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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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METHOD FOR PREVENTION OF COAGULOPATHIC BLEEDING DURING SURGERY FOR MECHANICAL JAUNDICE

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Abstract.

Background: Violation of hemostasis directly depends on the severity of hepatocyte dysfunction. Such patients may develop disseminated intravascular coagulation (DIC syndrome) and bleeding during and after surgery.

Objectives: To improve the results of treatment of coagulopathic bleeding during surgery for mechanical jaundice, through proactive therapy.

Methods: A prospective randomized clinical-controlled research was conducted according to the study protocol, which was based on the purpose of the study and objectives. The state of hemostasis was studied depending on the duration of jaundice in 79 patients with mechanical jaundice treated at the Semey Medical University Hospital, Non-Commercial Joint-Stock Company (NCJSC) at the age of 18 to 85 years, the average age was 62 years. (95% confidence interval (CI) 59.2/64.6 for average 61.9). The patients were distributed by gender in the following order: males – 30 patients (38%), females - 49 patients (62%). Inclusion criteria: all patients aged 18 and older with mechanical jaundice requiring surgical treatment. Exclusion criteria: includes children and adolescents under 18 years of age, patients who do not agree to participate, incapacitated, pregnant women are excluded from the study. The total number of the sample was n=79 (100%) patients for the study, the patients were divided into 2 groups: the main group n = 35 (44.3%), patients who were treated with L-carnitine and the control group n = 44 (55.7%). The prevention was based on a previously developed method of treating coagulopathies during surgery for mechanical jaundice, which includes a systemic effect on hemostasis and low invasiveness: treatment with levocarnitine at a dose of 5 ml intravenously slowly for 2-3 minutes, or drip in 100-200 ml of 0.9% sodium chloride.

Results: Changes in blood clotting parameters in patients with mechanical jaundice upon admission and on the 1st, 3rd and 5th days after treatment with the proposed method noticeably improve, so there is a shift in the indications APTT, Claus fibrinogen, INR and PT towards hypercoagulation already on day 1 (because they are specific markers of prolonged bleeding).

Conclusion: The proposed improved method of preventing coagulopathic bleeding during surgery for mechanical jaundice allowed to significantly reduce the incidence of coagulopathy in these patients, which is especially important, the frequency of their clinical manifestation, so Klausfibrinogen in the blood on the 5th day was 3.8 g/l, which turned out to be statistically significant U – 412.500 (P = 0.05) and improved PT by the 5th day was 12.3 seconds, the statistical significance of U was 208.500 (P = 0.05).

Key words. Coagulopathy, hemostasiopathy, mechanical jaundice, bleeding with mechanical jaundice, prevention and treatment of coagulopathy.

Bibliographic reference. Method for prevention of coagulopathic bleeding during surgery for mechanical jaundice.

Abbreviations. DIC Syndrome: Disseminated Intravascular Coagulation Syndrome; NCJSC «SMU»: Non-Commercial Joint-Stock Company «Semey Medical University»; CI: Confidence Interval; MJ: Mechanical Jaundice; APTT: Partially Activated Thromboplastin Time; INR: International Normalized Ratio; PT: Prothrombin Time; NH2: Terminal; TEG: Thromboelastogram; IBM SPSS: International Business Machines Corporation Statistical Package For The Social Sciences; CDA: Choledochoduodenoanastomosis; TNF: Tumor Necrosis Factor; IL: Interleukin; Alt: Alanine Aminotransferase; AsT: Aspartate Aminotransferase.

Introduction.

Prognostically severe are liver diseases that are a consequence of mechanical jaundice (MJ) with obstruction of choledochus [1]. A pathological syndrome that develops due to a violation of the outflow of hepatic bile through the biliary tract into the intestine due to mechanical obstacles is called Mechanical jaundice (MJ). One of the frequent causes of mechanical jaundice is most often cholelithiasis. Malignant tumors are not uncommon, as well as cicatricial stricture of the bile duct or the large duodenal papilla of the duodenum [2].

The liver is the main organ involved in metabolic processes in the organism and its functioning synthesizes a large amount of blood proteins, the restoration of anaerobic oxidation of substrates and the synthesis of many non-protein components. At the same time, the liver performing all complex metabolic processes is vulnerable to damaging factors [3,4]. Hemostasis depends on the full function of the liver, because the synthesis

of many coagulation factors occurs in the cells of the liver, and activation products in the cells of the reticuloendothelial system of the liver. Violation of hemostasis directly depends on the severity of hepatocyte dysfunction. Reduction of vitamin K-dependent factors (prothrombin, factors VII, IX and X, proteins C and S) in jaundice and at the same time other parameters may not change. Such patients may develop disseminated intravascular coagulation (DIC syndrome).

Despite oral (together with bile acids) or parenteