в наш центр стриктуру попытались пересечь с чрескожной чреспеченочной дилатацией. Поскольку неоднократные попытки интервенционной радиологии оказались безуспешными, потребовалось ревизионная операция. Несмотря на технические трудности, нам удалось успешно справиться с повторной операцией, выполнив резекцию печени и создав двойную гепатикоеюностомию по Ру с установкой чреспеченочного трансанастомотического стента.*

Заключение. *Стриктура гепатико-еюнального анастомоза является один из сложных и серьезных осложнений билиарной хирургии, приводящим к многочисленным повторным госпитализациям и процедурам. Сейчас во многих специализированных центрах лечение сужений гепатико-еюнального анастомоза может быть достигнуто такими нехирургическими методами как стентирование с эндоскопической ретроградной холангиопанкреатографией и с чрескожной чреспеченочной балонной дилатацией. В случаях неэффективности этих методов рассматривается оперативное лечение. Несмотря на то, что в последнее время при лечении стриктур билио-дигестивних анастомозов наблюдается тенденция к прекращению дренирования, в ряде ситуацийй этой процедуры не избежать. В нашем случае лучшим вариантом лечения было бигепатикоеюностомия на чреспеченочночном трансанастомотическом дренаже.*

Ключевые слова:
ятрогенные пороженияжелчевыводящих путей, стриктуры анастомозов, рецидивирующий холангит, гепатикоеюностомия по Ру, бигепатикоеюностомия.

Өт жолдарының холецистэктомиялық жарақатынан кейінгі гепатикоеюнальды анастомоздың алшақ стриктурасын емдеу

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Аңдатпа

Гепатикоеюностомияның стриктурасы гепатобилиарлық хирургияның күрделі асқынуы болып табылады және емдемеген жағдайда бауырішілік холангиолитиазға, қайталама холангитке, билиарлық циррозға және бауыр функциясының бұзылуына әкелуі мүмкін. Біз өт жолдарының ятрогендік зақымдануынан кейін гепатокоенальды анастомоздың кейінгі стриктурасынан туындаған қайталама холангиттің бір жылдан астам тарихы бар жағдай туралы баяндаймыз.

Клиникалық жағдай. *Науқасқа ауылдық ауруханада ашық холецистэктомия кезінде өт жолдарының ятрогендік зақымдануынан кейін бауыр арқылы дренажбен Ру гепатикоеностомиясы жасалды. 11 жылдан кейін жедел рецидивті холангит және бауырішілік холангиолитиаз ұстамаларымен гепатикоеналды анастомоз стриктурасының клиникасы пайда болды. Біздің орталыққа түскенге дейін тері арқылы бауыр арқылы стриктураны көлденеңінен шығару әрекеті жасалды. Интервенциялық радиологияның қайталама әрекеттері сәтсіз болғандықтан, тексеру операциясы қажет болды. Техникалық қиындықтарға қарамастан, біз бауыр резекциясын жасау және бауыр арқылы трансанастомотикалық стент орнату арқылы Ру бойынша қосарлы гепатикоеностомияны жасау арқылы қайталама операцияны сәтті жүргізе алдық.*

Қорытынды. *Бауыр анастомозының стриктурасы билиарлық хирургияның күрделі және ауыр асқынуларының бірі болып табылады, бұл көптеген қайталама госпитализациялар мен процедураларға әкеледі. Қазіргі уақытта көптеген мамандандырылған орталықтарда гепатикоеностомиялық анастомоздың тарылуын емдеуге эндоскопиялық ретроградтық холангиопанкреатография мен стенттеу және тері арқылы трансанастомотикалық балондарын ұзарту сияқты хирургиялық емес әдістер арқылы қол жеткізуге болады. Бұл әдістер тиімсіз болған жағдайда хирургиялық емдеу қарастырылады. Соңғы уақытта билио-дигестивті анастомоздардың стриктурасын емдеуде дренажды тоқтату үрдісі байқалғанына қарамастан, кейбір жағдайларда бұл процедураны қолдануға тура келеді. Біздің жағдайда емдеудің ең жақсы нұсқасы бауыр арқылы трансанастомотикалық дренажда бигепатикоеюностомия болды.*

Түйін сөздер:
өт жолдарының ятрогендік зақымдануы, анастомоздардың стриктуралар, қайталама холангит, Ру гепатикоеюностомиясы, биггепатоэюностомия

Introduction

Most of extrahepatic bile ducts injuries of the are iatrogenic and occur during laparoscopic or open cholecystectomies. Correct management of iatrogenic bile duct injuries is very important because if improperly treated, serious complications like biliary stricture, cholangitis, biliary cirrhosis portal hypertension and even death can occur [1, 2, 3]. Therapeutic options for the iatrogenic bile duct injuries can be divided into two groups: non-surgical (endoscopic approach and radiological interventions) and surgical. In general, minor bile duct injuries can be successfully treated endoscopically, but proximal and complex injuries require surgical treatment [4]. Roux-en Y hepaticojejunostomy (RYHJ) is the most preferred biliary reconstruction method for the management of iatrogenic biliary injuries [3, 5].

Despite RYHJ has excellent long-term outcomes (nearly-90%) it´s also associated with some complications, including anastomotic stricture, which sometimes leads to recurrent cholangitis and intraductal stone formation [6]. In many cases, non-surgical methods (endoscopic sphincterotomy or balloon dilatation, percutaneous interventions) may be useful, but in selected cases surgical revision is still considered as a standard of treatment of anastomotic strictures after iatrogenic bile duct injuries. Here we report a case of late development anastomotic stricture presenting 11 years after hepaticojejunostomy due iatrogenic biliary injury after open cholecystectomy.

Case presentation

A 46 year-old female patient was admitted to our clinic with the jaundice, fever and acute recurrent cholangitis. Eleven years earlier she had undergone RYHJ with transhepatic drain due to high (Strasberg E2) iatrogenic injury of the common hepatic duct (CHD) during open cholecystectomy in rural hospital. Her postoperative course was uneventful. The transhepatic drain was changed several times and removed after 2 years. Eleven years later she presented acute cholangitis with fever, jaundice and vomiting which treated conservatively with antibiotics several times. Before admitting to our center she was referred to another hospital for percutaneous transhepatic ballon dilatation (PTBD). Her cholangiogram showed high grade of RYHJ stricture. But multiple attempts of across the stricture was failed, because of due to the presence of intrahepatic stones stricture was non-crossable with conventional interventional radiology. In the end, it was decided to perform revision surgery in our hospital and renew the cicatrized anastomosis. On examination she was icteric and there was pain and tenderness in

right subcostal region. Laboratory tests showed white blood cell count (WBC)17.94*109/l, C-reactive protein (CRP) 264mg/l, total bilirubin 4,75mg/dl, direct bilirubin 4.55mg/dl, alanine aminotransferase (ALT) 30.6U/l, aspartate transaminase (AST) 27U/l, gamma-glutamyl transferase (GGT) 232U/l, and alkaline phosphatase (ALP)-272U/l.

Magnetic resonance cholangiopancreatography (MRCP) revealed stricture of HYS near the confluence zone and mild dilation of the intrahepatic biliary ducts associated with intrahepatic lithiasis.

During in multidisciplinary meeting including surgeons, radiologists and hepatogastroenterologists revision surgery was indicated as a treatment strategy. Subsequently revision surgery was performed. During surgery to expose the intrahepatic ducts partial liver resection was performed. Then, to correctly assess the anatomy of biliary tract intraoperative cholangioscopy was used which revealed multiple intraductal sludges and stones.

The stones and sludges removed from intrahepatic ducts. In further examination it was noticed that, as the result of recurrent cholangitis a very severe scar and fibrous tissue formed on anastomosis. Therefore it was decided to resect previous anastomosis and create a new, mucosa-mucosa, tension-free, double-barell RYHJ on a transhepatic transanastomotic drain.

In early postoperative period she was complicated with right side pneumonia which is successfully managed conservatively. The patient was discharged from the hospital on the 20 postoperative day in good general condition and satisfactory laboratory results. Six month after surgery transhepatic drains was changed and repeated cholangiogram showed well-functioning RYHJ. The patient was doing good through two-years of follow-up.

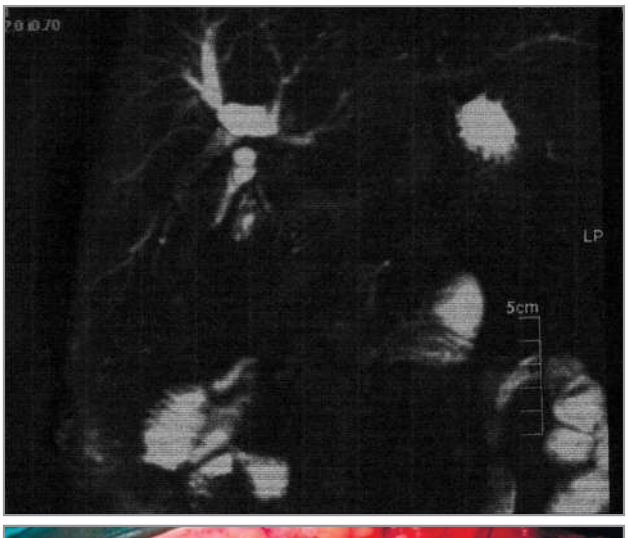

Figure 1.
Preoperative MRCP

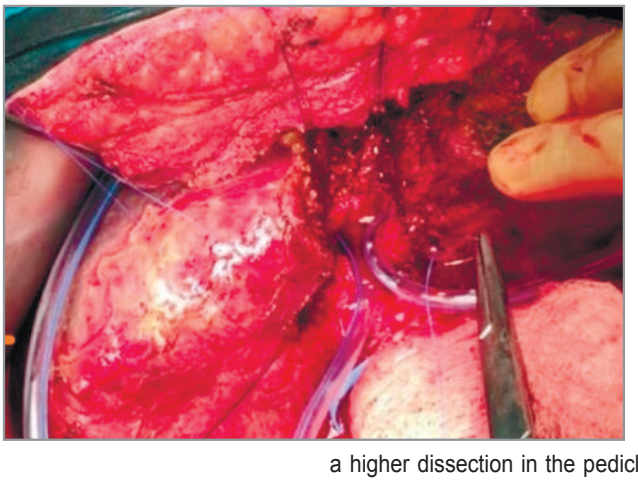

Figure 2.
Intraoperative picture of construction of the double-barrel anastomosis

Discussion

Nowadays in many centers, patients with a bilioenteric anastomotic strictures due iatrogenic biliary injuries are treated by dilatation and /or stent insertion with either an endoscopic or percutaneous approach. Surgical revision may be needed in patients with unsuccessful endoscopic or percutaneous treatment [7, 8]. Redo surgery for the bilio-enteric anastomotic stricture represent high grade of challenge for hepatobiliar surgeon because every new attempt of reconstruction inevitably implies tissue resection and a higher dissection in the pedicle with damage to the vascularization of the biliary tree. These factors affect both the course of surgery and the postoperative success rate so as it has been proposed that the failure rate of redo surgerys for the recurrent strictures ranges between 5-30% compared to nearly 90 % success in primary reconstruction in specialized centers [6, 9]. The traditional surgical approach to bile duct stricture repair involves Roux-en-Y hepaticojejunostomy. RYHJ failure can be associated with several other pathogenic factors including recurrent cholangitis, intrahepatic

calculi, intrahepatic stricture, and improper technical construction of the Roux-en-Y limb [10].

The most common of these late complications are anastomotic stricture and recurrent cholangitis. Recurrent cholangitis almost invariably is attributed to anastomotic stricture, however this assumption has been questioned recently [10, 11].

In the study of Okabayashi et al. postoperative cholangitis rate reported 7.7% (45) in a group of 583 patients who had undergone biliary-enteric anastomoses. Among patients with postoperative cholangitis anastomotic stenosis developed in 57.8% patients, (26/45) [12]. In a study by AbdelRafee et al. on 120 patients undergoing hepaticojejunal anastomosis for treatment of iatrogenic bile duct injuries, anastomotic stenosis occurred in 11.6% of the patients and postoperative cholangitis occurred in 14.2% of the total group and in 53.6% of the patients with anastomotic stenosis [13].

In our case recurrent cholangitis occurred in the absence of normal biliary drainage as a result of anastomotic stricture. Before admitting to our clinic she experienced several cholangitis attacs which is treated with antibiotics. As the last conservative therapy failed due development of antibiotic-resistant bacterial strains and multiple attempts of PTBD also failed, the surgical intervention was required. The main goal of revision surgery was provide adequate biliary excretion by creating wide RYHJ. For achievement of adequate boundary of healthy (non-ischemic, noninflammation and non-scarred) ducts and improvement of the surgical space we performed hepatic resection. This maneuver also helped to remove intrahepatic stones and sludges without difficulties. However, the use of transhepatic stents for supporting bile ducts is controversial we have followed stent use recommendations issued by Mercado et al. and Sampaio et al.in cases with small nondilated ducts to minimize the risk of stricture formation.2,9 We also think that despite poor impact to the patients quality of life in selected cases the transhepatic trananastomotic stents should be necessarily used.

Conclusion

Redo surgery for the late anastomotic stricture following hepaticojejunostomy after iatrogenic bile duct injuries always demonstrate technical difficulties for the hepatobiliary surgeons. It is very important to create wide, mucosa-to-mucosa, tension free bilioenteric-anastomosis with optimal length of Roux limb. Despite recently in the management of re-strictures of HYS the trend is not to drain anymore still in a number of situations this procedure cannot be avoided. In our case, double-barell HYS with placement transhepatic transanastomotic stent was the best choice of treatment.

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MODERN PRINCIPLES OF TREATMENT OF ACUTE DESTRUCTIVE PANCREATITIS

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

Abstract

Objective. *To improve the results of endovideosurgical treatment of patients with acute destructive pancreatitis.*

Material and methods. *The research was carried out at the bases of the Nur-Sultan Multifunctional City Hospital №2 and the Nur-Sultan Multifunctional City Hospital №1. Statistical analysis of the results was carried out using the methods of variation statistics with the calculation of M ± SD. Differences between comparison groups were analyzed using the Wilcoxon-Man-Whitney test and were considered statistically significant at p≤ 0.05.*

From 2017-2021, 64 patients with acute destructive pancreatitis were treated according to the developed and implemented treatment algorithm:

Of these: AP without organ failure and local or systemic complications -10 people. AP of moderate and severe form -54 people. Lethal outcomes-1; The average length of stay in the hospital is 20.8±1.2 days; The mean age was 43 ± 1.3 years.

The control group - treatment of patients with moderate and severe acute biliary pancreatitis without the use of ulinostatin (hereinafter US) was n = 122;

Lethal outcomes-8.

An algorithm for the use of US was developed and implemented depending on the severity of the course of destructive pancreatitis in the complex treatment of patients with AP.

Results. *10 patients were treated conservatively. 54 - surgical treatment was combined with the appointment of US according to the developed scheme. Endoscopic surgery was performed in 51 patients; 3 patients were operated on by laparotomy. The average duration of hospital stay in the main group was 3.5±0.34 days less than in the control group.*

Conclusion. *The research results showed the high efficiency of the developed algorithm for endovideosurgical treatment of AP in combination with the use of the US. Received AC №14704 dated January 27, 2021 (www.kazpatent.kz).*

Keywords
acute destructive pancreatitis, ulinostatin, endovideosurgical methods of treatment

Жедел деструктивті панкреатитті хирургиялық емдеуді оңтайландыру

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Аңдатпа

Мақсаты. *Жедел деструктивті панкреатитпен ауыратын науқастарды емдеудің эндовидеохирургиялық әдісінің нәтижелерін жақсарту.*

Материал және әдістер. *Зерттеулер ҚР «№1 қалалық ауруханасы» ШЖҚ ММК базасында және ҚР «Нұр-Сұлтан қаласының №2 қалалық ауруханасы» ШЖҚ ММК базасында жүргізілді.*

Нәтижелерді статистикалық талдау вариациялық статистика әдістерін қолдану арқылы M±SD есептей отырып жүргізілді. Салыстыру топтарының арасындағы айырмашылықтар Уилкоксон-Ман-Уитни тестінің көмегімен талданды және p≤ 0.05 кезінде статистикалық маңызды деп саналды.

2017-2021 жылдар аралығында әзірленген және енгізілген емдеу алгоритмі бойынша жедел деструктивті панкреатиті бар 64 науқас емделді.

Олардың ішінде: орган жеткіліксіздігі және жергілікті және/немесе жүйелік асқынусыз ОП -10 адам

ЖП орташа және ауыр түрі – 54 адам. Өлімге әкелген жағдайлар-1. Ауруханада болған орташа ұзақтығы- 20,8±1,2 тәулік. Ерлер – 35 адам. (54,7%). әйелдер – 29 адам. (45,3%) . Орташа жасы 43±1,3 жасты құрады.

Бақылау тобы- жедел деструктивті панкреатиті бар науқастарды улиностатинсіз емдеу – 122 науқас. Өлімге әкелген жағдайлар-8.

Жедел деструктивті панкреатиті бар науқастарды кешенді емдеуде деструктивті панкреатит ағымының ауырлығына байланысты улиностатинді қолдану алгоритмі әзірленді және енгізілді. Әзірленген схемаға сәйкес улиностатинді тағайындаумен біріктірілген.

***Нәтижелер.** 10 науқасқа консервативті ем жүргізілді. 54 - хирургиялық емдеу әзірленген схема бойынша улиностатин тағайындаумен біріктірілді. 54 науқастың 51-іне эндоскопиялық операция жасалды; 3 науқасқа лапаротомия әдісімен операция жасалды. Басты топ бақылау топқа қарағанда ауруханадан 3,5±0,34 тәулікке ертерек жазылып шыққан*

***Қорытынды.** Зерттеу нәтижелері протеаза тежегіші улиностатинді қолданумен бірге жедел панкреатитті эндовидеохирургиялық емдеу алгоритмінің жоғары тиімділігін көрсетті. 2021 жылғы 27 қаңтардағы АС № 14704 (www.kazpatent.kz) алынды.*

Түйін сөздер
жедел деструктивті панкреатит, улиностатин, емдеудің эндовидеохирургиялық әдістері

Оптимизация хирургического лечения острого деструктивного панкреатита

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Аннотация

***Цель.** Улучшить результаты эндовидеохирургического метода лечения пациентов с острым деструктивным панкреатитом.*

***Материал и методы.** Исследование проводилось на базах РГК на ПХВ «Городская больница №1» и РГП на ПХВ «Городская больница №2» города Нур-Султан РК.*

Статистический анализ результатов проводили с использованием методов вариационной статистики с расчетом M±SD. Различия между группами сравнения анализировали с использованием критерия Вилкоксона-Мана-Уитни и считали статистически значимыми за p≤ 0,05.

С 2017-2021гг. пролечено по разработанному и внедренному алгоритму лечения 64 пациентов с острым деструктивным панкреатитом:

Из них: ОП без органной недостаточности и местных и/или системных осложнений -10 чел. ОП средней и тяжелой формы -54.чел.

Летальные исходы-1; Средняя продолжительность нахождения в стационаре-20,8±1,2 суток; Средний возраст составил - 43 ± 1,3 лет.

Контрольная группа - лечение больных с средним и тяжелым острым билиарным панкреатитом без использования улиностатина (далее УС) составила n = 122; Летальные исходы-8.

Разработан и внедрен алгоритм применения улиностатина в зависимости от степени тяжести течения деструктивного панкреатита в комплексном лечении больных с острым деструктивным панкреатитом.

***Результаты.** 10 больных пролечено консервативно. 54 – хирургическое лечение сочеталось с назначением улиностатина по разработанной схеме. Из 54 пациентов, эндоскопические операции были произведены 51 пациентам; 3 пациента были прооперированы с помощью лапаротомии. Средняя продолжительность нахождения в стационаре у основной группы была на 3,5±0,34 суток меньше, чем контрольной.*

***Заключение.** Результаты исследований показали высокую эффективность разработанного алгоритма эндовидеохирургического метода лечения острого панкреатита в сочетании с применением ингибитора протеаз улиностатина.*

Получено АС №14704 от 27.01.2021г.(www.kazpatent.kz)

Ключевые слова
острый деструктивный панкреатит, улиностатин, эндовидеохирургические методы лечения

Relevance:

Despite the progressive development of modern medicine, the relevance of the treatment of patients with acute pancreatitis remains, as the mortality rate with this pathology is growing steadily. Today, this is a rather serious problem and requires considerable attention.

Numerous publications of endovideosurgical methods for the treatment of acute pancreatitis in combination with drug treatment indicate that surgeons are constantly searching for the optimal integrated approach to the treatment of this severe surgical disease.

The introduction of new drugs and technologies is necessary to improve treatment. The incidence of acute pancreatitis both abroad and in Kazakhstan tends to increase. The proportion of patients with destructive pancreatitis is 15-20%. At the same time, mortality, depending on the volume and severity of the pathology, remains at the level of 20% and above. The incidence of acute pancreatitis since 2000 in the Russian Federation has come out on top, accounting for 35-45% in the structure of acute surgical diseases of the abdominal organs (Kovalenko A.A., 2007; Vashetko R.V., 2012; Gostishchev V.K., 2012; Ostrovsky A.G., 2012; Bagnenko S.F., 2013), and the upward trend in the number of patients continues. In 15 - 20% of cases, the development of acute pancreatitis is destructive (Saveliev V.S., 2008). Among patients with acute pancreatitis, men average 55 - 75%, and women - 25 - 45% (Kuznetsov N.A., 2004). Most cases occur in people of working age from 21 to 60 years (65%). Among patients under 45 years old (76%) are men, which is mainly associated with alcohol abuse. A high incidence rate (up to 80%) among women over 60 years of age is associated, first of all, with a history of often exacerbating cholecystitis, as a manifestation of cholelithiasis (Shapovalyants S.G., Mikhailusov S.V., 2000). An increase in the number of patients with acute pancreatitis has led to an increase in the frequency of its destructive forms and their complications. So the formation of infected pancreatic necrosis is almost 60% of cases, parapancreatitis - more than 45%, omentobursitis - almost 30% (Tolstoy A.D., 2003).

The search and introduction of new drugs in combination with endovideosurgical technologies are necessary to improve the treatment and increase the effectiveness of the treatment of severe complications of acute pancreatitis.

Scientific novelty:

For the first time in the Republic of Kazakhstan, on the basis of the Nur-Sultan Multifunctional City Hospital №2 and the Nur-Sultan Multifunctional City Hospital №1, scientific studies were carried out on the use of the infusion solution “Ulinastatin”. An algorithm for the treatment of acute destructive pancreatitis with endovideosurgical interventions in combination with the use of a protease inhibitor has been developed, depending on the severity of the course of the disease. The use of ulinostatin in patients of the main group was carried out according to the developed algorithm: AC No. 14704 dated January 27, 2021.

Purpose of the study.

To improve the results of endovideosurgical treatment of patients with acute destructive pancreatitis.

Materials and methods.

The study was conducted on the basis of the Nur-Sultan Multifunctional City Hospital №2 and the Nur-Sultan Multifunctional City Hospital №1 of the Republic of Kazakhstan.

CT, MRI, ZORING unit, Karl Stors endoscopic stand, Karl Stors argon-plasma coagulator, GelPort (Applied Medical), abdominal radiography, abdominal ultrasound, ERCP; clinical and laboratory research. Statistical analysis of the results was carried out using the methods of variation statistics with the calculation of M±SD. Differences between comparison groups were analyzed using the Wilcoxon-Manh-Whitney test and considered statistically significant at p≤0.05.

From 2017-2021, 64 patients with acute destructive pancreatitis were treated according to the developed and implemented treatment algorithm:

Of these: AP without organ failure and local and / or systemic complications -10 people. AP of moderate and severe form -54 people.

Lethal outcomes-1; The average length of stay in the hospital is 20.8±1.2 days;

Men - 35 (54.7%), women – 29 (45.3%) . The mean age was 43 ± 1.3 years.

The control group - treatment of patients with moderate and severe acute biliary pancreatitis without the use of ulinostatin (hereinafter US) was n = 122;

Lethal outcomes-8; The average duration of stay in the hospital is 24.3±1.6 days.

Patients of the main group - in addition to traditional therapy received US (Bharat Serums and Vaccines Ltd., India) twice a day at 10:00 and 22:00 at a dose of 100 thousand IU for 5 days, no later than 48 hours after moment of hospitalization

Of these, 37% (20 people) of patients underwent ERCP;

13% (7 people) of patients were operated on (laparoscopy, open surgery);

50% (27 people) treatment of patients is limited conservatively: drug treatment + EPST (Fig. 1).

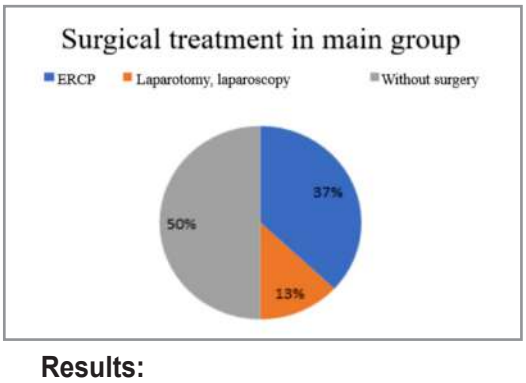


Figure 1.
Types of treatment in the main group

Results:

According to the developed algorithm, 54 patients with acute biliary pancreatitis of moderate and severe severity were treated. Of these, 29 were women and 35 were men (Fig. 2). The mean age of the patients was 43 ± 1.3 years. All patients received therapy in accordance with the approved clinical protocol «Acute

Figure 2.
Distribution of patients by gender

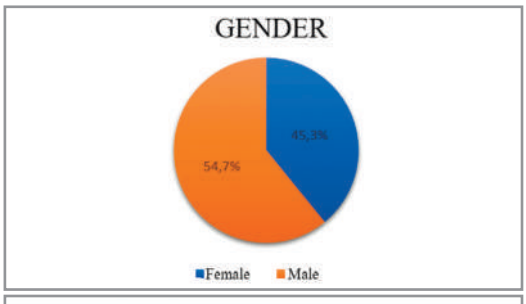


Figure 3.
Types of Surgical treatment

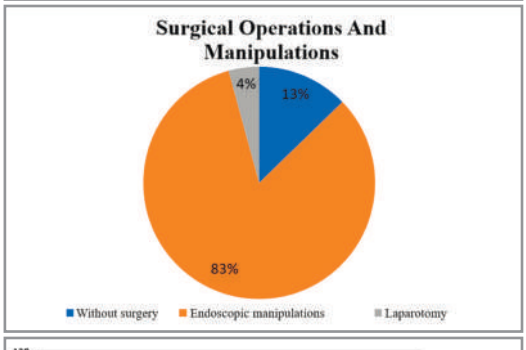


Figure 4.
The level of total bilirubin in dynamics

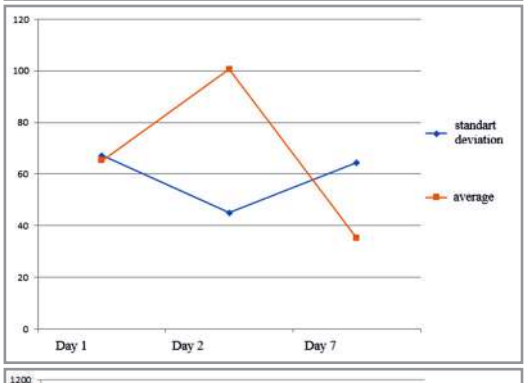


Figure 5.
Amylase level in dynamics

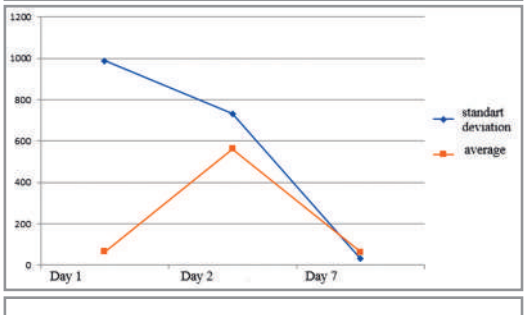
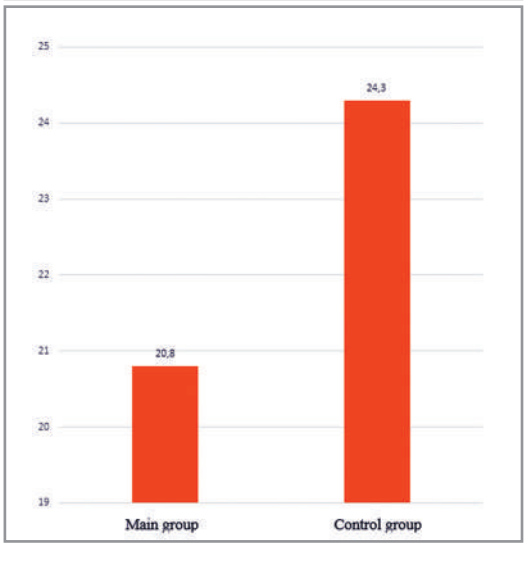


Figure 6.
Average duration of hospitalization of the main and control groups



pancreatitis» (dated March 29, 2019, Protocol №. 60, Ministry of Health of the Republic of Kazakhstan), clinical protocol «Chronic pancreatitis» (dated December 14, 2017 Protocol №. 35 of the Ministry of Health of the Republic of Kazakhstan).

Surgical operations and manipulations

10 patients were treated conservatively. 54 people have – surgical treatment combined with the appointment of ulinostatin according to the developed scheme.

Of the 54 patients, endoscopic surgery was performed in 51 patients. Only 3 patients were operated on in an open manner using laparotomy (Fig. 3).

Patients underwent a biochemical blood test at least three times: on admission, 1 day after the start of treatment, control tests at discharge. As a result: the average value of the level of total bilirubin after treatment decreased from 65 μmol/l at admission to 35 μmol/l with an equal statistical deviation (Fig. 4). The mean post-treatment amylase level decreased from 65 U/L on admission to 63 U/L (Fig.5). The drug has proven itself on the good side, it showed the highest efficiency after ERCP and EPST were performed in patients.

The average length of stay in the hospital in the main group was 3.5±0.34 days less, which also correlates with the dynamics of biochemical blood tests.

Algorithm for the use of ulinostatin depending on the severity of the course of destructive pancreatitis

The drug has established itself as an active inhibitor of pancreatic proteases; showed the highest efficiency after ERCP and EPST were performed in patients.

Our clinical studies have revealed: in moderate pancreatitis, it is effective and safe to administer Ulinastatin 100,000 units 2 times intravenously dissolved in saline or 5% glucose solution 100.0 ml for 1-3 days. In severe pancreatitis - 100,000 units x 2 times per 100.0 ml of saline solution or 5% glucose solution intra-arterially selectively for 5-7 days in combination with endovideosurgical interventions in the hepatopancreatoduodenal zone.

Conclusions: The results of our studies showed the high efficiency of the developed algorithm for the endovideosurgical method for the treatment of acute pancreatitis in combination with the use of the protease inhibitor ulinostatin.

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DIAGNOSIS AND TREATMENT OF OBSTRUCTIVE UROPATHY IN CHILDREN

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Conflict of interest
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Keywords
children, obstructive uropathy, endoscopic treatment

Abstract

Material and methods. *The study is based on the results of diagnosis and treatment of 444 children with congenital obstructive diseases of the urinary tract. They were in the urology department of NRCMCH since August 2007. To differentiate organic and functional obstructive uropathy were conducted high-tech, informative and noninvasive imaging diagnostic methods. On the basis of which were provided a differentiated treatment.*

Results.*Children with functional hydronephrosis and vesico-dependent version of urodynamic disorders in obstructive megauretera received conservative treatment. In ureteral type of the functional form of obstructive megauretera and 2-3 stage of vesicoureteral reflux were provided mini invasive endoscopic treatment. Effectiveness of endoscopic treatment of obstructive megauretera was - 85%, while the vesicoureteral reflux of 2nd stage - 100%, grade 3 - 80%. The use of mini lumbotomy front-side access for hydronephrosis, allowed towork locally in the area of ureteropelvic segment, to avoid injury of the kidneys and paranephritis.*

Conclusion. *Thus, the use of an integrated approach to diagnosis using minimally invasive, highly informative methods made it possible to pathogenetically substantiate the choice of tactics for the treatment of obstructive uropathy in children and significantly improve the results of this complex category of patients.*

Диагностика и лечения обструктивных уропатий у детей

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Конфликт интересов
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Ключевые слова
дети, обструктивные уропатии, эндоскопическое лечение

Аннотация

Материал и методы. *В основу работы положены результаты обследования и лечения 444 детей с врожденными обструктивными заболеваниями мочевых путей, находившихся в отделении урологии АО «ННЦМД» с августа 2007 года. Для дифференциации органической и функциональной обструктивной уропатий проводились высокотехнологичные, информативные и малоинвазивные визуализирующие методы диагностики, на основании которых проводилось дифференцированное лечение.*

Результаты. *Дети с функционально обусловленным гидронефрозом и пузырно-зависимым вариантом нарушения уродинамики при обструктивном мегауретере получали консервативное лечение. При мочеточниковом варианте функциональной формы обструктивного мегауретера и ПМР 2-3 ст. проведены миниинвазивные эндоскопические методы лечения. Эффективность эндоскопического лечения обструктивного мегауретера составила - 85%, при ПМР 2 ст.- 100%, 3 степени – 80%. Применение мини люмботомного передне-бокового доступа при гидронефрозе позволило локально работать в зоне ЛМС, без излишнего травмирования почки и паранефрия.*

Заключение. *Таким образом, использование комплексного подхода к диагностике с использованием миниинвазивных, высокоинформативных методов позволило патогенетически обосновать выбор тактики лечения обструктивныхуропатии у детей и значительно улучшить результаты этой сложной категории пациентов.*

Балалардағы обструктивтік уропатияның диагностикасы және емі

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Аңдатпа

Материал және әдістер. *Жұмыс 2007 жылғы тамыз айынан бері «ҰҒАБО» АҚ урология бөлімшесінде жатқан зәр шығару жолдарының туа біткен обструктивті аурулары бар 444 баланы қарап-тексеру және емдеу нәтижелеріне негізделген. Органикалық және функционалды обструктивті уропатияны саралау үшін жоғары технологиялық, ақпараттық және миниинвазивті бейнелеу диагностикалық әдістері жүргізілді, оның негізінде сараланған емдеу жүзеге асырылды.*

Нәтижелер. *Функционалды түрде анықталған гидронефроз және обструктивті мегауретердегі уродинамикалық бұзылулардың қуыққа тәуелді нұсқасы бар балалар консервативті ем алды. Обструктивті мегауретер және ҚНР 2-3 с. функционалдық түрінің несепағар нұсқасы мен емдеудің миниинвазивті эндоскопиялық әдістері орындалды. Обструктивті мегауреттерді эндоскопиялық емдеудің тиімділігі – 85%, 2 дәрежелі ҚНР кезінде - 100%, 3 дәреже кезінде 80%-ды құрады. Гидронефрозға арналған мини-люмботомиялық алдыңғы-бүйірлік тәсілді қолдану бүйрек пен паранефрияның шамадан тыс зақымдануынсыз ШНС аймағында жергілікті түрде жұмыс істеуге мүмкіндік берді.*

Қорытынды. *Осылайша, миниинвазивті, жоғары ақпараттық әдістерді қолдана отырып, диагностикаға кешенді тәсілді қолдану балалардағы обструктивті уропатияны емдеу тактикасын таңдауды патогенетикалық тұрғыдан негіздеуге және осы күрделі санаттағы науқастардың нәтижелерін айтарлықтай жақсартуға мүмкіндік берді.*

Мүдделер қақтығысы
Авторлар мүдделер қақтығысының жоқтығын мәлімдейді

Түйін сөздер
балалар, обструктивтік уропатия, эндоскопиялық ем

Introduction

The term “Obstructive uropathy” (OU) combines a complex of structural and functional changes in the renal parenchyma, predominantly of the tubulointerstitial type, which develop as a result offunctional or organic origin disorders of the urine passage at the level of the pyelocaliceal, pelvic-ureteral, vesicoureteral segments or a consequence of infravesical obstruction [1,2]. Obstructive uropathy in children most often includes hydronephrosis, vesicoureteral reflux, and obstructive megaureter. Obstructive uropathy without timely diagnosis and adequate treatment, can cause functional developmental delay of the kidneys, and when secondary changes are added, a complete loss of kidney function. Therefore, the assessment of the degree of preservation of renal function determines both, the choice of treatment for obstructive uropathy and the prognosis of the disease. At the same time, the degree of preservation of renal function directly depends on the state of renal hemodynamics [3,4].

Currently, the assessment of the upper urinary tract condition with obstructive uropathy is- complex and unthinkable, without the using of new technologies. This research is devoted to study these issues, as well as the search for new ways to correct the detected changes.

Material and methods

The study is based on the results of examination and treatment of 444 children with congenital obstructive diseases of the urinary tract, who were in the department of urology of the NRCMCH since August 2007, of all children 202 (45.5%) consist- hydronephrosis, 79 (17, 8%)-had megaureter and 163 (36.7%) were with vesicoureteral reflux (VUR) (Table 1).

Table 1.
Distribution of children with obstructive uropathy depending on nosology, sex and age

Diagnosis	under 3years		4-7years		8-11years		12-15years		Total
	boys	girls	boys	girls	boys	girls	boys	girls	
Hydronephrosis	69	28	38	9	24	10	12	12	202 (45,5%)
Megaureter	36	19	4	10	3	4	2	1	79 (17,8%)
VUR	38	22	6	39	11	24	9	14	163 (36,7%)
Total:	143	69	48	58	38	38	23	27	**444 (100%)**
	212 (47,7%)		**106 (23,9%)**		**76 (17,1%)**		**50 (11,3%)**		

As can be seen from the table above, children under 3 years of age predominated - 212 (47.7%). This unequivocally indicates an earlier diagnosis of Congenital Malformation of Urinary System . This positive trend is primarily due to the widespread introduction of prenatal ultrasound of the fetus into the protocol for examining pregnant women.

Attention is drawn to the distinct dynamics of the decrease in the frequency of OU with age, which correlates with the age-related regression of neurogenic urinary disorders in children. In this regard, we can assume a close relationship of the existing detrusor hyperreflexia with the development of OU.

All patients with obstructive uropathy during their stay in the hospital were examined according to the accepted plan, including the study of anamnesis, clinical laboratory, radiological (CT angiography, MRI - urography), ultrasound, urodynamic and endoscopic methods of research. To differentiate organic and functional obstruction, an ultrasound study was performed with a pharm test (lasix) - diuretic ultrasound (DUS), Dopplerography of the kidney vessels andureterovesical ejection of urine.

Results and discussion

In functional obstruction of pelvic-ureteral segment (PUS) zone and the uretero-vesical segment (UVS), the maximum expansion of the pelvis was noted in 15 minutes, but did not exceed 30% of the initial parameters, and the return to the original size occurred by 45-60 minutes.

On Dopplerography of the renal vessels: the vascular tree is preserved, the blood flow is determined in all parts of the parenchyma. Renal blood flow was assessed by the resistance index (IR). Normally, IR values fluctuated within 0.78 in children of the first months of life, 0.68 in older children. The spread of IR values at different levels of the renal artery did not exceed 0.03.

Dopplerography of ureterovesical ejection of urine was performed in all children. Emissions from the ureter were characterized by unchanged qualitative characteristics and frequency of ejection, the direction of the ejections was oriented towards the opposite wall of the bladder, their trajectories intersected in the projection of the midline and were alternating, independent of each other (Table 2).

Table 2.
Dopplerographic indicators of ureteral ejection in health children (n-45) and with functional OU (n-203)

Age	Vmax, cm/s		Vмin, cm/s		RI	
	normal	FOU	Норма	FOU	Норма	FOU
1 - 3 years	18,8±0,05	16,2±0,03	5,5±0,03	4,05±0,04	0,70±0,02	0,86±0,03
4 - 7 years	22,7±0,02	19,1±0,02	7,6±0,03	6,1±0,03	0,65±0,02	0,79±0,02
8 - 12 years	33,1±0,03	27,0±0,03	11,6±0,02	9,0±0,02	0,63±0,02	0,75±0,03

Following the table, the quantitative parameters of Dopplerograms with functional obstruction approach those of the control group (normal). In the organic form of obstruction, the expansion of the pelvicalyceal system was observed in 30-40 minutes after the administration of lasix, in the absence of regression of values by the 60th minute of the study. Emissions from the ureter are characterized by a significant decrease in the resistance index, a decrease in the frequency and speed of urine ejection, as well as a violation of renal hemodynamics, which are reliable hallmarks of organic obstruction (FO).

With vesicoureteral reflux of I-II degree, echographic and Doppler parameters of the kidneys corresponded to the standards. In children with grade III VUR, the size of the kidneys on the side of the lesion was reduced, differentiation into the cortical and medulla of the parenchyma was indistinct. Diffuse or focal impoverishment of blood flow was determined in CDI and ED.

In order to determine the nature of kidney vascularization, we used a high-tech, minimally invasive and informative method: magnetic resonance urography (MRU) with an angiographic phase. The advantage of this technique, in addition to improving the visualization of the PCS and ureters, was that after the introduction of the diuretic, there was an acceleration of blood flow in the vessels of the kidney, including additional ones, which in turn significantly improved the conditions for visualization of the vessels and allowed in most cases (78%) to diagnose an accessory vessel in the area of the LMS or in/3 of the ureter (Fig. 1).

The conducted complex examination allowed us to make a differentiated approach to the choice of treatment tactics.

Children with functional hydronephrosis 119 (59%) received a course of conservative treatment.

From 83 patients with an organic form of hydronephrosis, 67 patients underwent plastic surgery of the pyeloureteral segment according to the Hines-Andersen method. The remaining 16 children underwent laparoscopic nephroureterectomy due to the lack of kidney function.

Since 2007, we have been using a minimally invasive lumbotomy anterior-lateral approach (Figure 2).

This access allows to work locally in the area of the UPJ, without excessive injury to the paranephria of the kidney.

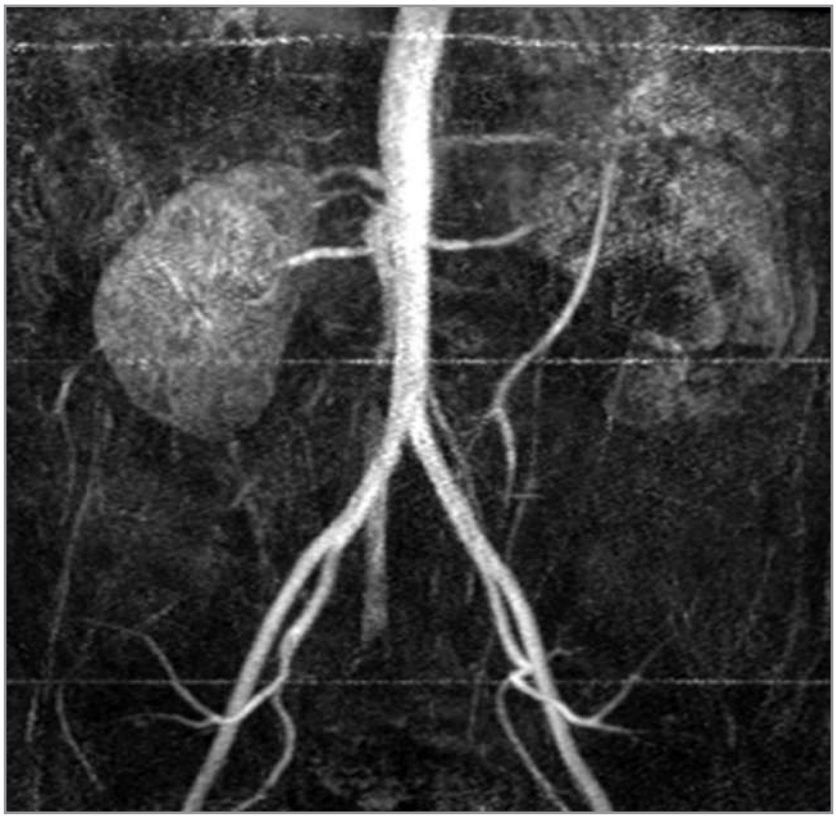

Figure 1.
Left-sided hydronephrosis. MR angiography

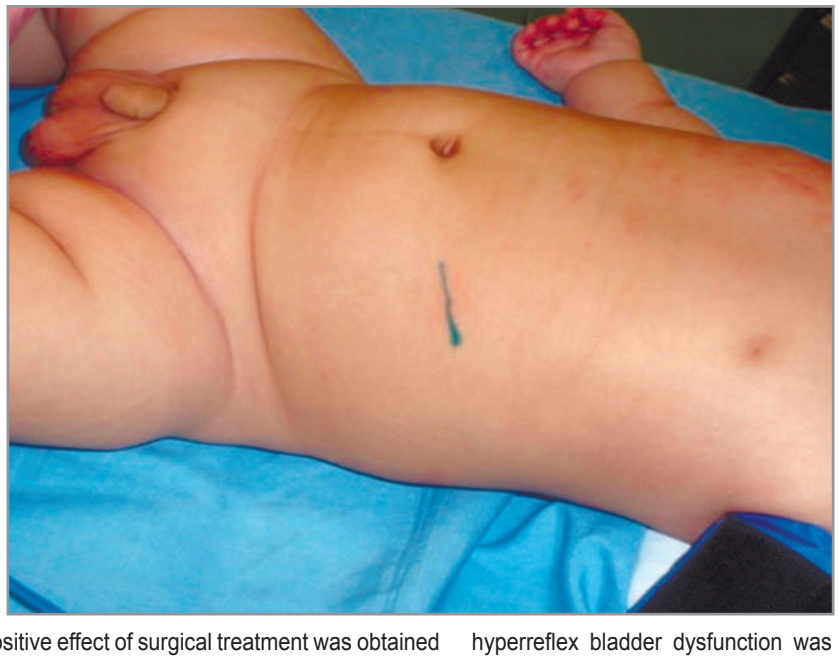

Figure 2.
Anterior-lateral
access for hydronephrosis
(surgical navigation)

A positive effect of surgical treatment was obtained in 64 (95.5%) patients, of which in 46 (71.9%) it was regarded as good - complete recovery or significant improvement in urodynamics and kidney function, in 18 (28.1%) as satisfactory - a slight improvement or stabilization of the function of the operated kidney, preservation of preoperative obstructive manifestations of urodynamic insufficiency - expansion of the pelvis and a violation of its evacuation function. In 3 (4.4%) patients, worsening of kidney function was noted.

A bladder-dependent variant of urodynamic disturbance in obstructive megaureter due to neurogenic hyperreflex bladder dysfunction was detected in 53 (67.1%) patients (Group I). These patients received conservative treatment for neurogenic bladder. In 16 (20.2%) patients, the ureteral variant of the functional form of obstructive megaureter was diagnosed (group II). These patients underwent endovideoscopic treatment (bougienage, dilatation and stenting) of the ureterovesical segment. In general, positive results of endovideosurgical treatment of OMU were obtained in 85% of cases.

In all these children, the course of chronic pyelonephritis from the stage of constant exacerbations

passed into a stable phase of remission, the amount of antibiotic therapy was significantly reduced. The developed technique for endosurgical treatment of the ureteral variant without resection of the ureterovesical segment made it possible to change the existing concept of active surgical treatment of children with obstructive megaureter, in particular, to sharply limit the indications for open surgical treatment and expand the scope of endosurgical interventions.

Group III - children with an organic form of obstruction of urodynamic disorders, which was detected in 10 (12.7%) patients. Children of this group underwent various types of antireflux surgery.

In the treatment of VUR, we have identified 3 main methods: conservative, endoscopic and surgical methods. In the presence of VUR of 1-2 degrees, a course of conservative treatment was performed. In case of grade 3 VUR, as well as in case of failure of conservative therapy in grade 1-2 VUR, we performed endoscopic correction with glycogel.

The effectiveness of endoscopic treatment for VUR of stage 1-2, according to our data, was 100%, for stage 3 - 80%, of which the elimination of reflux from the first injection of glycogel was achieved in 45%, in another 20% of patients reflux was eliminated with repeated administration through 3 months, and in 15% due to the persistence of reflux, a third injection of glycogel was required, after which a positive result was obtained.

At the same time, even against the background of reflux persistence, almost all patients showed a decrease in its degree, as well as a decrease in the phenomena of bladder dysfunction and the frequency of exacerbations of pyelonephritis.

Thus, the use of an integrated approach to diagnosis using minimally invasive, highly informative methods made it possible to pathogenetically substantiate the choice of tactics for the treatment of obstructive uropathy in children and significantly improve the results of this complex category of patients.

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SURGICAL TREATMENT OF CONGENITAL PTOSIS OF THE UPPER EYELIDS

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

Keywords
congenital pathology, ptosis of the eyelids, tendon

Abstract

In childhood, closing the pupil with the upper eyelid leads to the development of amblyopia in 20-70%. The main methods of surgical treatment of blepharoptosis in the absence of the function of the muscle that lifts the upper eyelid are suspension operations.

Material and methods. *A 2-year-old child presented with congenital ptosis of the right upper eyelid. Palpebral fissure versus right narrowed by 0.5 cm. Excursion of the left upper eyelid 0.9 cm, right 0.3 cm.*

After the written consent of the parents, the child underwent an operation to eliminate ptosis of the right upper eyelid by implantation parts of the superficial flexor of the hand.

Results. *The variety of suspension operations for blepharoptosis is associated not only with the many options for conducting a suspension suture (single and double diamond-shaped, triangular, U-shaped, etc.), but also with the materials used - biological and synthetic.*

Conclusion. *According to our research, synthetic materials allow you to get a more stable good result, but we used a tendon.*

Вариант хирургического лечения врожденного птоза верхних век

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Ключевые слова
врожденная патология, птоз век, сухожилие

Аннотация

В детском возрасте закрытие зрачка верхним веком приводит к развитию амблиопии в 20-70%. Основными методами хирургического лечения блефароптоза при отсутствии функции мышцы, поднимающей верхнее веко, являются подвешивающие операции.

Материал и методы. *У ребенка 2-х лет врожденный птоз правого верхнего века. Глазная щель относительно правого сужена на 0,5 см. Экскурсия левого верхнего века 0,9 см, правого 0,3 см. С письменного согласия родителей ребенку была проведена операция по устранению птоз правого верхнего века имплантацией части поверхностного сгибателя кисти.12*

Результаты. *Разнообразие подвесных операций при блефароптозе связано не только с множеством вариантов проведения подвесного шва (одинарный и двойной ромбовидный, треугольный, П-образный и др.), но и с применяемыми материалами - биологическими и синтетическими.*

Заключение. *По нашим исследованиям, синтетические материалы позволяют получить более стабильный хороший результат, но наш опыт применения сухожилия может быть предложен как один из методов лечения.*

Туа біткен үстіңгі қабақ птозының хирургиялық емдеу әдісінің түрі

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Аңдатпа

Балалық шақта қарашықты жоғарғы қабақпен жабу 20-70% амблиопияның дамуына әкеледі. Жоғарғы қабақты көтеретін бұлшықеттің қызметі болмаған кезде блефароптозды хирургиялық емдеудің негізгі әдістері көтерме операциялары болып табылады.

Материал және әдістер. *2 жасар балада оң жақ қабақтың туа біткен птозы бар. Пальпебральды жарықшақ оң жаққа қарағанда 0,5 см тарылған.Сол жақ жоғарғы қабақтың экскурсиясы 0,9 см, оң жақ қабақтың экскурсиясы 0,3 см. Ата-анасының жазбаша келісімімен балаға оң жақ қабақтың птозын жою операциясы жасалды. Қолдың сіңірінің имплантациясы арқылы оң жақтың жоғарғы қабағының пластикасы жасалды.*

Нәтижелер. *Блефароптозға арналған көтерме операцияларының әртүрлілігі қос алмас тәрізді, үшбұрышты, U-тәрізді және т.б.) ғана емес, сонымен қатар қолданылатын материалдармен - биологиялық және синтетикалық.*

Қорытынды. *Біздің зерттеулерімізге сәйкес, синтетикалық материалдар тұрақты жақсы нәтиже береді, бірақ сіңірге қатысты тәжірибеміз емдеу әдістерінің бірі ретінде ұсынылуы мүмкін.*

Түйін сөздер
туа біткен патология, қабақтың птозы,сіңір

Introduction

In childhood, closing the pupil with the upper eyelid leads to the development of amblyopia in 20-70%. The main methods of surgical treatment of blepharoptosis in the absence of the function of the muscle that lifts the upper eyelid are suspension operations.

Currently, autogenous materials are used to eliminate congenital ptosis of the upper eyelids: hip fascia, temporal fascia. Synthetic materials - polypropylene, silicone, supramide nylon seam. [1,2, 3,4].

We present a case report of congenital ptosis of the right upper eyelid which was removed using by our an improved method applying a tendon graft.

Materials and methods

The informed consent was obtained from the child's parents involved in this study according to the Institutional Review Board and all procedures were in accordance with the institutional and national ethical standards.

A 2-year-old child presented with congenital ptosis of the right upper eyelid. Palpebral fissure versus right narrowed by 0.5 cm. Excursion of the left upper eyelid 0.9 cm, right 0.3 cm.

Under general anesthesia, the child underwent surgery to eliminate ptosis of the right upper eyelid by implanting a superficial flexor of the wrist.

In the lower third of the right forearm over the tendon superficial flexor of the hand carried out two transverse skin incision 0.5 cm long (Figure 1. 1) and took part of the superficial flexor of the hand, 5 cm long (Figure 1. 2).

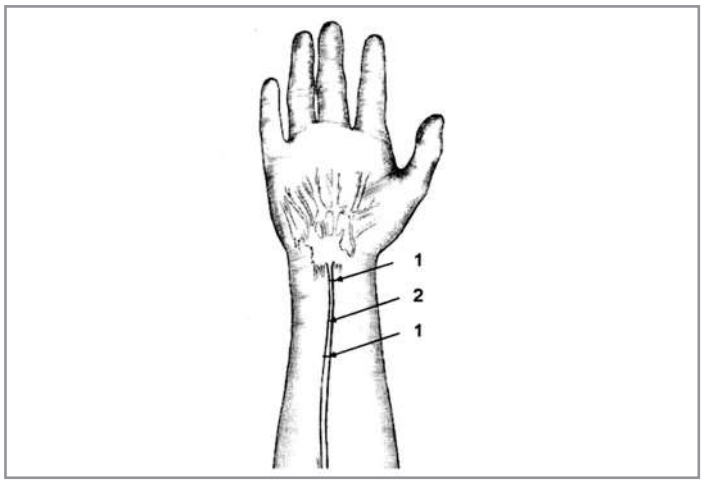

Figure 1.
Superficial flexor of the hand for the grafting

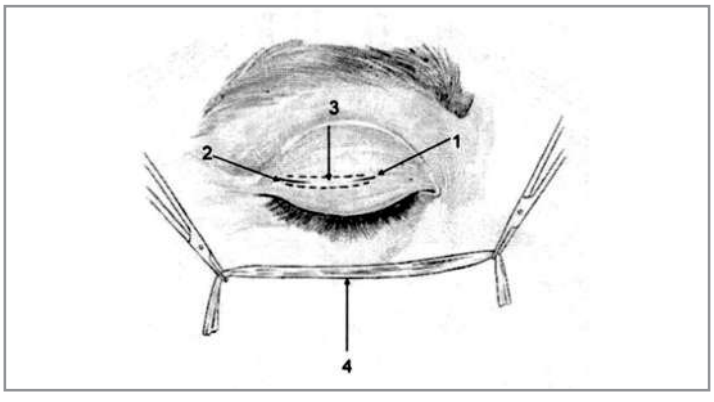

Figure 2.
П-shaped channel

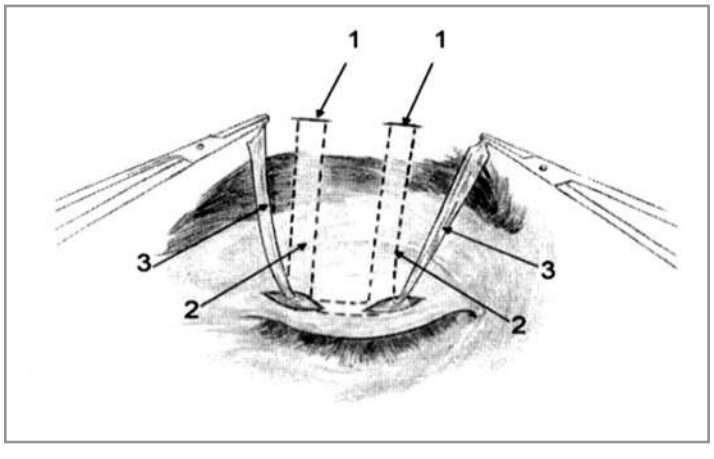

Figure 3.
Transplant fixation in the superciliary region

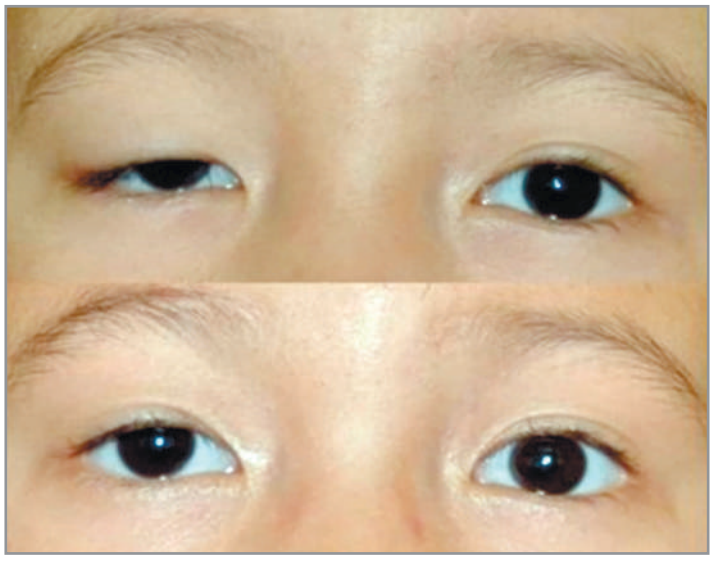

Figure 4.
The result after 8 months of operation

In the middle third of the upper eyelid at the level of the upper the cartilage of the eyelid performed two incisions (Figure 2. 1, 2), Between two skin incisions, we formed the first subcutaneous canal (Figure 2. 3). Part of the tendon of the superficial flexor of the hand-prepared for insertion into the formed П-shaped channel (Figure 2. 4).

Two small incisions are also made in the superciliary region (Figure 3. 1). Perpendicular to the first channel, two other subcutaneous canals to the frontal muscle (Figure 3. 2). Then an autograft was performed (part of the tendon superficial flexor of the hand (Figure 3. 3) in formed П-shaped channel starting from the first one, which is formed at the level of the upper cartilage of the century in the middle third of the century. Ends autograft (Figure 1. 3) is fixed (Figure 1. 3) to superciliary muscle, so that the eyelid covers the pupil of the eye on ¾.

Post-operative course and long term result

On the 3rd day after surgery: edema of the upper eyelid asleep. The palpebral fissures are symmetrical. Closing upper eyelid function restored. 8 months after surgery, the patient recurred ptosis of the upper eyelid and the development of the cicatricial process was not observed (Figure 4).

Result and discussion

The variety of suspension operations for blepharoptosis is associated not only with the many options for conducting a suspension suture (single and double diamond-shaped, triangular, U-shaped, etc.), but also with the materials used - biological and synthetic. According to our research, synthetic materials allow you to get a more stable good result, but we used a tendon. However, many foreign authors prefer autofascia due to the high percentage of successful operations up to 90% in the early postoperative period. The long-term suspension effect from the use of allomaterials persisted only in half of the cases [5, 6]. All patients who came to us after implantation of autofascia showed deformity of the upper eyelid and the development of contractures. In all cases of weakening the effect and the development of an infectious process, we performed the removal of auto- and allo-materials, which was complicated by the germination of the implant by fibrovascular tissue [7, 8]. According to the literature, polypropylene threads are used as a suspension in young children to prevent the development of amblyopia. The advantage of their use is that they do not grow into fibrovascular tissue and are easily removed in patients who are scheduled for implantation of the latissimus fascia at an older age [9, 10]. The literature describes cases of rupture and cutting of polypropylene threads [11]. According to our study, suppuration and the development of suture granulomas, as well as a change in the shape of the upper eyelid, can be considered a disadvantage of polypropylene threads. The same complications are typical for silicone threads. Their use as a suspension often led to the development of re-ptosis, since this material is very elastic, stretches well and often unties and shifts.

This method of performing ptosis elimination upper eyelid improves results restoration of the function of the upper eyelid and the continuation of research in this direction is relevant[12,13].

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HYPERTROPHIC CARDIOMYOPATHY. LITERATURE REVIEW

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Abstract

Hypertrophic cardiomyopathy is a common hereditary heart disease with a heterogeneous clinical picture and a natural history. Recent advances in diagnosis and treatment methods have played an important role in reducing the incidence of adverse clinical events; however, the complete elimination of sudden cardiac death is still an unattainable achievement. Despite the heterogeneous clinical profile and complex pathophysiology, effective treatment strategies are available, including implantable defibrillators to prevent sudden death, medical and surgical myectomy (or, alternatively, alcohol ablation of the septum) to alleviate outflow obstruction and symptoms of heart failure, as well as pharmacological strategies (and possibly radiofrequency ablation) to control atrial fibrillation and prevent embolic stroke. Now, after more than 50 years, hypertrophic cardiomyopathy has been transformed from a rare and largely untreatable disorder to a common genetic disease with management strategies that permit realistic aspirations for restored quality of life and advanced longevity. This article discusses some aspects of this condition: epidemiology, clinic, diagnosis and surgery technique.

Objective.*Evaluate the effectiveness of surgical treatment of patients with hypertrophic cardiomyopathy.*

Material and methods.*This literature review was carried out in accordance with the PRISM statement. The databases searched in this review included Pubmed, Web of Science, Scopus, and Cochrane for systematic reviews.*

Conclusion. *The diagnosis of HCMP is based mainly on echocardiographic variables including the dynamic parameters of LV, LVOT the distribution of increased muscle thickness, the mechanism and severity of MR as well as the degree of diastolic dysfunction.*

Keywords
HCMP, echocardiography, left ventricle.

Гипертрофическая кардиомиопатия. Обзор литературы

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Аннотация

Гипертрофическая кардиомиопатия - распространенное наследственное заболевание сердца с неоднородной клинической картиной и естественным анамнезом. Последние достижения в методах диагностики и лечения сыграли важную роль в снижении частоты неблагоприятных клинических проявлений; однако полное устранение внезапной сердечной смерти по-прежнему остается недостижимым достижением. Несмотря на неоднородный клинический профиль и сложную патофизиологию, доступны эффективные стратегии лечения, включая, имплантируемые дефибрилляторы для предотвращения внезапной смерти, медикаментозную и хирургическую миэктомию (или, альтернативно, алкогольную абляцию перегородки) для облегчения обструкции оттока и симптомов сердечной недостаточности. А также фармакологические стратегии (и, возможно, радиочастотная абляция) для контроля фибрилляции предсердий и предотвращения эмболического инсульта. Теперь, по прошествии более чем 50 лет, гипертрофическая кардиомиопатия превратилась из редкого и в значительной степени неизлечимого заболевания в распространенное генетическое заболевание со стратегиями лечения, которые позволяют реалистично стремиться к восстановлению качества жизни и увеличению продолжительности жизни. В этой статье рассматриваются некоторые аспекты этого состояния: эпидемиология, клиника, диагностика и методика хирургического вмешательства.

Цель исследования. *Оценить эффективность хирургического лечения пациентов с гипертрофической кардиомиопатией.*

Материал и методы. *Этот литературный обзор был выполнен в соответствии с заявлением PRISM. Базы данных, в которых проводился поиск в этом обзоре, включали базы данных Pubmed, Web of Science, Scopus и Cochrane для систематических обзоров.*

Заключение.*Диагноз ГКМП основывается преимущественно на эхокардиографических переменных, включая динамические показатели ЛЖ, ВОЛЖ, распределение увеличенной толщины мышц, механизм и тяжесть МН, а также степень диастолической дисфункции.*

Конфликт интересов
Авторы заявляют об отсутствии конфликта интересов

Ключевые слова
ГКМП, эхокардиография, левый желудочек

Гипертрофиялық кардиомиопатия. Әдебиет шолу

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Аңдатпа

Гипертрофиялық кардиомиопатия-гетерогенді клиникалық көрінісі және табиғи тарихы бар жалпы тұқым қуалайтын жүрек ауруы. Диагностикалық және емдеу әдістеріндегі соңғы жетістіктер қолайсыз клиникалық көріністердің жиілігін төмендетуде маңызды рөл атқарды; алайда кенеттен жүрек өлімін толығымен жою әлі де қол жетпейтін жетістік болып қала береді. Біртекті емес клиникалық профильге және күрделі патофизиологияға қарамастан, тиімді емдеу стратегиялары бар, соның ішінде кенеттен өлімнің алдын-алу үшін имплантацияланатын дефибрилляторлар, ағып кетудің және жүрек жеткіліксіздігінің белгілерін жеңілдету үшін дәрі-дәрмектер мен хирургиялық миэктомия (немесе алкогольді септальды абляция). Сондай-ақ, атриальды фибрилляцияны бақылауға және эмболиялық инсульттің алдын алуға арналған фармакологиялық стратегиялар (және мүмкін радиожиілікті абляция). Енді 50 жылдан астам уақыттан кейін гипертрофиялық кардиомиопатия сирек кездесетін және көбінесе емделмейтін аурудан жалпы генетикалық ауруға айналды, бұл өмір сүру сапасын қалпына келтіруге және өмір сүру ұзақтығын арттыруға нақты ұмтылуға мүмкіндік беретін емдеу стратегиялары бар. Бұл мақалада осы жағдайдың кейбір аспектілері қарастырылады: эпидемиология, клиника, диагностика және хирургиялық әдіс.

Мақсаты. *Гипертрофиялық кардиомиопатиясы бар науқастарды хирургиялық емдеудің тиімділігін бағалау.*

Материал және әдістер. *Бұл әдеби шолу орындалды prism мәлімдемесіне сәйкес. Өткізілген деректер базасы бұл шолуда іздеу Pubmed, Web of Science, Scopus және жүйелі шолулар үшін Cochrane.*

Қорытынды. *Гипертрофиялық кардиомиопатия диагнозы негізінен өтірік динамикалық көрсеткіштерін қоса, эхокардиографиялық айнымалыларға негізделген, СҚ, СҚШБ бұлшықет қалыңдығының таралуы, механизмі мен ауырлығы, сондай-ақ диастолалық дисфункция дәрежесі.*

Түйін сөздер
ГКМП, эхокардиография, сол жақ қарынша

Relevance

Hypertrophic cardiomyopathy is a common hereditary cardiovascular disease occurring in one out of 500 people in the whole population [1-3]. It is caused by more than 1400 mutations in 11 or more genes [4-8] encoding cardiac sarcomere proteins. Although hypertrophic cardiomyopathy is the most common cause of sudden death in young people (including trained athletes) [9, 10] and can lead to functional disability as a result of heart failure and stroke, most affected people probably remain undiagnosed, and many do not have a significant reduction in life expectancy or significant symptoms. The diagnosis is most often made by echocardiographic assessment of left ventricular hypertrophy, gradients of the left ventricular outlet tract, systolic and diastolic function, as well as mitral valve anatomy and function. Magnetic resonance imaging of the heart also plays a diagnostic role, determining the degree and localization of left ventricular hypertrophy, and anatomical abnormalities of the mitral valve and papillary muscles.

Pathophysiology in HCMP

HCMP is defined as an abnormal thickening of the LV without expansion of the chamber, which is usually asymmetric, develops in the absence of an identifiable cause (for example, aortic valve stenosis, hypertension) and is associated with a violation of myocardial fibers [11, 12]. The main structural anomalies underlying HCMP are [1] disorder of myocardial cells when the cells are in an unorganized state, in contrast to the normal parallel arrangement of myocytes; [2] dysfunction of the coronary microcirculatory bed due to an increase in the wall/lumen ratio; and [3]remodeling changes [13, 14]. In intramiocardial arterioles <80 microns, studies have shown a 2-fold increase in the wall-to-lumen ratio, predisposing patients with silent myocardial ischemia, ongoing myocardial damage and fibrosis. Moreover, these changes are not limited to the areas of LVH and myocardial remodeling, which occur as a compensatory mechanism and may include changes in myocytes, fibroblasts and interstitials. These changes develop over many years before symptoms appear. Disorganized pattern of myocytes, increased wall/lumen ratio of coronary arteries and remodeling changes in patients with HCMP lead to impaired coronary reserve, diastolic dysfunction, supraventricular and ventricular rhythm disturbances, and sudden death. LV remodeling may include fibrosis, diffuse, asymmetric, focal or concentric hypertrophy, as well as a decrease in the size of the cavity [15, 16]. Obstruction of the excretory tract of the left ventricle occurs with HCMP, and it was initially thought that basal septum hypertrophy invading the LVOT caused the obstruction. However, later studies have shown that during ventricular systole, the flow against the incorrectly positioned mitral valve apparatus (MV) leads to the appearance of resistance forces

on part of the valves, which are then pushed into LVOT [17-21] anomalias of the MK apparatus may include displacement of papillary muscles in front, hypertrophied papillary muscles in contact with the septum, elongated mitral flaps or abnormal insertion of the papillary muscle into the anterior mitral flap [18, 21, 22].

The enlargement of the left ventricle may be accelerated or aggravated by a decrease in the final diastolic volume or systemic arterial resistance or an increase in contractility or heart rate [23].

Modern classification of diseases:

Idiopathic hypertrophic subaortic stenosis.

Asymmetric hypertrophy of the septum without changes from the aortic and mitral valves, without obstruction of the LV exit tract.

Apical HCMP with restriction of the hypertrophy zone to the apical region. Symmetrical HCMP with concentric LV myocardial hypertrophy.

The last 3 forms are rare and are not accompanied by the development of obstruction of the LV outflow tract.

Classification of the New York Heart Association's HCMP:

- I degree - pressure gradient not higher than 25 mm Hg.
- II degree - pressure gradient from 25 to 36 mm Hg.
- III degree - pressure gradient from 36 to 44 mm Hg.
- IV degree - pressure gradient 45 mm Hg.

Classification by degree of hypertrophy:

* moderate - the thickness of hypertrophy is 15-20 mm;
* average - hypertrophy thickness of 21-25 mm;
* pronounced - the thickness of hypertrophy is more than 25 mm.

Nonspecific Electrocardiogram changes associated with hypertrophic cardiomyopathy
- Hypertrophy of the left ventricle (S-shaped wave in V1 ≥35 mm; R-shaped wave in V5 >35 mm)
- Left axis deviation/left front hemiblock
- Intraventricular conduction delay (QRS >0.12 ms)
- Enlargement of the left atrium (wide toothed wave P in lead II; deeply inverted wave P in V1)
- Pathological Q-waves
- Poor progression of the R wave in precordial leads
- Supraventricular arrhythmias (most often atrial fibrillation)
- Full block of package branches
- ST segment depression
- Inverted T-waves in ≥2 consecutive leads

Table 1.
Electro-and Echocardiographic examinations at HCMP

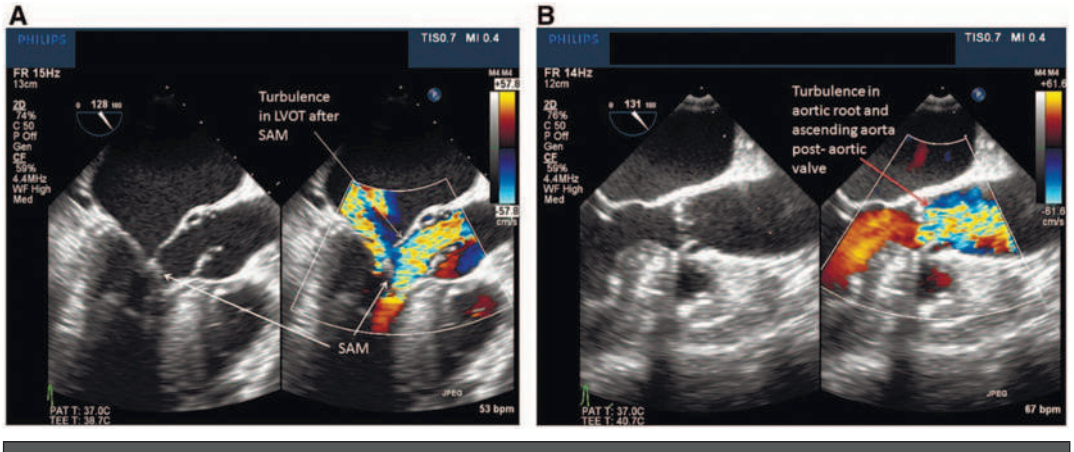

Figure 1.
A, image of transesophageal echocardiography (TEE) -color flow Dopplerography (CFD) images of the middle long axis of the esophagus (ME-LAX) in a patient with hypertrophic cardiomyopathy with turbulence in the excretory tract of the left ventricle (LVOT) at the level of systolic anterior movement of the mitral valve (SAM) (proximal to the aortic valve). B, TEE-CFD image of the ME-LAX image in a patient with valvular aortic stenosis showing laminar flow in the LVOT and turbulence distal to the affected aortic valve. (Hypertrophic cardiomyopathy: a review Nadia Hensley 1, Jennifer Dietrich, Daniel Nyhan, Nanhi Mitter, May-Sann Yee, MaryBeth Brady)

Echocardiographic focus in hypertrophic cardiomyopathy
1. The presence of hypertrophy and its distribution; report measurements of the size of the left ventricle, wall thickness (septum, posterior, maximum)
2. Left ventricular ejection fraction
3. Pancreatic hypertrophy and the presence of dynamic pancreatic obstruction
4. The volume of the left ventricle, indexed by body surface area
5. Diastolic function of the left ventricle (pressure of relaxation and filling)
6. Systolic pressure in the pulmonary artery
7. Dynamic obstruction at rest and with Valsalva, the place of obstruction and the slope
8. Evaluation of the mitral valve and apparatus, details of mitral regurgitation (i.e. mechanism, severity);

Table 2.
Echocardiographic focus in hypertrophic cardiomyopathy

Surgical technique: In this article we will carefully focus on the technique: transaortic myoectomy. An attempt at a basal septum myectomy using transaortic access was originally described by Morrow in 1961 [25-31], but it was first performed in 1958 and subsequently described by Kleland in 1963 [32-37]. The initial report described a limited myectomy without a specific anatomical resection. The technique of formal basal myectomy was later published in 1975. Initially, this method involved excision of a rectangular segment of the septum myocardium under the flap of the right coronary aortic valve which extended apically to the

point of contact of the septum of the anterior flap of the mitral valve. This point is usually delimited by a fibrous scar which develops a second time due to the constant contact of the valve leaf with the septum myocardium during systole. The total myocardial sample excised during Morrow's myectomy is approximately 3-4 cm long, 1 cm wide and 1.5 cm deep [27]. More recently the standard transaortic procedure has turned into an extended septal myectomy. This procedure creates a longer myocardial excision and opens the LVOT more apically than the Morrow procedure. Following the initiation of artificial circulation (CPB), the exposure of the left ventricle is achieved by an oblique aortotomy performed through the midpoint of the non-coronary sinus of the aorta and ending about 1 cm above the aortic ring. Polypropylene seams remain or not. The Ross retractor keeps the aorta open, and the suction tip for cardiotomy is used to retract and protect the anterior flap of the mitral valve. Depending on the surgeon's preferences, scalpel No. 10 or 11 is used to cut the septum, starting directly under the nadir of the right aortic valve leaf and directed to the left. to the anterior flap of the mitral valve, removing the basal part of the hypertrophied septum. The incision in this area is carefully marked, because a tissue rupture further to the right of the midpoint of the right valve leaf will increase the risk of damage to the membranous septum and disruption of the conductive tissue, thereby significantly increasing the likelihood of complete heart block. Then, starting again from the area of the initial incision, the area of the cut-out septum is lengthened to the apex of the heart, making sure that the excision is performed outside the endocardial fibrous scar and in the apical trabeculations. The completed myectomy extends from the subaortic level, about 5 mm below the aortic ring, to the level of the middle ventricle, opposite the base of the anterior papillary muscle of the mitral valve, with a total length of about 7 cm.

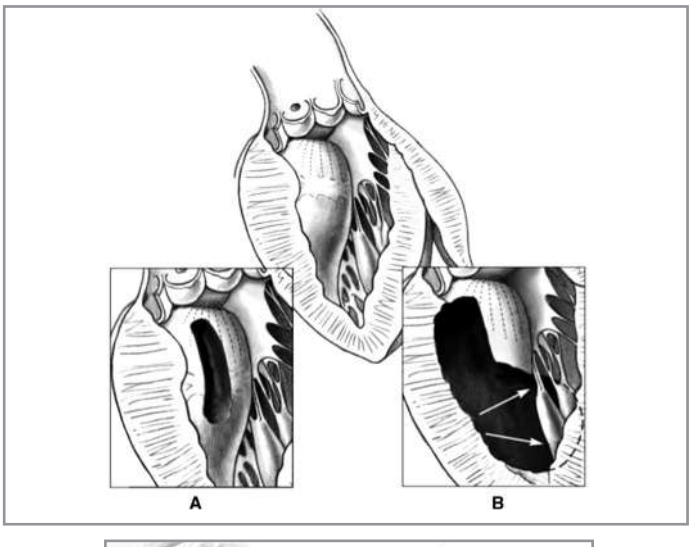

Figure 2.
Comparison of the classic Morrow procedure (A) with the modification of the extended septal myectomy (B). The resection of the septum wall expands to the top, to the free wall on the left side of the image, and then to the right, as indicated by the white arrows. The dotted lines in the basal septum represent the bundles of the left bundle emanating from the membranous septum

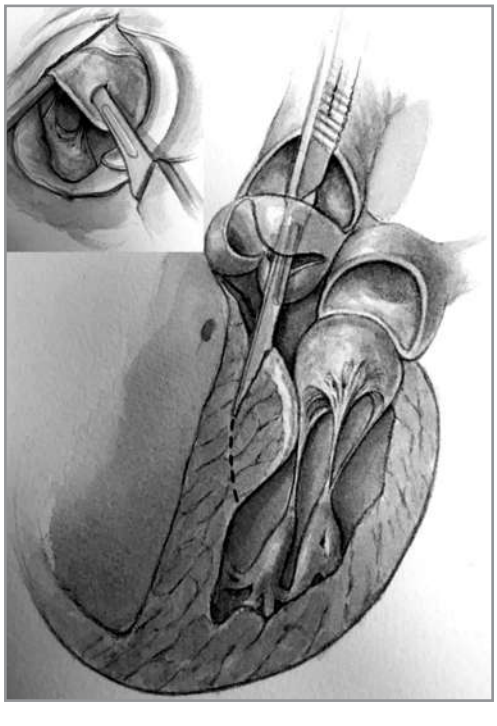

Figure 3.
(a) Extended thymectomy of the basal septum using supravalvular aortotomy. (b) The surgeon's view through the aortotomy, determining the hypertrophied septum directly below the right coronary aortic valve leaf

Conclusion. The diagnosis of HCMP is based mainly on echocardiographic variables including the dynamic parameters of LV, LVOT the distribution of increased muscle thickness, the mechanism and severity of MR as well as the degree of diastolic dysfunction. Current indications for surgical intervention include patients with symptoms that are immune to drug therapy who can tolerate the risk of surgical intervention and patients with pronounced outflow gradients, even if they are asymptomatic.

Despite the ambiguity the mechanism underlying the improvement of symptoms, LV condition and long-term survival after myectomy is at least partially due to LV regression. It is extremely important for cardiac surgeons to understand the mechanisms of this disease in order to best manage these patients in perioperative conditions. It is very important to diagnose these HCMP patients in time, provide the necessary therapy and hospitalization for surgical treatment.

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COMPARATIVE EVALUATION OF A CONTROLLED CLINICAL TEST OF APPARATUS INTRAOPERATIVE REINFUSION OF BLOOD COLLECTED FROM THE PLEURAL CAVITY UNDER SLOW AND FAST MODES

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

Abstract

Objective. *An analysis of the study, in the mode of fast and slow blood exfusion, controlled clinical trials showed that the number of platelets was significantly reduced.*

Material and methods. We have conducted a series of researches in 44 patients with cavitary blood loss, which is 34.3% of the total number of the examined patients (n-128), for whom an IOBR apparatus technology was used. The studies were also conducted during the surgery in the first 2 hours.

Results. *Controlled clinical trials (CCT) have shown that blood exfusion after intraoperative blood reinfusion, the degree of destruction of erythrocytes and leukocytes with slow blood exfusion is 35%, and with fast - 48%. Osmotic resistance is reduced by 3 times. With rapid hardware exfusion, blood hemolysis is more than 28%, which should be taken into account when performing hardware intraoperative blood reinfusion. Controlled clinical trials have shown that the faster the machine exfusion is performed, the greater the decrease in protein and bilirubin content. In the blood collected in the mode of rapid apparatus exfusion, a higher concentration of K +, residual N and urea is noted. Controlled clinical trials have shown that platelet counts are significantly reduced, especially when using a rapid blood collection regimen. Against this background, the process of aggregation is reliably slowed down, and with a fast mode of blood collection - 2 times in comparison with the control. Plasma recalcification time is reliably reduced by 40% when using a high-speed blood collection mode in comparison with the control values, which is almost 3 times higher than when using slow blood aspiration.*

Conclusion. *The article provides an analysis of scientific research, CCT, experimental control, clinical control and practical work. The work is interdisciplinary in nature, written at the intersection of surgery and anesthesiology, to increase the effectiveness of emergency surgery and anesthesiology-resuscitation in critical abdominal and luminal blood loss based on the optimization of intraoperative infusion-transfusion therapy.*

Keywords
controlled clinical trials, instrumental intraoperative blood reinfusion, pleural cavity.

Сравнительная оценка контролируемого клинического испытания аппаратной интраоперационной реинфузии крови, собранной из плевральной полости в условиях медленного и быстрого режимов

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Аннотация

Цель. *Анализ изучения, в режиме быстрой и медленной эксфузии крови, контролируемые клинические испытания показали, что количество тромбоцитов достоверно снижается.*

Материал и методы. *Нами проведена серия исследований у 44 больных с полостной кровопотерей, что составляет 34,3% от общего числа обследованных больных (n-128), у которых применялась аппаратная технология интраоперционной реинфузии крови (ИО РИК). Исследования также проводились во время операции в первые 2 часа.*

Результаты. *Контролируемые клинические испытания (ККИ) показали, что эксфузия крови после ИО РИК, степени разрушаемости эритроцитов и лейкоцитов при медленной эксфузии крови составляет 35%, а при быстрой – 48%. Осмотическая резистентность снижается в 3 раза.*

Конфликт интересов
Авторы заявляют об отсутствии конфликта интересов

При быстрой аппаратной эксфузии гемолиз крови составляет более 28%, что следует учитывать при выполнении аппаратной интраоперационной реинфузии крови. ККИ показали, что чем быстрее выполнена аппаратная эксфузия, тем значительнее снижение содержания белка и билирубина. В крови, собранной в режиме быстрой аппаратной эксфузии отмечается более высокая концентрация К+, остаточного N и мочевины. ККИ показали, что количество тромбоцитов достоверно снижается, особенно при использовании быстрого режима сбора крови. На таком фоне процесс агрегации достоверно замедляется, причем при быстром режиме сбора крови - в 2 раза в сравнении с контролем. Время рекальцификации плазмы достоверно уменьшается на 40% при использовании высокоскоростного режима сбора крови в сравнении с контрольными показателями, что почти в 3 раза выше, чем при применении медленной аспирации крови.

***Заключение.** В статье дано анализ научных изысканий, ККИ, экспериментального контроля, клинического контроля и практической работы. Работа имеет междисциплинарный характер, написана на стыке хирургии и анестезиологии, повысить результативность экстренной хирургии и анестезиологии-реаниматологии при критических полостных и просветных кровопотерях на основе оптимизации интраоперационной инфузионно-трансфузионной терапии.*

Ключевые слова
контролируемые клинические испытания, аппаратная интраоперационная реинфузия крови, плевральная полость

Баяу және жылдам режимдер жағдайында плевра қуысынан жиналған қанның аппараттық интраоперациялық реинфузиясының бақыланатын клиникалық сынамасын салыстырмалы бағалау

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Аңдатпа

***Мақсаты.** Қанның жылдам және баяу эксфузиясы режимінде жүргізілген зерттеуді талдау, бақыланбалы клиникалық зерттеулер тромбоциттер санының айтарлықтай азайғанын көрсетті.*

***Материал және әдістер.** Біз қуыстық қан жоғалтуы бар 44 науқаста бірқатар зерттеулер жүргіздік, бұл тексерілген науқастардың жалпы санының 34,3%-ы (n-128), олар интраоперациялық қан реинфузиясының аппараттық технологиясын (ИО ҚРАТ) пайдаланды. Алғашқы 2 сағатта операция кезінде де зерттеулер жүргізілді.*

***Нәтижелер.** Бақыланбалы клиникалық сынамалар (БКС) ИО ҚРАТ-тан кейін қанның эксфузиясы, қанның баяу эксфузиясы кезінде эритроциттер мен лейкоциттердің жойылу дәрежесі – 35%, ал жылдам қан эксфузиясы кезінде 48% екенін көрсетті. Осмостық төзімділік 3 есе азаяды. Жылдам аппараттық эксфузия кезінде қанның гемолизі 28%-дан асады, бұл аппараттық интраоперациялық қан реинфузиясын жүргізу кезінде ескерілуі керек. БКС аппараттық эксфузия неғұрлым жылдам орындалса, ақуыз мен билирубин мөлшерінің азаюы соғұрлым жоғары болатынын көрсетті. Жылдам аппараттық эксфузия режимінде жиналған қанда К+, қалдық N және несепнәрдің жоғары концентрациясы байқалады. БКС тромбоциттер санының айтарлықтай азайғанын көрсетті, әсіресе жылдам қан жинау режимін пайдаланған кезде байқалды. Осының аясында агрегация процесі айтарлықтай баяулайды, ал қан алудың жылдам режимінде - бақылаумен салыстырғанда 2 есе баяулайды. Бақылау мәндерімен салыстырғанда жоғары жылдамдықты қан жинау режимін пайдаланған кезде плазманы қайта кальцификациялау уақыты айтарлықтай 40%-ға қысқарады, бұл қанның баяу аспирациясын пайдаланған кездегіден 3 есе дерлік жоғары.*

***Қорытынды.** Мақалада ғылыми зерттеулер, БКС, эксперименттік бақылау, клиникалық бақылау және практикалық жұмыстарға талдау жасалған. Жұмыс интраоперациялық инфузионды-трансфузионды терапияны оңтайландыру негізінде қуыстық мен жарық аралық қан жоғалту кезінде жедел хирургиялық және анестезиологиялық-реаниматологиялық тиімділігін арттыру мақсатында хирургия мен анестезиологияның тоғысында жазылған пәнаралық сипатқа ие.*

Мүдделер қақтығысы
Авторлар мүдделер қақтығысының жоқтығын мәлімдейді

Түйін сөздер
бақыланбалы клиникалық сынамалар, аппараттық интраоперациялық қан реинфузиясы, өкпеқап қуысы

According to a number of authors, a decrease in fibrinogen and the number of platelets is apparently connected with their consumption during clotting in the cavity, and partly - with destruction in the aspiration system [2-4, 5-7, 9-10]. Meanwhile, an increase in thromboplastic activity, probably, on the one hand, is a consequence of the ingestion of tissue factors from the tissues damaged during the intervention into the collected blood, and on the other hand, it may be the result of hemolysis [1, 8-10].

An extensive experience in the use of intraoperative blood reinfusion (IOBR) apparatus has been accumulated in the national surgical practice. Kobzeva E.N. (2002) has developed a differentiated tactics of intraoperative fractioning of cavity and wound autoblood [6]. Kobzeva E.N. notes that the electronic microscopic studies of Nunaeva E.S. (1997) showed that erythrocytes used for IOBR have a method of apparatus processing, have normal structural and functional properties, which makes them capable of full functioning after IOBR [6].

Purpose

Comparative characteristics of the results of the following studies performed from the perspective of the controlled clinical trials (CCT):

1) experimental control (EC) - examination of the blood collected from the pleural and abdominal cavities before and after instrumental intraoperative blood reinfusion (IOBR) in conditions of simulating injuries to the abdomen and chest in animals with the corresponding formation of hemothorax and hemoperitoneum;

2) clinical control (CC) - examination of the blood collected from the abdominal and thoracic cavities before and after an IOBR apparatus in patients with injuries and wounds of the chest and abdomen with the corresponding formation of hemothorax and hemoperitoneum.

Material and methods

We have conducted a series of researches in 44 patients with cavitary blood loss, which is 34.3% of the total number of the examined patients (n-128), for whom an IOBR apparatus technology was used. The studies were also conducted during the surgery in the first 2 hours. The breakdown into clinical groups is shown on Table 1. As shown on Table 1, rapid mode of collection of the outflowing blood was used in 18 (40.9%) patients (group A), and slow mode (group B) was used in 26 (59.1%) patients. Moreover, 18 patients represented the clinical group for evaluation of physical-chemical state of the blood from the pleural cavity, while 26 - from the abdominal cavity.

Table 1.
Clinical groups for evaluation of physicochemical state of the blood collected from the abdominal and pleural cavity (A, B), as well as evaluation of the effectiveness (C, D) of IOBR in conditions of rapid and slow blood collection for IOBR (n-44)

Groups	Clinical control	n,%
Blood suitability evaluation		
A	Evaluation of physicochemical state of blood aspirated from the pleural and abdominal cavities in a slow mode	18 40,9%
B	Evaluation of physicochemical state of blood aspirated from the pleural and abdominal cavity in a rapid mode	26 59,1%
IOBR effectiveness evaluation		
C	Evaluation of the effectiveness of IOBR against the background of slow exfusion of blood from the cavities	26 59,1%
D	Evaluation of the effectiveness of IOBR against the background of rapid exfusion of blood from the cavities	18 40,9%

*IOBR – intraoperative blood reinfusion
CC – clinical control

OBR effectiveness evaluation was conducted in all 44 patients in whom the blood from the cavities was collected in various modes. Moreover, under the conditions of rapid mode (group C), the evaluation was conducted in 18 (40.9%) patients, and under the conditions of slow mode (group D) - in 26 (59.1%) patients.

We have developed the simplest apparatus IOBR technique. The device consists of a programmable time relay connected to a micro-vibration compressor and a suction unit. The compressor has knobs for adjusting the degree of vacuum generation. The compressor, from its part, is connected to a sealed, graduated sterile blood collection container.

The device works as follows: the free end of the line is connected to the tip, with a help of which the surgeon aspirates the blood that has poured into the chest or abdominal cavity during the surgery. The specified modification consists in the fact that a calibrated siliconized vessel with a capacity of 1000 ml and connected to a vacuum aspirator is used to collect blood.

The aspirated blood flows into a graduated reservoir with a blood stabilizer. For general practice, we recommend using the traditional TSIPK ampoule with TSOLIPK-7b. When using modern disposable systems for intravenous infusion, blood is sufficiently reliably filtered and returned by gravity into the patient's vein.

Results and discussion: Table 2 shows the dynamics of the morphology of the blood collected from the chest cavity at slow (1st group) and rapid (2nd group) modes.

Table 2.
Parallels of clinical control (CC) and experimental control (EC) of hemographic parameters at different blood aspiration for IOBR

Control	Indicators	Baseline	1st group	2nd group
CC	Er.	3,3±0,8	2,8±0,2*	2,3±0,3*,**
	CI	0,7±0,02	0,5±0,02	0,5±0,04*
	Hb	66,2±5,5	54,4±2,8*	51,0±2,2*,**
	Ht	32,2±2,2	31,5±2,2*	29,5±2,1*,**
	Leuk.	4,8±0,2	4,2±0,1*	4,2±0,2*
EC	Er.	3,5±0,3	2,8±0,1*	2,2±0,2*,**
	CI	0,8±0,01	0,6±0,01	0,5±0,02*
	Hb	98,6±7,4	80,1±3,6*	56,3±5,5*,**
	Ht	30,2±3,1	20,2±2,0*	14,8±2,2*,**
	Leuk.	6,6±0,4	3,4±0,2*	2,5±0,1*,**

Note: * - reliable in comparison with baseline level;
** - reliable in comparison with the 3rd group

As shown on Table 1, in both EC and CC, the number of Er. in the 2nd group decreases more significantly than in the 1st group (P <0.05). In CC and EC, similar dynamics are observed for CI, Hb, and Ht. The value of all indicators of hemogram in the 2nd group is reduced in comparison with those of the 1st group. Thus, for example, in EC, the Ht indicator in the 4th group is 2 times less than the baseline value (P <0.05). In CC, the gradient of the decline in this indicator is slower, but the trend remains as in EC. That is, in the 2nd group it is more noticeable than in the 1st group. According to EC data, the number of leukocytes decreases in the 1st group by almost half, and in the 2nd group - almost threefold (P <0.05 and P <0.05). According to CC, the decrease in leukocytes in the 1st and 2nd groups respectively is 0.8 times.

Table 3 shows the physical-colloid characteristics of the blood collected from the chest cavity, depending on the speed of its apparatus exfusion (slow and rapid modes).

Table 3.
Parallels of clinical control (CC) and experimental control (EC) of physicoloid parameters at different blood aspiration rates for IOBR

Control	Indicators	Baseline	1st group	2nd group
CC	Osm. resist. Er. (%)	0,8±0,01	0,7±0,01*	0,3±0,02*
	Hemolysis,% to total Hb	3,1±0,4	8,2±0,02*	10,8±0,3*,**
	Free Plasma Hb, mg%	1,0±0,01	6,6±0,6*	10,4±1,0*,**
EC	Osm. resist. Er. (%)	0,8±0,003	0,6±0,02*	0,4±0,02*
	Hemolysis,% to total Hb	6,3±0,3	8,8±0,07*	12,3±1,2*,**
	Free Plasma Hb, mg%	3,3±0,03	7,7±1,1*	31,2±2,5*,**

Note: * - reliable in comparison with baseline level;
** - reliable in comparison with the 3rd group

As shown on Table 3, in EC, osmotic resistance of erythrocytes during apparatus exfusion decreases: in the 1st group - by 1.5 times, and in the 2nd group - by 2 times (P <0.05 and P <0.05). The specific gravity of free plasma Hb significantly and sharply increases in both groups (P <0.05). Meanwhile, in a comparative aspect, the increase in free Hb in CC is less pronounced than in EC.

Thus, in EC, blood hemolysis with a slow mode of exfusion (group 1) is 8.8 ± 0.07%, and in the 2nd group - 12.3 ± 1.2% (P <0.05 and P < 0.05). In CC, 8.2 ± 0.02% and 10.8 ± 0.3% (P <0.05 and P <0.05) respectively.

Thus, the specific gravity of destruction of the blood corpuscles during rapid mode of apparatus blood exfusion reaches 48% in EC and 35% in CC.

Table 4 shows the dynamics of the content of protein and its fractions in blood collected from the pleural cavity for IOBR at slow (1st group) and rapid (2nd group) modes.

Control	Indicators	Baseline	1st group	2nd group
CC	Protein	54,2±6,6	50,2±2,2*	43,2±2,0*,**
	Albumen	30,2±6,2	42,5±2,3*	32,8±6,6
	Globulin	42,5±2,2	58,8±2,5*	55,3±3,8*
	A/G ratio	1,0±0,05	0,7±0,01*	0,6±0,05*,**
EC	Protein	59,2±4,1	53,4±3,3*	41,6±5,1*,**
	Albumen	41,4±3,9	40,0±5,1*	33,5±2,8
	Globulin	59,2±8,1	59,4±4,4*	65,9±3,6*,**
	A/G ratio	0,7±0,01	0,6±0,01*	0,5±0,05*,**

Table 4.
Parallels of CC and EC of proteinogram indicators at different blood aspiration rates for IOBR

Note: * - reliable in comparison with baseline level;
** - reliable in comparison with the 1st group

As shown on Table 4, in EC, the decrease in the concentration of the total protein, as well as its albumin fraction, is more pronounced in the 2nd group (P <0.05 and P <0.05). In CC the situation is the same (P <0.05 and P <0.05). Such dynamics is also typical for the albumin content, both in EC and CC. Moreover, the gradient of the decrease in this fraction of protein in plasma is more pronounced in the 2nd group, that is, during rapid mode of aspiration of cavity blood (P <0.05 and P <0.05).

Table 5 shows the dynamics of a number of biochemical parameters of the blood collected from the chest cavity at slow (1st group) and rapid (2nd group) collection modes.

Control	Indicators	Baseline	1st group	2nd group
CC	Bilirubin	15,3±2,4	18,8±1,2*	21,5±2,2*,**
	Residual N	19,3±1,01	28,2±1,5*	33,4±2,1*,**
	Urea	4,8±0,4	25,8±2,6*	36,2±2,0*,**
	Na^{++}	140,2±5,5	142±2,2	145±3,1
	K^{+}	4,1±0,2	5,0±0,1*	5,0±0,3*
EC	Bilirubin	5,2±0,3	5,6±0,4	5,2±0,1
	Residual N	31,4±9,2	33,6±2,3*	56,2±6,2*,**
	Urea	8,2±0,9	23,6±251*	66,7±7,7*,**
	Na^{++}	144,5±3,8	136±8,8	144±5,9
	K^{+}	5,1±0,3	5,3±0,1*	5,9±0,3*,**

Table 5.
Parallels of clinical control (CC) and experimental control (EC) of biochemical parameters at different blood aspiration rates for IOBR

Note: * - reliable in comparison with baseline level;
** - reliable in comparison with the 1st group

As shown on Table 5, in EC, the concentration of bilirubin is practically the same in the compared groups, while the residual N and blood urea increased several times in comparison with the baseline values (P <0.05 and P <0.05). Moreover, in the 2nd group, a similar tendency is more pronounced than in the 1st group.

In CC, there is a tendency to an increase in the concentration of bilirubin. In particular, in the 1st group up to 18.8 ± 1.2 mmol/L and in the 2nd group - up to 21.5 ± 2.2 mmol/L (P <0.05 and P <0.05). Such dynamics is also typical for the content of the residual N and urea. By the way, the trend towards hyperkalemia is more pronounced for EC.

Discussion. Based on the extended hemostasiogram of the blood collected from the chest cavity, depending on the rate of apparatus blood exfusion (slow and rapid modes of aspiration) in EC, we found that

the number of platelets in EC significantly decreases in both groups (P <0.05 and P <0.05). Moreover, in the 2nd group, this process is more pronounced than in the 1st group. Similar dynamics and regularity are also characteristic of platelet aggregation and adhesion (P <0.05 and P <0.05).

Thus, during rapid apparatus collection, the blood clotting process increases. This is evidenced by the fact that in EC there is a more rapid rate of shortening of Lee-White coagulation time in siliconized and non-siliconized trial tubes. It should be noted that in the 2nd group this fact is noticeable more clearly.

In the 2nd group, the plasma recalcification time decreases by almost 2 times in comparison with the baseline level (P <0.05), and the kaolin and kaolin-cephalin time of plasma - > 2 times (P <0.05 and P <0.05), making, respectively, 30.1 ± 1.9 sec (against the baseline value - 64.4 ± 3.8 sec) and 25.5 ± 1.0 sec (against the baseline value - 62.4 ± 8.8 sec).

In both groups, there was a synchronous shortening of thrombin and prothrombin times (P <0.05 and P <0.05). Moreover, the same regularity remains as was the case with respect to the time of blood coagulation. That is, in the 2nd group, the dynamics of the shortening of time is more pronounced than in the 1st group. Moreover, the prothrombin time is shortened more rapidly than the thrombin time.

Against this background, the content of fibrinogen in both groups increases. In particular, in the 1st group - up to 2.4 ± 0.3 g/L and in the 2nd group - up to 3.1 ± 0.2 g/L versus the control value - 1.9 ± 0.2 g/L (P <0.05 and P <0.05). It was found that the duration of euglobulin fibrinogen also increased (P <0.05). Meanwhile, in all periods of the ACT reactions (6, 8 and 10 minutes), on the contrary, they are shortened. Especially, this process is noticeable in the 2nd group (P <0.05).

On the basis of the extended hemostasiogram of blood collected from the chest cavity, depending on the rate of apparatus blood exfusion (slow and rapid modes of aspiration) in CC we found that in the compared groups there was a synchronous decrease in the number of platelets, as well as their aggregation and adhesion (P <0.05 and P <0.05). In both 1st and 2nd groups, a shortening of thrombin and prothrombin times is observed.

It should be noted that such a synchronicity and such a pattern persists in relation to the time of blood coagulation. Moreover, a certain synchronicity is manifested in EC and CC.

Thus, in CC and EC, it is noticeable that in the 2nd group the dynamics of time shortening is more intense than in the 1st group. Moreover, in both materials (experimental and clinical), the prothrombin time is shortened more rapidly than the thrombin time.

As for the concentration of fibrinogen, in the compared groups it clearly increases, both according to EC data and according to CC data. In particular, in EC in the 1st group, fibrinogen increases to 2.4 ± 0.3 g/L, and in the 2nd group - to 3.1 ± 0.2 g/L versus the control value - 1.9 ± 0.2 g/L (P <0.05 and P <0.05).

In CC, the indicators are 2.6 ± 0.2 g/L and 3.3 ± 0.6 g/L, respectively (P <0.05 and P <0.05). Simultaneously with this process, the duration of euglobulin fibrinogen (P <0.05) also increases in both research materials. It was found that the ACT reaction (6, 8 and 10 min) are shortened during all periods, especially in the 2nd group - 2 times in average (P <0.05).

Conclusion

Starting the conclusion, it should be noted that the results of systematization of long-term and multifaceted scientific and practical data provide the ground for classification of the problem of emergency blood replacement in cases of intraoperative bleeding (cavity, luminal) as a poorly structured subject area. This is due to the fact that, as a rule, new methods are applied to new research objects at different stages of research.

These methods often belong to different methodological clusters. We mean the use of experimental, clinical, statistical, probabilistic studies, each method of which has its own interval of abstraction. In this aspect, we believe that the scientific justification of the adapted IO ITT (intraoperative infusion-transfusion therapy) program should be based on the comparative characteristics of the data obtained in the result of using the methods of various methodological clusters (EC, CC, CCI).

One way or another, at some stage of the study of the problem, it becomes necessary to perform a conceptual unfolding of an object in the form of a set of its projection in various methodological clusters.

Taking into account the above, we have put a target to increase the effectiveness of emergency operation and anesthesiology and resuscitation in critical cavity and luminal blood loss based on the optimization of IO ITT. Moreover, the optimization was supposed to be built on the basis of many years of research, which are purely experimental, clinical, statistical, methodological, probabilistic in nature.

First, there is a clear parallel between CC and EC, indicating the relevance of experimental and clinical laboratory research methods;

Second, there is a clear connection between the timing of hemoperitoneum and hemothorax, as well as the nature of changes in the hemostasis system in the blood collected, respectively, from the abdominal and thoracic cavities. The degree of destruction of formed elements in the blood collected from the pleural cavity exceeds the one in the blood collected from the abdominal cavity and, in general, the process of hemolysis of the blood poured into the pleural cavity is more intense than the one in the blood poured into the abdominal cavity.

Third, there is a clear parallel between CC and EC data that the main function of the collected blood – transportation of O2 is preserved to a sufficient extent, regardless of the pleural or abdominal cavity. At the same time, due to the more pronounced hemolytic ability of the pleural cover, the quality of the blood collected from the pleural cavity is inferior to the one of the blood collected from the abdominal cavity.

In our opinion, the results of CCI with determination of the relevance of CC and the effectiveness of IO BRI (intraoperative blood reinfusion) apparatus are in the following evidence:

First, there is a clear parallel between CC and EC, indicating the relevance of experimental and clinical laboratory research methods;

Second, in case of EC after IO BRI, the degree of destructibility of erythrocytes and leukocytes in case of slow blood exfusion is 35%, and in case of rapid blood exfusion is 48%. Osmotic resistance is reduced by 3 times. With rapid apparatus exfusion, blood hemolysis is more than 28%, which should be taken into account when performing the apparatus IO BRI;

Third, the faster the apparatus exfusion is performed, the more significant is the decrease in the protein and bilirubin content both in case of EC and CC. A higher concentration of K+, residual N and urea is noted in the blood collected in the mode of rapid apparatus exfusion;

Fourth, platelet count is significantly reduced, especially when using a rapid blood collection mode. Against this background, the process of aggregation is reliably slowed down, and in case of rapid mode of blood collection - 2 times in comparison with the control. Plasma recalcification time is reliably reduced by 40% when using a rapid blood collection mode in comparison with the control parameters, which is almost 3 times higher than when using the slow blood aspiration;

Fifth, in case of EC, 4 hours after IO BRI using the technology of slow blood exfusion, hemographic and biochemical parameters increase. When using the technology of rapid blood exfusion, the number of platelets decreases and the degree of their aggregation and adhesion decreases.

After IO BRI under the conditions of the given rates of apparatus exfusion of autologous blood, the concentration of K + and Na ++ in the blood plasma increases, and after rapid exfusion - to critical values.

We investigated the limits of justification of the adapted IO ITT program for critical luminal blood loss, depending on the rate of bleeding and the severity of the patient's condition. They demonstrated the following results:

First, in case of profuse bleeding, the proportion of lethality with expectant tactics is 10%, while in case of active bleeding it is 2 times less (5%). At the same time, the proportion of postoperative complications is 4 times lower with active tactics than with active expectant tactics;

Second, against the background of using the adapted ITT program, the chances of a favorable outcome of the operation increase by 30% when using active tactics in patients, and the level of risk of an unfavorable outcome in case of using the expectant tactics is 2 times less (15%);

Third, in a serious condition of patients, the proportion of mortality in case of active tactics is 6.2%, and in case of active-expectant tactics it increases almost 7 times, amounting to 41.6%;

Fourth, against the background of implementation of the adapted ITT program in patients in extremely serious condition and in whom active operative tactics were undertaken, the chances of a favorable outcome of the operation increase by 82%, and the level of risk of an unfavorable outcome in case of using active expectant tactics increases by 15%.

This is what our studies have demonstrated regarding the limits of justification of the adapted IO ITT program for critical luminal blood loss, depending on the massive blood loss and the old age of patients:

First, in patients with the III stage of blood loss and in whom active operative tactics were undertaken, postoperative complications were observed in 25% of patients, while in patients in whom active expectant tactics were undertaken, complications developed in 50% of patients. Moreover, in patients in whom active tactics were undertaken, mortality was observed only in 6.2% of patients, while in patients in whom active expectant tactics were undertaken - in 41.6% of patients;

Second, in patients with the III stage of blood loss and in whom active operative tactics were undertaken, the chances of a favorable outcome of the operation increase by 30%, and the level of risk of an unfavorable outcome in case of using the active-expectant tactics increases by 15%;

Third, in patients with the II stage of blood loss and in whom active operative tactics were undertaken, postoperative complications developed in 10% of patients, whereas in patients with the same degree of blood loss, but operated on in a delayed period, according to their active expectant tactics, complications were noted in 40% of patients. Thus, there is a 4-fold increase in postoperative complications. At the same time, the proportion of mortality in case of active tactics is 10%, while in patients operated on in delayed periods - 5%;

Fourth, in patients with the II stage of blood loss and who underwent the operation in the early stages, the chances of a favorable outcome of the operation increase by 60%, and the level of risk of an unfavorable outcome in case of a delay in the operation increases by 15%;

Fifth, the proportion of mortality in patients at the age of > 60 in case of active surgical tactics is 6.4%, and in case of active-expectant tactics it increases 9 times (57.1%). The proportion of postoperative complications in case of active tactics is 24.3%, and in case of active-expectant - 29.2%. The chances of a favorable outcome in case of active tactics increases by 82%, and the level of risk of an unfavorable outcome in case of active-expectant tactics is 7.5 times less (15%).

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

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

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)*

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).

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

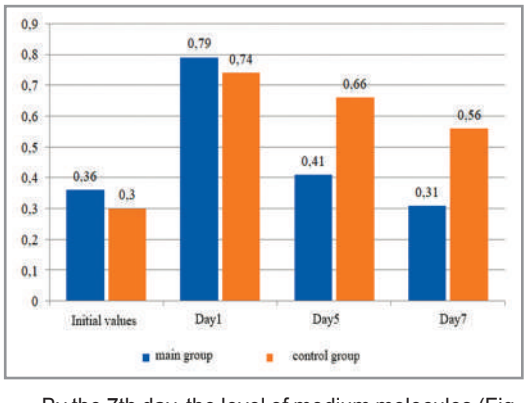
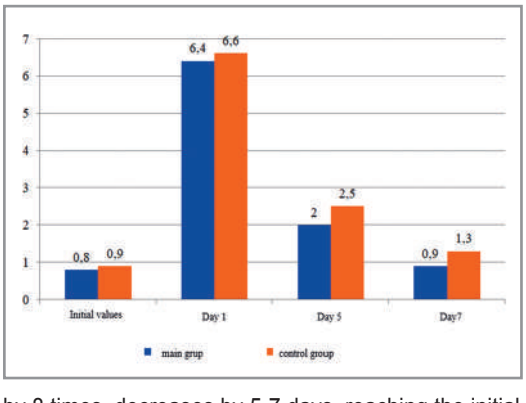


Figure 2.
HII-hematological index of intoxication



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

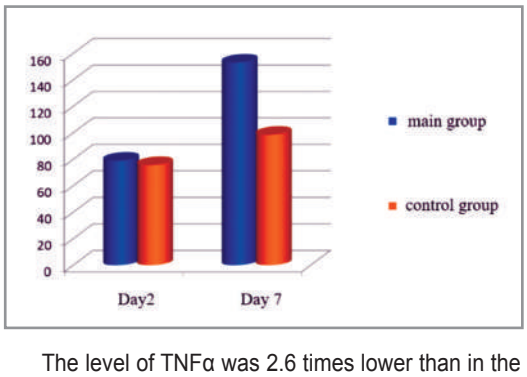
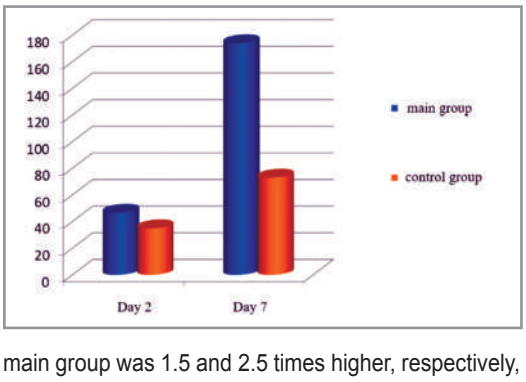


Figure 4.
Interleukin 2



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 ($p < 0.05$).

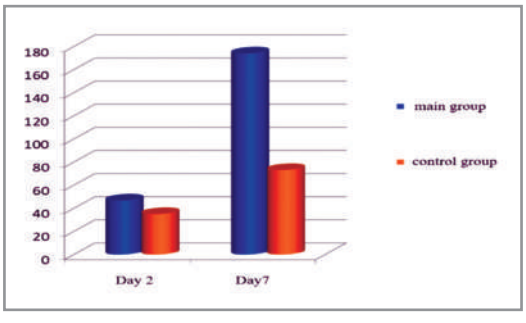
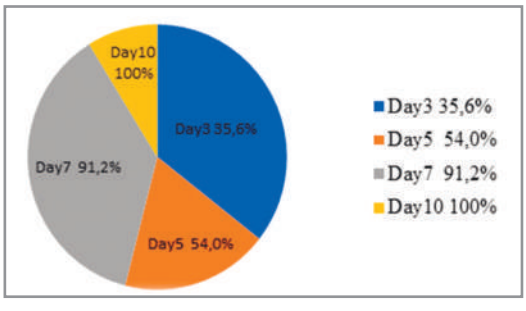


Figure 5.
TNFα in dynamics



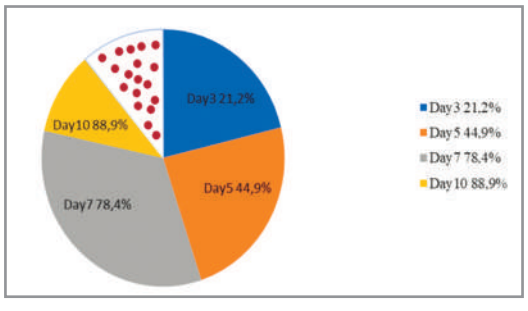


Figure 6.
Wound healing rate of the main group

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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CORONARY PULMONARY FISTULA

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

Keywords
coronary fistula, vascular anomaly, congenital defect

Abstract

Coronary arteriovenous fistula (CAF) is a rare form of congenital heart disease. However, it is the most common type of congenital anomaly of the coronary arteries. [1] When there is the connection between the coronary artery and the chambers of the heart, it is called a coronary chamber fistula. The fistula may also be between a coronary artery and another adjacent vessel from the pulmonary or systemic circulation. An open fistula provides low-resistance flow by directing blood from an artery into a vein, heart chamber, or other low-pressure vessel such as the pulmonary artery. Patients with CAF may develop symptoms at birth or later in life, depending on the type of fistula and the presence of collateral circulation. Studies have reported an association between ventricular arrhythmias and sudden cardiac death syndromes in young adults and athletes with certain types of coronary anomalies, such as anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) [2-5]. The most common symptom is a myocardial ischemia. The purpose of this article is to present a clinical case of endovascular treatment of coronary pulmonary fistula. As a result of a modern diagnostic methods, such as CT angiography with three-dimensional reconstruction, it is not difficult to assess the degree and nature of the pathology. Having assessed the tactics, modern doctors are able to cope with coronary arteriovenous fistulas with great success using minimally invasive X-ray endovascular technologies.

Коронарно-пульмональная фистула

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Ключевые слова
коронарная фистула, аномалия сосудов, врожденный порок

Аннотация

Коронарная артериовенозная фистула (КАФ) является редкой формой врожденного порока сердца. Тем не менее, это наиболее распространенный тип врожденных аномалий коронарных артерий. Когда он находится между коронарной артерией и камерами сердца, он называется коронарно-камерным свищом. Свищ также может быть между коронарной артерией и другим соседним сосудом из легочного или большого круга кровообращения. Открытая фистула обеспечивает поток с низким сопротивлением, направляя кровь непосредственно из артерии в вену, сердечную камеру или другой сосуд с низким давлением, такой как легочная артерия. У пациентов с КАФ симптомы могут развиваться при рождении или в более позднем возрасте, в зависимости от типа фистулы и наличия коллатерального кровообращения. В исследованиях сообщалось о связи между желудочковыми аритмиями и синдромами внезапной сердечной смерти у молодых людей и спортсменов при определенных типах коронарных аномалий, таких как аномальное отхождение левой коронарной артерии от легочной артерии (ALCAPA). Одышка при физической нагрузке и стенокардия из-за ишемии миокарда являются самыми частыми симптомами. В данной статье представлен клинический случай эндоваскулярного лечения коронарно-пульмональной фистулы. На данный момент, благодаря современным методам диагностики, таких как КТ ангиография, с трехмерной реконструкцией, оценить степень и характер патологии не составляет труда. Оценив тактику, современные врачи с большим успехом способны справиться с коронарными артериовенозными фистулами с использованием малоинвазивных рентгенэндоваскулярных технологий.

Коронарлық өкпе фистуласы

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Аңдатпа

Коронарлық артериовенозды фистула (КАФ) туа біткен жүрек ақауының сирек түрі болып табылады. Дегенмен, бұл коронарлық артериялардың туа біткен аномалиясының ең көп таралған түрі. Коронарлық артерия мен жүрек камералары арасында болса, оны коронарлық-камералық фистуласы деп атайды. Сондай-ақ, фистула коронарлық артерия мен өкпе немесе жүйелі қан айналымынан басқа іргелес тамыр арасында болуы мүмкін. Ашық фистула қанды артериядан тікелей тамырға, жүрек камерасына немесе өкпе артериясы сияқты басқа төмен қысымды тамырға бағыттау арқылы төмен қарсылық ағынын қамтамасыз етеді. КАФ бар емделушілерде фистула түріне және коллатеральды қан айналымының болуына байланысты туылғанда немесе кейінгі өмірде сипаттамалар дамуы мүмкін. Зерттеулер өкпе артериясынан сол жақ коронарлық артерияның аномалиялық шығу тегі (ALCAPA) сияқты коронарлық аномалиялардың белгілі бір түрлері бар жас ересектер мен спортшылардағы қарыншалық аритмиялар мен кенеттен жүрек өлімі синдромдары арасындағы байланыстарды хабарлады. Миокард ишемиясының әсерінен күш түскендегі ентігу және стенокардия - ең жиі кездесетін белгілер. Бұл мақалада коронарлық өкпе фистуласының эндоваскулярлық емінің клиникалық жағдайы берілген. Қазіргі уақытта үш өлшемді реконструкциямен КТ ангиографиясы сияқты заманауи диагностикалық әдістердің арқасында патологияның дәрежесі мен сипатын бағалау қиын емес. Тактиканы бағалай отырып, заманауи дәрігерлер минималды инвазивті рентгендік эндоваскулярлық технологияларды қолдана отырып, коронарлық артериовенозды фистулаларды үлкен табыспен жеңе алады.

Мүдделер қақтығысы
Авторлар мүдделер қақтығысының жоқтығын мәлімдейді

Түйін сөздер
коронарлық фистула, қан тамырлары аномалиясы, туа біткен ақау

Relevance

A coronary artery fistula or coronary arteriovenous fistula is a congenital or acquired defect characterized by an abnormal connection of a coronary artery with a pulmonayr or systemic circulation, as well as with one or more chambers of the heart, bypassing the capillary blood flow. Coronary arteriovenous fistulas occur in the population in 0.002% of cases, and in 0.25% of patients undergoing coronary angiography [6–9].

CAF was first described by Krause in 1865. [10], revealed by coronary angiography. Haller and Little described the characteristic clinical triad of CAF: murmurs, left-to-right atrial or ventricular shunt, and dilated, tortuous coronary arteries. CAF can lead to severe hemodynamic disorders such as myocardial ischemia, cardiac arrhythmias, heart failure, and infective endocarditis in adults [11]. The classification according to Sakakibara (12) is often used to classify CAF, according to which the division according to the type of vessel origin is important: from the proximal or distal segment of the coronary arteries.

The proximal type of fistula discharge is characterized by normal diameters of the involved coronary arteries. In the case of the distal type, the entire coronary artery often expands and often ends in the right heart.

The main pathogenetic mechanism is related to the drainage of blood from high pressure blood vessels into a low pressure system through a fistula.

Causes of CAF can be congenital or acquired. More than 90% of CAFs are congenital [13]. During early fetal development, the sinusoids feed the primitive myocardium, which is associated with the primitive tubular heart. Later, in adulthood, sinusoids usually transform into Thebesian vessels and capillaries. Persistent sinusoids that do not regress may contribute to a fistulous connection between coronary arteries and heart chambers [14, 15]. There is also a residual primitive connection between the coronary arteries and other mediastinal vessels (eg, bronchial, pericardial, or mediastinal arteries) or the superior vena cava, which may contribute to the development of a coronary arteriovenous fistula [16]. Acquired CAF results from iatrogenic events such as coronary stenting, coronary artery bypass grafting, trauma, and chest radiation [17, 18]. Some diseases, such as coronary vasculitis and myocardial infarction, can lead to the development of CHF in the chronic phase [19].

Description of the clinical case

The purpose of this article is to present a clinical case of endovascular treatment of coronary pulmonary fistula. Patient M., 60 years old, a resident of the Almaty region, was admitted to JSC «NSC of surgery named after Syzganov A.N.'' with a diagnosis of Congenital heart disease. Coronary pulmonary fistula. Atrial fibrillation. Cryoablation in 2021. CH II FC by NYHA.

The first time patient was admitted to our center in September 2021. with complaints related to cardiac arrhythmias, interruptions in the work of the heart, the patient was additionally examined at the center. Due to the AF Cryoablation was performed. Selective polypositional coronary angiography re-

vealed anomalies associated with the coronary arteries. Because of the low ejection fraction by echocardiography (29%), was made a decision to implant a cardioverter defibrillator. The patient was discharged with an improvement in his general condition, and inncreasing in EF up to 36% was noted during the control EchoCG.

In January 2022 the patient is re-admitted to the Department of Interventional Cardiology, Arrhythmology and Endovascular Surgery of our Center. According to EchoCG, LV EDV is noted: 151 ml, LV ESV: 74 ml, SV 77 ml, EF 51%. interventricular septum thickness 1.2 cm. RVSP 24 mm Hg. The valves are intact. According to the ECG: Horizontal position of the electrical axis. LV hypertrophy. Myocardialischemia of the posterior wall of the left ventricle. The patient complains of shortness of breath, mild angina pectoris, and general weakness. The patient was taken to the «cath lab»: after processing the surgical access was secured through the right radial artery using the Seldinger method. Selective polypositional coronary angiography revealed: LCA trunk - stenosis up to 30%, passable. LAD - stenosis in the proximal third up to 80%. There is an aberrant vessel in the CxA, which has a tortuous course with angiomatous nodes with a transition to an aneurysmal expansion in the final segment up to 3.0 mm and a fistula into the left pulmonary artery, the diameter of the fistula is 4.5-5.0 mm. C type by Sakakibara. RCA - in the proximal third there is an aberrant vessel with a tortuous course, expanded to 5.0 mm in the final segment and a fistula with a diameter of 4.5 mm communicating with the pulmonary artery trunk. A coronary guidewire was inserted into the coronary pulmonary fistula, into it is supply vessel, on which a microcatheter «Maestro Merit» was delivered. A Nester Embolization Coil was passed through the microcatheter and delivered. During embolization, the number of coils was not enough, and therefore it was decided to use a coronary stent Ultimaster 4.5-15 mm, which was implanted in the distal third of the OA at the site of the coronary-pulmonary fistula. During control coronary angiography, the discharge of contrasted blood through the coronary-pulmonary fistula was eliminated and completely occluded.

There were no complications during the operation. The patient was transferred to the ward for dynamic observation. The patient was discharged a few days later. Subsequently, the patient is scheduled to undergo embolization of the RCA fistula and stenting of the LAD of the LCA. As a result of treatment, the patient's general condition improved, chest pains ceased to bother, shortness of breath decreased.

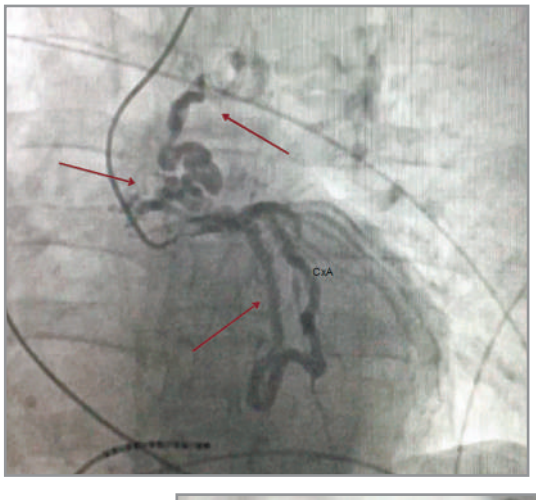

Figure 1.
Selective coronary angiography of the LCA, direct projection. The arrows indicate tortuous aberrant vessels originating from the CxA

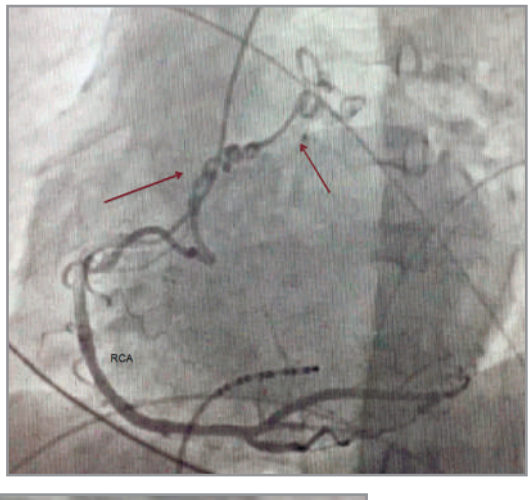

Figure 2.
Selective coronary angiography of the RCA, direct projection. Arrows indicate tortuous aberrant vessels originating from the RCA RCA CxA

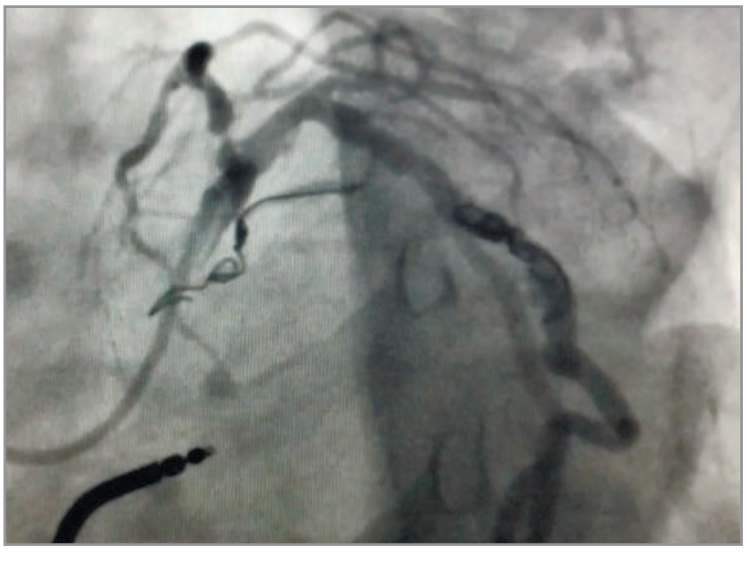

Figure 3.
Selective coronary angiography of the CxA, direct projection. Final view after embolization of the aberrant vessels

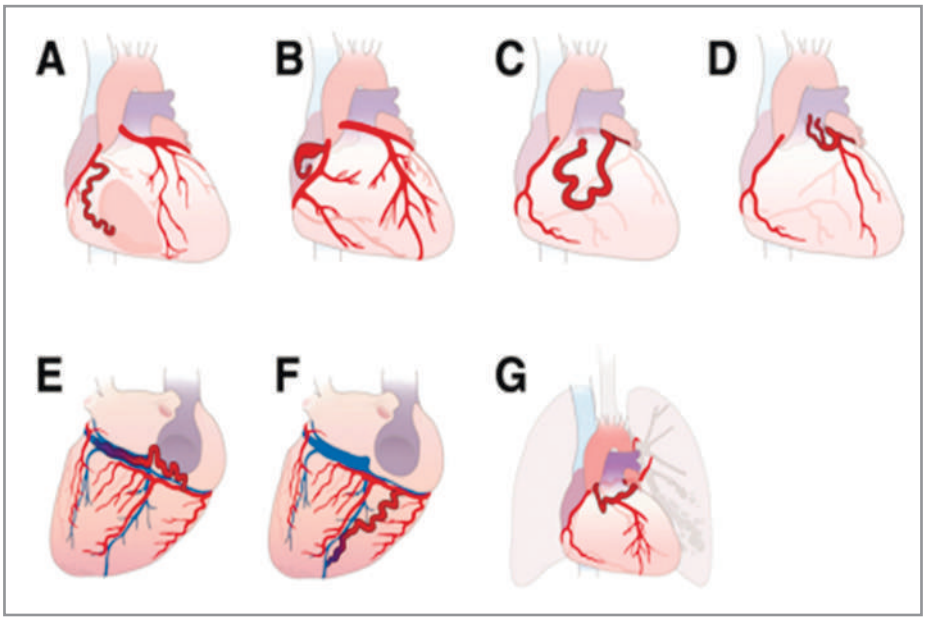

Figure 4.
Classification of CAF according to the type of drainage [12]
A - fistula with communication of the chamber of the right ventricle; B — fistula involving the right atrial chamber; C - fistula from the coronary artery to the pulmonary artery, with the presence of one large fistulous tract; D - coronary artery - pulmonary artery, fistula with multiple small fistulas; E - coronary artery fistula communicates with the coronary sinus; F - coronary artery-venous fistula; G - coronary artery-fistula of the bronchial artery.

Discussions

Unfortunately, at the moment there are no single accepted protocols for the postoperative management of patients with this pathology. According to some authors, 10% of cases of transcatheter or surgical treatment were subject to CAF recanalization [20].

Zhang and colleagues [21] reported that CAF recanalization occurs within 1 year, suggesting the importance of assessing the residual shunt in the early postoperative period. Although a residual shedding of less than 2–3 mm can be observed without further intervention, careful monitoring during the postoperative follow-up period is necessary [21, 22].

Other possible complications after coil embolization or surgical ligation of the coronary arteries include persistent dilatation or aneurysmal changes in the ostia and coronary arteries, as well as the formation of blood clots, which can lead to myocardial ischemia and even infarction [23].

According to some authors, ECG changes and arrhythmias may also occur during and after transcatheter closure [24]. In CAF with a large fistulous tract, coil migration is possible [25]. On the other hand, in patients with small branching vessels, incomplete shunt occlusion may occur if coils are placed distal to the branching point [26]. Incomplete CAF occlusion or the presence of a foreign body increases the risk of infective endocarditis [17].

Conclusion

CAF is one of the rare pathologies with a high variability of clinical manifestations, which include such formidable complications as myocardial infarction and heart failure. As a result of a modern diagnostic methods, such as CT angiography with three-dimensional reconstruction, it is not difficult to assess the degree and nature of the pathology. Having assessed the tactics, modern doctors are able to cope with coronary arteriovenous fistulas with great success using minimally invasive X-ray endovascular technologies.

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FEATURES OF AFP EXPRESSION LEVEL AT DIFFERENT STAGES AND GRADATIONS OF HCC, CORRELATION ANALYSIS BETWEEN SERUM AFP

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

Keywords
hepatocellular carcinoma, serum alpha-fetoprotein, immunohistochemistry, stage, grade

Abstract

Hepatocellular carcinoma (HCC) is a malignant tumor of the liver which accounts for up to 90% of all liver cancers.

In recent years, there has been an increase in the incidence of HCC all over the world, including in Kazakhstan. Diagnostic issues are still important. Alpha-fetoprotein (AFP) is a specific marker most widely used in the diagnosis of HCC. The article describes of the features of the AFP expression level in immunohistochemical studies with different stages and gradation of hepatocellular carcinoma, as well as a correlation analysis with serum AFP.

Material and methods. *A total of 50 patients with HCC were analyzed. Blood serum tests were performed to determine the level of AFP and an IHC study to assess the expression of AFP.*

Results. *When analyzing the serological AFP, it was found that in the vast majority of cases (n=33), values were between 10-20 units/ml. In 83% cases HCC, cytoplasmic and nuclear expression of AFP was determined in malignant cells in IHC. The expression of the AFP was high in 32% cases, moderate in 46% cases, and low or not detected in 22% cases. The area of AFP - immunopositive cells node averaged 37.25±15.47%. When conducting a correlation analysis, it was found that the overall Pearson correlation coefficient between serum AFP and the degree of AFP staining was r = +0.0089.*

Conclusion. *Critically high AFP values correlate with the degree of HCC differentiation. The results of IHC showed that in 83% of patients with HCC, cytoplasmic and nuclear expression of AFP, which indicates a high sensitivity of the marker regarding the definition of malignancy. Given the absence of a correlation, it can be assumed that the serum AFP value cannot be associated with AFP expression data in immunohistochemistry and can be used as a separate value for HCC differentiation.*

Гепатоцеллюлярлық карциноманың түрлі сатылары мен градацияларындағы афп экспрессиясы деңгейінің ерекшеліктері, сарысулық афп арасындағы корреляциялық талдауы

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Аңдатпа

Гепатоцеллюлярлы карцинома - гепатоциттерден пайда болатын бауырдың қатерлі ісігі, бауырдың барлық қатерлі ісіктерінің 90% құрайды.

Соңғы жылдары бүкіл әлемде, оның ішінде Қазақстандада гепатоцеллюлярлық карциноманың алғашқы анықталған жағдайларының кездесу жиілігінің артуы байқалады. Қазіргі уақытта диагностикалық мәселелер әлі де маңызды болып қала береді. Альфафетопротеин ерекше маркер, ГЦК диагнозында кеңінен қолданылады. Мақалада әртүрлі сатымен және гепатоцеллюлярлық карциноманың градациясымен иммуногистохимиялық зерттеу кезінде АФП экспрессия деңгейінің ерекшеліктерін талдау, сондай-ақ сарысулық АФП-мен корреляциялық талдау сипатталады.

Мүдделер қақтығысы
Авторлар мүдделер қақтығысының жоқтығын мәлімдейді

Материал және әдістер. *Ашық хирургиялық ота жоспарлаған ГЦК-ы бар 50 пациенттің деректері талданды. Барлық пациенттерде АФП деңгейін анықтау үшін қан сарысуын зерттеу және АФП экспрессиясын бағалау үшін ИГХ зерттеу жүргізілді.*

Нәтижелер. *Серологиялық АФП деңгейін талдау кезінде басым көпшілік жағдайларда (n=33) АФП мәндері 10-20 бірлік/мл арасында болғаны анықталды, жүргізілген иммуногистохимиялық зерттеулердің нәтижелері ГЦК-ы бар науқастардың 83% - ында қатерлі жасушаларда АФП цитоплазмалық және ядролық экспрессиясы анықталатынын көрсетті. ГЦК түйініндегі АФП маркерінің экспрессия деңгейі 32% (n=16) жағдайда жоғары, 46% (n=23) жағдайда - орташа және 22% (n=11) жағдайда - төмен немесе мүлдем анықталмаған. ГЦК торабындағы АФП-иммунопозитивті жасушалардың ауданы орта есеппен 37,25±15,47% - ды құрады. Корреляциялық талдау жүргізу кезінде сарысулық АФП мен ИГХ-дағы АФП бояу дәрежесі арасындағы Пирсонның жалпы корреляция коэффициенті r = +0,0089 құрағаны анықталды.*

Қорытынды. *АФП-нің сыни жоғары мәндері ГЦК саралау деңгейімен байланысты. ИГХ нәтижелері патологиялық жасушаларда ГЦК бар науқастардың 83%-ында α-фетопротеиннің цитоплазмалық және ядролық экспрессиясы анықталатынын көрсетті, бұл қатерлі ісікті анықтауға қатысты маркердің жоғары сезімталдығын көрсетеді. Корреляциялық байланыстың жоқтығын ескере отырып, сарысулық АФП мәні иммуногистохимия кезінде АФП экспрессиясының деректерімен байланысты болмайды және ГЦК дифференциалдау үшін жеке мән ретінде қолданылуы мүмкін деп болжауға болады.*

Түйін сөздер
гепатоцеллюлярлық карцинома, сарысулық альфафетопротеин, иммуногистохимия, сатысы, градациясы

Особенности уровня экспрессии афп при различных стадиях и градациях гцк, корреляционный анализ между сывороточным афп

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Аннотация

Гепатоцеллюлярная карцинома – злокачественная опухоль печени, происходящая из гепатоцитов, составляет до 90% всех раков печени. В последние годы наблюдается увеличение частоты встречаемости первично выявленных случаев гепатоцеллюлярной карциномаы во всем мире, в том числе и в Казахстане. В настоящее время вопросы диагностики остаются все еще важными. Альфафетопротеин специфичный маркер, наиболее широко используемый в диагностике ГЦК. В статье описывается анализ особенностей уровня экспрессии АФП при иммуногистохимическом исследовании с различной стадией и градацией гепатоцеллюлярной карциномы, а также корреляционный анализ с сывороточным АФП.

Материал и методы. *Всего были проанализированы данные 50 пациентов с ГЦК, которым планировались открытые хирургические вмешательства. У всех пациентов были выполнены исследования сыворотки крови для определения уровня АФП и ИГХ исследование для оценки экспрессии АФП.*

Результаты. *При анализе уровня серологического АФП было выявлено, что в преобладающе большинстве случаев (n=33) значения АФП находились между 10-20 ед/мл. Результаты проведенных иммуногистохимических исследовании показали, что у 83% больных с ГЦК в злокачественных клетках определяется цитоплазматическая и ядерная экспрессия АФП. Уровень экспрессии маркера АФП в узле ГЦК в 32% (n=16) случаях был высоким, в 46% (n=23) случаях - умеренным, и в 22% (n=11) случаях - низким или же вовсе не определялся. Площадь АФП - иммунопозитивных клеток в узле ГЦК в среднем составила 37,25±15,47%. При проведении корреляционного анализа было выявлено, что общий коэффициент корреляции Пирсона между сывороточной АФП и степенью окрашивания АФП на ИГХ составил r = +0,0089.*

Заключение. *Критически высокие значения АФП коррелируют со степенью дифференцировки ГЦК. Результаты ИГХ показали, что у 83% больных с ГЦК в патологических клетках определяется цитоплазматическая и ядерная экспрессия α-фетопротеина, что свидетельствует о высокой чувствительности маркера касательно определения злокачественности. Учитывая отсутствия корреляционной связи, можно предположить, что значение сывороточной АФП не могут быть ассоциированы с данными экспрессии АФП при иммуногистохимии и могут быть применены как отдельное значение для дифференцировки ГЦК.*

Конфликт интересов
Авторы заявляют об отсутствии конфликта интересов

Ключевые слова
гепатоцеллюлярная карцинома, сывороточный альфафетопротеин, иммуногистохимия, стадия, градация

Introduction

Liver cancer is currently the second most common cancer-associated cause of death worldwide [1]. Hepatocellular carcinoma (hepatoma, hepatocellular carcinoma), a malignant liver tumor originating from hepatocytes, accounts for up to 90% of all liver cancers [2].

In recent years, there has been an increase in the frequency of HCC throughout the world, for example, more than 600,000 newly diagnosed cases are recorded annually [3].

According to GLOBOCAN 2018, in the structure of oncopathology in terms of the incidence of HCC, it ranks 6th after lung and breast cancer, colorectal cancer, prostate and stomach cancer, and in terms of mortality it takes 4th place after lung cancer, colorectal cancer and cancer of stomach. However, in men, the incidence of morbidity and mortality from HCC is 2-3 times higher than in women, therefore, the incidence and mortality rates in men ranked 5th and 2nd, respectively [4, 5].

The etiology of HCC is multifactorial [6]. The main reasons for the development of HCC worldwide are chronic hepatitis (hepatitis B and C virus infections) and liver cirrhosis [7]. Aflatoxin B1 (AFB1) and chronic alcohol abuse may also be additional factors [8].

The highest HCC rates are observed in countries with economies in transition with a low human development index, for example, in some countries in Africa (Egypt, Gambia, Guinea) and East and Southeast Asia (Mongolia, Cambodia, and Vietnam). In Mongolia, the incidence of HCC is significantly higher than in any other country [4, 5].

Major risk factors vary by region. In regions with the highest risk of HCC (China, East Africa), chronic HBV infection and exposure to aflatoxin are the main determinants, while in other countries (Japan, Egypt), HCV infection is considered the predominant cause. In Mongolia, HBV and HCV infection, coinfection with HBV with HCV or HBV with a δ (delta) agent, as well as alcohol abuse, are the main risk factors for the development of HCC [4, 5].

Hepatocellular carcinoma is a serious medical and social problem in many countries of the world, including Kazakhstan. In recent years (2013 - 2017) in the Republic of Kazakhstan there has been an increase in the incidence of HCC to 5.5 cases per 100 thousand population, and the mortality rate remains at a high level (about 1000 people annually). In 2017, 82.3% of the observed HCC patients died by the end of the year. The five-year survival rate was 23.7% [9].

HCC is characterized by an aggressive course, in most cases, an unfavorable prognosis. The five-year survival rate for HCC does not exceed 18%, and the postoperative recurrence rate is about 50% [10].

In recent years, the immunohistochemical (IHC) research method has been widely used in the diagnosis of malignant neoplasms. IHC is an informative method not only in the differential diagnosis of HCC, but also in determining the degree of histological differentiation of cancer, which has a prognostic value in the course of the disease [11].

Alpha-fetoprotein (AFP) is a glycoprotein produced by fetal cells of the fetus in the fetal gastrointestinal tract, liver and yolk sac [12]. The reasons for the formation of AFP in liver cancer of adult patients have not yet been established. It is assumed that embryospecific cells appear in a malignant tumor with impaired intercellular-matrix interactions and a reduced level of differentiation of new generations of tumor cells, which resume the synthesis of AFP [13].

Since the 1970s, AFP has been used as a tumor marker for the diagnosis of HCC. An increase in the AFP level by more than 10 μg/l was noted in almost 75% of cases with HCC [14]. Serum AFP results are still considered the most important marker for the diagnosis of HCC today and, together with ultrasound techniques, can increase the diagnostic value. However, its values can be high in some non-malignant liver diseases (hepatitis, cirrhosis without HCC nodes), as well as it can be low in some patients with HCC [15].

In addition to the use of serum AFP and ultrasound as diagnostic tools, there are biological tumor markers of AFP in IHC that play an important role in the following aspects: monitoring of treatment outcomes, prognostic information, and detection of disease recurrence after removal [16].

The article analyzes the parameters of serum AFP, the expression of AFP-immunopositive cells depending on the stage and gradation of HCC, in addition, the degree of correlation between the values of the two methods is determined.

Purpose:

Comparative analysis of the level of AFP expression in IHC, depending on the stage and gradation of HCC, correlation analysis of serum AFP and the level of AFP expression of immunopositive HCC cells.

Materials and methods

A total of retrospectively analyzed data from 50 patients with HCC who underwent surgical treatment (resection, transplantation) at the Syzganov's NSCS in 2014 - 2019. There were 28 men, 22 women, aged 34 to 74 years (average age 49.7 ± 0.2 years). All patients underwent a serological blood test to determine the AFP level. The postoperative material was subjected to immunohistochemical examination to determine the area of staining, the degree and intensity of expression of AFP-immunopositive cells.

Immunohistochemical study

Paraffin sections were dewaxed and rehydrated according to a standard technique. The protocol included preheating to 65 °C, antigen recovery for 20 minutes at a temperature of 97 °C and further cooling to 65 °C. Then the slides were washed for 1-3 minutes with TBS-buffer (Dako), then staining was carried out in a Bio-Optica slide master, in manual mode with FLEX Polyclonal rabbit antibody by human Alpha-1-Fetoprotein. The Reveal Polyvalent HRP-DAB Detection System was used to visualize the immunohistochemical reaction. Sections were counterstained with Mayer's hematoxylin; Bio-Mount balm was used for the conclusion.

Evaluation of the expression of antigens in IHC studies was carried out according to generally

accepted methods. The intensity and area of staining was evaluated, the value of staining was determined. Negative expression was noted as 0; low expression, 1% -10% of the area was marked as «+», moderate expression, 10% -50% of the area - «++», and high expression, > 50% - «+++».

The statistical analysis was performed using Microsoft Excel 2007 software.

Results:

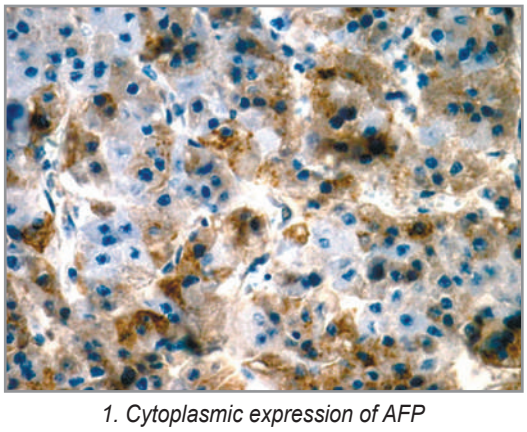
When analyzing the level of serological AFP, it was revealed that in the overwhelming majority of cases (n = 33) the AFP values were between 10-20 μg/l. At the same time, a critically high level of AFP (> 1000 μg/l) was found in 16% of cases (Table 1).

The results of the carried out immunohistochemical studies showed that in 83% of patients with HCC, cytoplasmic and nuclear expression of AFP is determined in malignant cells (Figure 1, 2).

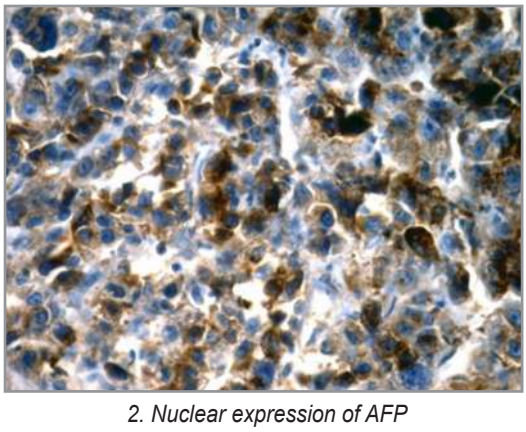
Table 1.
Distribution of patients with HCC by AFP level

AFP level, μg/l	HCC	
	n=50	%
10-20	33	66
20-100	3	6
100-200	3	6
200-500	1	2
500-1000	2	4
›1000	8	16

Figure 1,2.
HCC neoplastic cells with pronounced AFP expression. IHC x 200.



1. Cytoplasmic expression of AFP



2. Nuclear expression of AFP

To determine the characteristics of HCC, a comparative analysis was carried out according to the stages of the oncological process and the level of differentiation (gradation). Histological TNM classification was used to determine the stage of HCC. It was found that in most cases pT2 (34%), pT3 (32%), pT1 (16%) HCC stages were encountered in our sample. pT3 b and pT4 stages of the oncological process were detected in isolated cases. According to the degree of HCC differentiation (gradation), moderately differentiated HCC was detected in 46% (23) cases, low-differentiated HCC - in 30%, (15) cases, and highly differentiated HCC - in 24% (12) cases (Table 2).

Table 2.
Distribution of the HCC stage with the degree of differentiation (gradation)

Stage/ Gradation	n=50	n%	G1 n=12	G2 n=23	G3 n=15
pT1	8	16	8	-	-
pT2	17	34	2	12	3
pT3	16	32	2	6	8
pT3a	6	12	-	5	1
pT3b	2	4	-	-	2
pT4	1	2	-	-	1

The expression level of the AFP marker in the HCC node was high in 32% (n = 16) cases, moderate in 46% (n = 23) cases, and in 22% (n = 11) cases, the expression level of this hepatic glycoprotein was low or it was not determined at all (table 3). The area of AFP-immunopositive cells in hepatocellular liver cancer averaged 37.25 ± 15.47%. When analyzing the level of AFP expression depending on the HCC stage,

it was revealed that a high level of AFP expression was observed at pT2 - in 4% (2) cases, at pT3 and pT3a stages - 12% (6) cases in each, and at pT3b and pT4 stages - 2% (1) of cases in each. In most cases, moderate expression of AFP was observed at pT2 and pT3 stages of HCC (in 24% (12) and 20% (10) cases, respectively) (Table 3).

Table 3.
Expression level of AFP antigen at different stages of HCC

Expression Level/ Stage	pT1	pT2	pT3	pT3a	pT3b	pT4
Low	7	3	-	-	1	-
Moderate	1	12	10	-	-	-
High	-	2	6	6	1	1

Analyzing table 3, it can be revealed that high expression of AFP is observed in the HCC stages starting from pT2, pT3 and ending with pT4. Moderate expression of AFP is observed at stages pT2 and pT3 in relatively equal amounts. A low level of AFP can be seen mainly at the pT1 stage. Therefore, it can be assumed that the expression level increases from low to high depending on the stage of HCC (from pT2 to pT4). In total, it was revealed: in 46% of cases, moderate, in 32% of cases, high and in 22% - low expression of AFP. When analyzing the level of AFP depending on the gradation of HCC, it was found that, a low level of expression in 14% of cases out of 24% with highly differentiated HCC (G1 gradation), a moderate level of expression in 28% of cases out of 46% with moderately differentiated HCC (gradation G2), a high level of expression in 16% of cases out of 30% with low-differentiated HCC (gradation G3) (table 4).

Table 4.
Distribution of the AFP expression level by the level of HCC differentiation (gradation)

Expression level/ Gradation	n=50	n%	G1	G1%	G2	G2%	G3	G3%
Low	11	22	7	14	2	4	2	4
Moderate	23	46	4	8	14	28	5	10
High	16	32	1	2	7	14	8	16

Therefore, according to the data obtained, it can be concluded that the level of expression is directly proportional to the degree of HCC differentiation (gradation), i.e. with highly differentiated HCC (G1), the level of expression will be low, and with low-differentiated HCC (G3), the level of expression will be high. Correlation analysis revealed that the overall Pearson correlation coefficient between serum AFP and the degree of AFP staining on IHC was r = +0.0089, which corresponds to almost no correlation between these values (Figure 3). Accordingly, it can be assumed that serum AFP values will not be associated with AFP expression data during immunohistochemistry and can be used as a separate value for HCC differentiation.

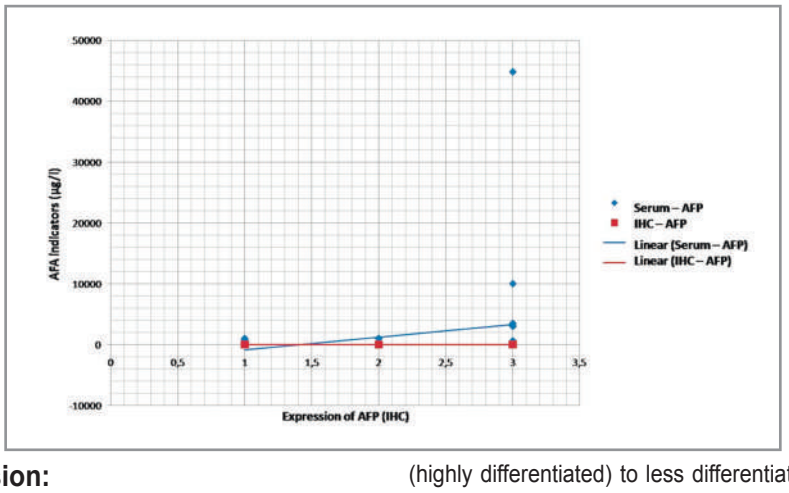


Figure 3.
Correlation of serum AFP parameters and expression of AFP-immunopositive cells

Conclusion:

Thus, in a comparative analysis of the level of alphafetoprotein expression with the stage and degree of HCC differentiation, the data obtained showed a relationship between these variables. A direct dependence of the AFP expression level on the HCC stage is noted; the expression level increases from pT1 to pT4. There is also an increase in the level of AFP expression from more differentiated HCC (highly differentiated) to less differentiated HCC (low-differentiated).

In our study the correlation analysis between serum AFP and the level of AFP expression in IHC revealed a weak correlation in the general cohort. It can be assumed that serum AFP values cannot be associated with data on AFP expression during immunohistochemistry and can be used as a separate value for HCC differentiation.

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THE USE OF INTRAVENOUS IBUPROFEN IN POSTOPERATIVE PERIOD

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

Keywords
intravenous ibuprofen, postoperative analgesia, pediatric esophagocoloplasty

Abstract

The article reflects the role of non-steroidal anti-inflammatory drugs in postoperative period. The study was conducted on the data of 94 operations of children aged from 10 months to 15 years (mean age 4.4 years). All patients of our center with esophagocoloplasty in the postoperative period received the drug «Intrafen» in injectable form, intravenously. Name of manufacturer of drug: GEN ILAC VE SAGLIK URUNLERI SANAYI VE TICARET, A.S. (Turkey). The main active substance of this drug is Ibuprofen 400mg/4ml for intravenous injection. Patients were injected intravenous ibuprofen at therapeutically effective doses for a minimal period of time. After receiving positive reactions to the drug at the initial stage of treatment, the dose and frequency of taking the drug was adjusted individually for each patient.

Objective. *This work is dedicated to evaluate the role of the intravenous Ibuprofen in the postoperative period in surgical practice.*

Material and methods. *The study included 94 pediatric patients with esophagocoloplasty. Age of patients: from 10 months to 15 years (mean age 4.4 years), of which: 90 (96%) patients had post-burn stricture of the esophagus; 3 (3%) patients with esophageal atresia; 1 (1%) patient with a short esophagus. The number of female children - 51 (54.3%) patients, male - 43 (45.7%) patients.*

Results. *The total number of patients receiving intravenous Ibuprofen in the postoperative period was 94. The optimal dose showed a good therapeutic effect. At the optimal dosage of 20 mg/kg/day, two patients experienced intra-abdominal bleeding. Follow-up time: 2 weeks after esophagocoloplasty.*

Conclusion. *In patients with esophagocoloplasty, preventive intravenous administration of Ibuprofen showed a good therapeutic result. Patients noted a decrease in pain, which in turn led to a decrease in the need for emergency analgesia.*

Отадан кейінгі кезеңде ибупрофенді көктамыр ішілік енгізу

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Аңдатпа

Мақалада отадан кейінгі кезеңдегі стероидтық емес қабынуға қарсы заттардың рөлі айқындалған. Зерттеу 10 ай мен 15 жас аралығындағы (орта жас - 4,4) балаларда болған 94 отаның негізінде жүргізілді. Орталықтағы эзофагоколопластикасы бар барлық науқастар отадан кейінгі кезеңде «Интрафен» дәрілік затын инъекциялық формада, көктамырішілік жолмен қабылдаған. Бұл дәрілік затты өндіруші ұйымның атауы: GEN ILAC VE SAGLIK URUNLERI SANAYI VE TICARET, A.S. (Түркия). Дәрілік заттың негізгі белсенді құрамы көктамыр ішіне енгізуге арналған Ибупрофен 400мг/4мл болып табылады. Науқастарға көктамырішілік Ибупрофенді терапиялық эффективті мөлшерде аз уақыт көлемінде тағайындадық. Емдеудің алғашқы сатысында-ақ дәрілік затқа оң жауап алғаннан кейін, дәрілік заттың мөлшері мен қабылдау жиілігі әр науқасқа жеке дара өзгертілді.

Мақсаты. *Бұл жұмыстың мақсаты хирургиялық тәжірибеде отадан кейінгі кезеңдегі көктамырішілік Ибупрофеннің рөліне баға беру болып табылады.*

Материал және әдістер. *Зерттеуге эзофагоколопластикасы бар 94 педиатриялық науқас алынды. Науқастардың жасы: 10 айдан 15 жасқа дейін (орта жас - 4,4), соның ішінде: 90 (96%) науқаста – өңештің күйіктен кейінгі стриктурасы; 3 (3%) науқаста – өңеш атрезиясы; 1(1%) науқаста – қысқа өңеш. Әйел жынысты балалар саны – 51 (54,3%) науқас, ер жынысты – 43 (45,7%) науқас.*

Нәтижелер. *Отадан кейінгі кезеңде көктамырішілік Ибупрофен қабылдаған пациенттердің жалпы саны-94. Оңтайлы доза жақсы терапиялық әсер көрсетті. Оңтайлы дозада тәулігіне 20 мг/кг екі науқаста құрсақішілік қан кету байқалды. Бақылау мерзімі: эзофагоколопластикадан кейін 2 апта.*

Қорытынды. *Эзофагоколопластикасы бар науқастарда Ибупрофенді превентивті көктамырішілік енгізу жақсы терапиялық нәтиже берді. Науқастар ауырсыну сезімінің азайғанын байқады, ол өз кезегінде шұғыл ауырсынуды басуға деген қажеттілікті азайтты.*

Мүдделер қақтығысы
Авторлар мүдделер қақтығысы туралы мәлімдеме жасаған жоқ

Түйін сөздер
көктамырішілік ибупрофен, отадан кейінгі анальгезия, балалар эзофагоколопластикасы

Применение внутривенного ибупрофена в послеоперационном периоде

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Конфликт интересов
Авторы заявили об отсутствии конфликта интересов

Аннотация

В статье отражена роль нестероидных противовоспалительных лекарственных средств в послеоперационном периоде. Исследование проводилось по данным 94 операции, у детей в возрасте от 10 месяцев до15 лет (средний возраст 4,4 года). Все пациенты нашего центра с эзофагоколопластикой в послеоперационном периоде получали препарат «Интрафен» в инъекционной форме, внутривенно. Наименование организации-производителя данного препарата: GEN ILAC VE SAGLIK URUNLERI SANAYI VE TICARET, A.S. (Турция). Главным активным веществом данного препарата является Ибупрофен 400мг/4мл для внутривенного введения. Пациентам внутривенный Ибупрофен ввели в терапевтически эффективных дозах в течение минимального периода времени. После получения положительных реакций на препарат на начальной стадии лечения, доза и частота приема препарата была скорректирована индивидуально для каждого пациента.

Целью *данной работы является оценка роли внутривенного Ибупрофена в послеопреационном периоде в хирургической практике.*

Материал и методы. *В исследование включены 94 педиатрических пациентов с эзофагоколопластикой. Возраст пациентов: от 10 месяцев до 15 лет (средний возраст 4,4 года), из них: у 90 (96%) пациентов - послеожоговая стриктура пищевода; 3 (3%) пациента с атрезией пищевода; 1(1%) пациент с коротким пищеводом. Количество детей женского пола – 51 (54,3%) больных, мужского пола – 43 (45,7%) больных.*

Результаты. *Общее количество пациентов, получавших внутривенный Ибупрофен в послеоперационном периоде – 94. Оптимальная доза показала хороший терапевтический эффект. При оптимальной дозировке 20 мг/кг/сутки у двоих пациентов было отмечено внутрибрюшное кровотечение. Сроки наблюдения: 2 недели после эзофагоколопалстики.*

Заключение. *У пациентов с эзофагоколопластикой превентивное внутривенное введение Ибупрофена показал хороший терапевтический результат. Пациенты отметили уменьшение боли, это в свою очередь привело к снижению потребности в неотложной анальгезии.*

Ключевые слова
внутривенный ибупрофен, послеоперационная анальгезия, детская эзофагоколопластика

Introduction

Causes of chemical damage: alkali “sparkling cauldron”, “mole” - in 65 (72.2%) patients; acids: acetic acid, battery electrolyte - in 19 (21%) patients and unknown chemicals - in 6 (6.7%) patient(Fig. 1).

At the moment, a hot topic in medicine is the treatment of acute postoperative pain. The main painkillers used in surgical practice are a group of analgesics based on opioid and non-steroidal anti-inflammatory drugs (NSAIDs). Ibuprofen is most commonly used for children and is prescribed according to age and weight.

We used Ibuprofen solution for intravenous administration of 400 mg/4 ml for our patients. When used intravenously, the drug immediately enters the bloodstream. Ibuprofen is a non-selective, cyclooxygenase (COX) inhibitory NSAID that has anti-inflammatory, analgesic, and antipyretic properties.

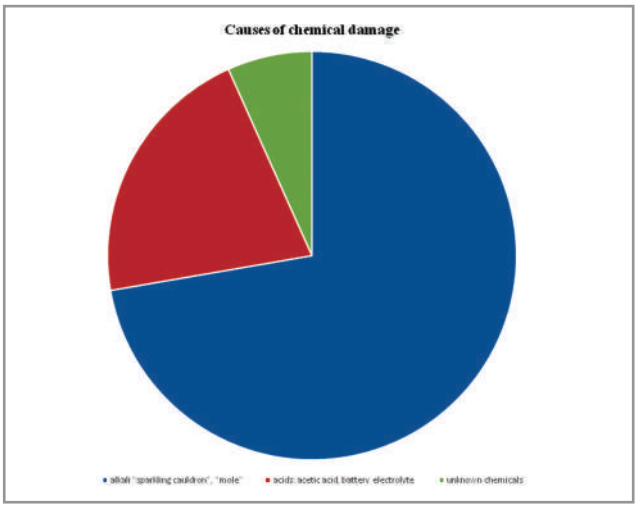

Figure 1.
Causes of chemical damage

The use of injectable forms of NSAIDs has an advantage in the speed of onset of the analgesic effect compared to taking standard tablets or capsules.

The use of several analgesics with different mechanisms of analgesic effect can help achieve the maximum level of pain relief when prescribing minimal therapeutic doses of several drugs that affect different levels of the nociceptive process. Thus, the analgesic effect of drugs increases, side effects decrease [1].

In patients in the postoperative period, the use of representatives of the NSAID group is pathogenetically justified, so we routinely prescribe them together with opioid analgesics. After extensive surgical interventions, the appointment of NSAIDs as basic analgesics can reduce the consumption of opioids by 20–60% [2].

For the treatment of pain syndromes with moderate to severe intensity, intravenous ibuprofen can be combined with intravenous opioid analgesics.

The use of NSAIDs helps to reduce the level of side effects inherent in «morphine-like» analgesics, such as paresis of the gastrointestinal tract, nausea, vomiting, sedation; improves the function of external respiration and pulmonary gas exchange, provides a quick awakening of the patient in the postoperative period. In the absence of the ability to take the last inside, we introduce them mainly intravenously in the form of a continuous infusion or bolus doses.

In multicenter studies, N. Moore et al. (1999) of the comparative efficacy and tolerability of first-line analgesics - acetylsalicylic acid, paracetamol and ibuprofen, used in 8677 patients, the authors demonstrate that the tolerability of the latter was comparable to that of paracetamol and was better than in cases of acetylsalicylic acid. Adverse events occurred more often in patients taking acetylsalicylic acid than in patients who were anesthetized with ibuprofen or paracetamol. The authors conclude that ibuprofen should be considered as the drug of choice in the practice of general practitioners in the short course, since there is a potential risk of developing a toxic effect when taking paracetamol. The most important advantage of ibuprofen over other NSAIDs is its high safety, proven by studies such as ARAMIS and PAIN [3].

Also, like most NSAIDs, ibuprofen is reversibly bound to plasma proteins (more than 99% at a concentration of 20 μg / ml). Protein binding is saturated, and at concentrations greater than 20 μg/ml, binding is non-linear. Dosage data for oral administration - the volume of distribution of ibuprofen varies according to age and temperature. In the human body, the release of ibuprofen is rapid and complete. More than 90% of the absorbed dose is excreted in the urine as metabolites or their conjugates. Adequate use of intravenous ibuprofen at an adequate dose in patients with acute postoperative pain resulted in analgesia after the first dose and at the end of the course of analgesia in 90 children. It is advisable to prescribe intravenous Ibuprofen within one week after surgery, every 12 hours at a rate of 20 mg / kg / day in case of pain syndrome of severe intensity or moderate intensity. The duration of intravenous drip should be at least 30 minutes. The highest recommended dose for children is 30 mg/kg/day.

NSAID use and risk of postoperative bleeding.

NSAIDs may have an antithrombotic effect and increase the risk of postoperative bleeding [4–8]. The possibility of this complication should always be considered when prescribing NSAIDs for patients undergoing surgery, even when it comes to outpatient interventions such as removal of the adenoids or tonsillectomy [9,10]. The frequency of bleeding from the area of the surgical wound in patients treated with NSAIDs exceeds 1%, but most of them are of low intensity and do not require repeated surgical intervention or blood transfusion. Risk factors are a large amount of surgical intervention, the presence of initial hemocoagulation disorders and the use of anticoagulants, which increases the risk of bleeding by 2-3 times [4,5].

All patients after esophagocoloplasty in the postoperative period received intravenous Ibuprofen for one week. A single dose of Ibuprofen for children is 5-10 mg/kg of the child's body weight 3-4 times a day. The maximum daily dose allowed in pediatric practice is 20-30 mg/kg of body weight. The duration of intravenous drip should be at least 30 minutes. We used a dosage of 20 mg/kg/day, every 12 hours. When using the above dosage, two patients received complications in the form of bleeding. Both patients had intra-abdominal bleeding, and therefore the drug was discontinued. Clinical, laboratory and instrumental research methods: In order to assess complications, postoperative bleeding in children, the results of a general blood test and coagulogram were used. Venous blood was used for the study. During the analysis of patient data, the following laboratory changes were obtained.

Patient M., 12 years old. Clinical diagnosis: Decompensated post-burn (means for cleaning cauldrons «sparkling cauldron», composition - alkali) cicatricial stenosis of the lower third of the esophagus. ICD disease code: K22.2. Obstruction of the esophagus (Table1, 2).

Component	Result	Comments	Normalvalues	Doneat
Hemoglobin	66,0 g/L	**Lowered**	120-140	29.10.2018 14:45:09
Erythrocyte	3,14 10^12/L	**Lowered**	3,9-4,7	29.10.2018 14:45:09
Hematocrit	23,20 %	**Lowered**	35-47	29.10.2018 14:45:09

Table1.
Hemogram. Patient M.

Table 2.
Coagulogram. Patient M.

Component	Result	Comments	Normal values	Done at
Prothrombin time (sec)	11.1 s		11 - 21	29.10.2018 15:58:12
Prothrombinindex	70 %	**Lowered**	80,00 - 110,00	29.10.2018 15:58:12
INR	0,95		0,85 - 1,40	29.10.2018 15:58:12
Thrombintime	16,2 s		14,0 - 21,0	29.10.2018 15:58:12
APTT	23,30 s	**Lowered**	24,00 - 35,00	29.10.2018 15:58:12
Fibrinogen	4,50 g/L	**Raised**	2,00 - 4,00	29.10.2018 15:58:12

Patient L., 7 years old. Clinical diagnosis: Decompensated post-burn (liquid "mole", sewage cleaner, the main substance is sodium hydroxide) cicatricial stenosis of the middle third of the esophagus. The presence of a gastrostomy. ICD disease code: K22.2. Obstruction of the esophagus (Table 3,4).

Table 3.
Hemogram.
Patient L.

Component	Result	Comments	Normalvalues	Doneat
Hemoglobin	69,0 g/L	**Lowered**	130-160	01.11.2021 6:57:47
Erythrocyte	2,54 10^12/L	**Lowered**	4,0-5,0	01.11.2021 6:57:47
Hematocrit	21,80 %	**Lowered**	39-50	01.11.2021 6:57:47

Table 4.
Coagulogram.
Patient L.

Component	Result	Comments	Normal values	Done at
Prothrombin time (sec)	won't clot		11 - 21	01.11.2021 6:27:51
Prothrombinindex	won'tclot		80,00 - 110,00	01.11.2021 6:27:51
INR	won'tclot		0,85 - 1,40	01.11.2021 6:27:51
Thrombintime	35,5 s	**Raised**	14,0 - 21,0	01.11.2021 6:27:51
APTT	36,70 s	**Raised**	24,00 - 35,00	01.11.2021 6:27:51
Fibrinogen	won'tclotg/L		2,00 - 4,00	01.11.2021 6:27:51

Main points regarding the development of complications associated with the use of NSAIDs.

All NSAIDs can cause complications in the gastrointestinal tract (GIT): dyspepsia, ulcers, bleeding and perforation of the upper and lower gastrointestinal tract, iron deficiency anemia (IDA) due to damage to the small intestine (NSAID enteropathy), cause exacerbation and complications of inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis (UC).

NSAIDs may increase the risk of bleeding after surgery and traumatic medical procedures.

The risk of complications can be significantly reduced with the use of drug prophylaxis. The main means of controlling the side effects of NSAIDs from the upper gastrointestinal tract are proton pump inhibitors (PPIs) [11-14]. At present, there is no doubt about the ability of this class of gastroprotectors to reduce the incidence of ulcers, gastrointestinal bleeding and dyspepsia, significantly improving the subjective tolerance of NSAIDs. The use of a proton pump inhibitor prevents the risk of damage to the mucosa of the gastrointestinal tract, justified transfusion of blood components prevents the risk of developing metabolic disorders and blood clotting disorders.

The main preventive method of complications is the individual consideration of risk factors and the appointment of a more adequate dose of NSAIDs for each patient. Therefore, NSAIDs, including ibuprofen, should be used with caution in patients with gastric

ulcers or gastrointestinal bleeding. In patients with peptic ulcer and/or gastrointestinal bleeding, taking NSAIDs, the risk of developing gastrointestinal bleeding is higher than in patients without these diseases.

To reduce the risk of side effects associated with the gastrointestinal tract, the dose of NSAIDs should be reduced to the minimum effective dose as soon as possible.

In the event of gastrointestinal bleeding and ulcer formation in patients taking intravenous ibuprofen, treatment should be discontinued.

Conclusion

Intravenous administration of ibuprofen in children was well tolerated for postoperative pain relief. The anti-inflammatory activity of intravenous ibuprofen helps prevent pain receptor sensitization and relieve tissue inflammation; stop the inflammatory cascade caused by invasive procedures. However, there are some safety concerns when using NSAIDs. Gastrointestinal and renal toxicity and the overall risk of bleeding are increased with the use of NSAIDs. However, many of these effects are associated with longer use. Intravenous ibuprofen is usually used on a short-term basis in hospitalized patients and in outpatient surgical procedures, which reduces the incidence of these problems.

We analyzed 94 studies using injectable ibuprofen, and all studies considered the efficacy of the optimal dose of intravenous ibuprofen in the postoperative period in children.

The present study showed that the preventive intravenous administration of ibuprofen led to a reduction in pain and a decrease in the need for emergency analgesia within one week after esophagocoloplasty in children.

Practical recommendations:

1. Indications for the use of intravenous Ibuprofen are pain syndrome of various etiologies, including postoperative pain; treatment of pain syndromes of moderate and severe intensity, as an adjunct to intravenous opioid analgesics. The use of intravenous ibuprofen reduces the undesirable side effects inherent in “morphine-like” analgesics, such as toxic effects on the central nervous system, respiratory depression, paresis of the gastrointestinal tract.

2. It is advisable to prescribe intravenous ibuprofen for three days after surgery, every 12 hours at a rate of 20 mg/kg/day in case of severe or moderate pain. The duration of intravenous drip should be at least 30 minutes. The highest recommended dose for children is 30 mg/kg/day.

3. To reduce the risk of side effects associated with the gastrointestinal tract, the dose of NSAIDs should be reduced to the minimum effective dose as soon as possible.

4. In the event of gastrointestinal bleeding and ulcer formation in patients taking intravenous ibuprofen, treatment should be discontinued.

5. The specific antidote for Ibuprofen is not known. In case of overdose, symptomatic treatment is recommended.

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К 80-ЛЕТИЮ ПРОФЕССОРА НУРМАКОВА АМАНА ЖАМЕЛОВИЧА

13 марта 2022 года исполняется 80 лет со дня рождения почетного профессора Казахского Национального медицинского университета им. С.Д.Асфендиярова, доктора медицинских наук, академика Академии профилактической медицины РК Нурмакова Амана Жамеловича.

Нурмаков А.Ж. родился в Егиндыбулакском (ныне Каркаралинском) районе Карагандинской области в семье рабочего. После окончания казахской средней школы №2 г. Караганды (в настоящее время школа им. Н.Н.Нурмакова), с 1959 по 1965 г. обучался на лечебном факультете Карагандинского государственного медицинского института.

Свою трудовую деятельность Нурмаков А.Ж. начал в качестве сельского врача в участковой больнице совхоза им. Абая Карагандинской области. В октябре 1967 г. поступает в аспирантуру при кафедре хирургических болезней Алма-Атинского государственного медицинского института. Под руководством заведующего кафедрой, заслуженного врача КазССР, доктора медицинских наук, профессора А.А. Сулейменова, в 1971г. защитил кандидатскую диссертацию на тему: «Клинико-экспериментальная оценка нового отечественного местного анестетика ринокаина», после чего был принят на должность ассистента кафедры хирургии, а в 1976 году избран доцентом данной кафедры. За период с 1976 по 1986 г. он проходит факультеты повышения квалификации в центральных вузах Москвы, Ленинграда, Киева и достигает высокой квалификации по своей специальности.

С 1986 по 1989 г. Нурмаков А.Ж. является докторантом кафедры общей хирургии 1-го Ленинградского медицинского института (ныне Санкт-Петербургский медицинский университет) им. акад. И.П.Павлова. Научным консультантом был назначен заслуженный деятель науки РФ, член-корреспондент РАМН, доктор медицинских наук, профессор Л.В. Поташов. В 1989г., после защиты докторской диссертации на тему: «Пути совершенствования диагностики и лечения желчнокаменной болезни и её осложнений», Нурмаков А.Ж. возвращается на родную кафедру, которую возглавил в 1995г. после избирания по конкурсу.

Сегодня профессор Нурмаков А.Ж. является известным в стране ученым, автором более 165 научно-методических работ, из которых 5 монографий и 4 учебника для студентов. Его монографии «Өт қуығында тас пайда болу ауруы» (2003) и «Хирургиялық аурулардың симптомдары мен синдромдары» (2005) являются первыми в стране монографиями по хирургии, изданными на государственном языке. Под его руководством были выполнены одни из первых диссертаций, защищенных на государственном языке.

Диапазон научных исследований профессора Нурмакова А.Ж. и его учеников охватывает разные области хирургии.

Под его руководством были проведены разносторонние и углубленные исследования по проблемам язвенной болезни желудка и двенадцатиперстной кишки, желчнокаменной болезни, разлитого гнойного перитонита, хирургической инфекции, гиперпаратиреоза, травматических повреждений селезенки, применения иглорефлексотерапии в хирургии и др. Впервые в стране было проведено комплексное исследование особенностей иммунопатогенеза, клиники, диагностики и лечения гнойной хирургической инфекции у больных наркоманией. По результатам научных исследований изданы монографии и методические рекомендации, получены официальные охранные документы Национального патентного ведомства РК, защищены докторские (2) и кандидатские (3) диссертации. В практическое здравоохранение с успехом внедрены разработанные оригинальные методы лечения, прежде всего это способы аутотрансплантации ткани селезенки; управляемой лапаростомии; местного лечения гнойных ран; профилактики и лечения хирургической инфекции с применением нейтрального анолита и системной энзимотерапии.

За 55 лет (1967-2022гг.) непрерывной работы в КазНМУ им. С.Д.Асфендиярова профессором Нурмаковым А.Ж. проводилась большая общественная работа. Он неоднократно избирался заместителем секретаря партийной организации факультета, был членом Ученого Совета института и факультетов, заместителем декана педиатрического факультета, деканом подготовительного отделения, председателем УМК и НППК по хирургическим дисциплинам. В настоящее время является почетным профессором КазНМУ им.С.Д.Асфендиярова, почетным членом Общества хирургов г. Алматы.

Много сил и душевной теплоты Нурмаков А.Ж. уделял воспитанию молодых кадров и студентов. В процессе обучения студентов особое внимание он уделял деонтологическому, нравственно-этическому и профессиональному воспитанию будущих врачей. Его ученики успешно трудятся в различных уголках страны и за рубежом (Индия, Непал, Россия).

Многолетняя плодотворная деятельность профессора Нурмакова А.Ж. отмечена значками «Отличнику здравоохранения СССР» и «Отличнику здравоохранения РК», почетными грамотами, дипломами МЗ СССР, МЗ КазССР, партии «Отан», медалями, грамотами, благодарностями университета и ценными подарками. Исключительное трудолюбие, скромность и доброжелательность, а также позитивная принципиальность снискали ему заслуженное уважение и авторитет среди друзей, коллег, студентов и пациентов.

ТРЕБОВАНИЯ ДЛЯ АВТОРОВ ЖУРНАЛА «ВЕСТНИК ХИРУРГИИ КАЗАХСТАНА»

Уважаемые авторы!

С 1 апреля 2018 года все статьи на публикацию принимаются на государственном или русском языках с обязательным переводом всей статьи на английский язык. Статьи без версии на английском языке будут отклонены.

Также учитывая требования Консультативной Комиссией (CSAB) Scopus об интернационализации авторов и аудитории редколлегия журналов рекомендуют публиковать статьи в соавторстве с учеными дальнего и ближнего зарубежья.

В журнале публикуются научные статьи и заметки, экспресс-сообщения о результатах исследований в различных областях естественно-технических и общественных наук.

Решение о публикации принимается редакционной коллегией журнала после рецензирования, учитывая научную значимость и актуальность представленных материалов. Статьи, отклоненные редакционной коллегией, повторно не принимаются и не рассматриваются. Рукописи, оформленные не по правилам, возвращаются авторам без рассмотрения.

Рукопись направляется на отзыв члену редколлегии и одному из указанных рецензентов; в спорных случаях по усмотрению редколлегии привлекаются дополнительные рецензенты; на основании экспертных заключений редколлегия определяет дальнейшую судьбу рукописи: принятие к публикации в представленном виде, необходимость доработки или отклонение. В случае необходимости рукопись направляется авторам на доработку по замечаниям рецензентов и редакторов, после чего она повторно рецензируется, и редколлегия вновь решает вопрос о приемлемости рукописи для публикации. Переработанная рукопись должная быть возвращена в редакцию в течение месяца после получения авторами отзывов; в противном случае рукопись рассматривается как вновь поступившая. Рукопись, получившая недостаточно высокие оценки при рецензировании, отклоняется как не соответствующая уровню или профилю публикаций журнала.

Авторы несут ответственность за достоверность и значимость научных результатов и актуальность научного содержания работ. Не допускается **ПЛАГИАТ** – умышленно совершаемое физическим лицом незаконное использование чужого творческого труда, с доведением до других лиц ложных сведений о себе как о действительном авторе.

Редакция принимает на рассмотрение рукописи только на английском языке, присланные через официальный сайт журнала **www.vhk.kz.**

Материал статьи – абстракт на казахском, русском и английском языках, список литературы, рисунки, подписи к рисункам и таблицы, оформляется одним файлом; дополнительно каждый рисунок оформляется в виде отдельного файла. Если пересылаемый материал велик по объему, следует использовать программы для архивирования. Все страницы рукописи, в том числе таблицы, список литературы, рисунки и подписи к ним, следует пронумеровать.

Представленные для опубликования материалы должны удовлетворять следующим требованиям:

1. Содержать результаты оригинальных научных исследований по актуальным проблемам в области физики, математики, механики, информатики, биологии, медицины, геологии, химии, экологии, общественных и гуманитарных наук, ранее не опубликованные и не предназначенные к публикации в других изданиях. Статья сопровождается разрешением на опубликование от учреждения, в котором выполнено исследование.
2. Размер статьи 7-10 страниц (статьи обзорного характера – 15-20 стр.), включая аннотацию в начале статьи перед основным текстом, которая должна отражать цель работы, метод или методологию проведения работы, результаты работы, область применения результатов, выводы (аннотация не менее 20 предложений (150»300 слов) - (на английском языке) через 1 компьютерный интервал), таблицы, рисунки, список литературы (через 1 компьютерный интервал, размер шрифта – 14), напечатанных в редакторе Word, шрифтом Times New Roman, поля – верхнее и нижнее – 2 см, левое –3 см, правое –1,5 см. Количество рисунков – 5-10.

Структура должна соответствовать международной формуле IMRAD, где I – introduction (вступление), M – Methods (методы), R – Results (исследование), A – и, D – conclusion+ discussion (заключение, обсуждение результатов и выводы).

Название • Отображает суть работы • Краткое • Без аббревиатур.

Необходимо официально закрепить название организации на английском и сокращение

Резюме • Структурировано • Без аббревиатур • Передает структуру статьи – Зачем (актуальность) – Какими методами?

– Что получено – Как это изменило картину знаний. Именно его читают в первую очередь, только хорошее резюме может привлечь внимание!

Вступление • Актуальность работы • Какая задача поставлена • Почему

Методы • Перечисление • Если известные - дать ссылку

Если модифицировали – указать как • Описывать так что б могли повторить • Статистика!

Результаты • Допускается не хронологическое, а логическое повествование • Основные, а не все что были сделаны • Иллюстрируются минимально необходимыми сводными данны- ми (исходные могут быть в дополнительных материалах)

Обсуждения • Не повторять результаты • Сопоставить полученные данные с имеющимися • Обсудить возможные причины и следствия

Функции списка литературы: • Аргументировать идею • Сопоставить с существующими аналогами • Обозначить место данного исследования • Избежать плагиата • Для журнала и ученого = признание • Часто указаны только собственные работы или очень старые (самоцитирование допускается только 10-15% от общего списка литературы) • Кочующие ошибки

Различайте • Ссылки • Список литературы • Библиография Что

могут цитировать • Книги, (монографии, главы) • Статьи научных журналов • Материалы конференций • Патенты • Диссертации • Неопубликованные данные • СМИ • Веб ресурсы (протоколы, веб странички) Источник должен быть надежным и легко доступным.

Статья начинается на английском языке. В начале, посередине страницы, идет название статьи прописными жирными буквами, название статьи должно быть коротким и емким, согласно проведенного анализа около 30-40 символов на английском языке.

Далее на следующей строчке – инициалы и фамилии авторов обычным жирным шрифтом, затем на следующей строчке – название организации(ий), в которой выполнена работа, город, страна, затем на новой строчке – адреса E-mail авторов. С красной строки идут ключевые слова **(Key words)**, а на новой строчке – сама аннотация (**Abstract** – не менее **150** и более **300** слов).

Далее, после отбивки одной строки, начинается на русском языке. В начале статьи вверху слева следует указать индекс **УДК, МРНТИ.**

Затем, посередине страницы, пишется: 1) название статьи; авторы; 3) название организации; с красной строки – **Ключевые слова,** затем – **Аннотация** (оформление шрифтов, как на английском языке).

Отбиваем одну строку и начинается сама статья. Следом за статьей идет список **Литературы.** Ссылки на литературные источники даются цифрами в прямых скобках по мере упоминания (не менее 20).

Для каждой статьи обязателен DOI (Digital Object Identifier) - это цифровой идентификатор документа. DOI выполняет функцию гиперссылки, которая всегда помогает найти нужный документ, даже если сайт, где он находился ранее, был впоследствии изменен. Благодаря этому индексу поиск научной информации в Интернете стал проще и эффективнее. Каждое издание, журнал размещает на своих веб-страницах в интернете, как текущие, так и архивные номера, и материалы. Таким образом, в открытом доступе можно увидеть резюме, которые включают в себя название статьи, фамилию, имя, отчество автора, аннотацию и ключевые слова, место выполнения работы, а также выходные данные опубликованных статей (название журнала, год издания, том, номер, страница).

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Статья в международном журнале:

1. Campry TS, Anders T. (1987) SNAP receptors implicated in vesicle targeting and fusion, Environ Pollut, 43:195-207. DOI: 10.1016/0269-7491(87)90156-4 (in Eng)

Статья в русскоязычном журнале, не имеющая англоязычной версии:

2. Ivanova TV, Samoilova NF (2009) Electrochemical Energetics [Elektrohimicheskaya energetika] 9:188-189. (In Russian)

Книги:

Timrat TA (2008) Soil pollution: origins, monitoring and remediation, second edition. Springer, Germany. ISBN: 978-3- 540-70777-6

Материалы конференции:

Monin S.A. (2012) Treatment techniques of oil-contaminated soil and water aquifers. Proceedings of International Conference on Water Resources and Arid Environment, Riyadh, Saudi Arabia. P.123.

Патенты:

Barin AB, Mukamedzhan NT (2000) A method for determination of 1,1-dimethylhydrazine and nitrosodimethylamine [Metodopredeleniya 1,1-dimetilgidrazina initrosodimetilamina]. Preliminary Patent of the Republic of Kazakhstan [Predvaritelnyi patent Respubliki Kazakhstan]. (In Russian)

Стандарты, ГОСТы:

RMG 61-2003. Indexes of accuracy, precision, validity of the methods of quantitative chemical analysis, methods of evaluation [GSI.Pokazatelitochnosti, pravilnosti, retsizionnosti metodik kolichestvennogo himicheskogo analiza. Metodyiotsenki]. Moscow, Russia, 2003. (In Russian)

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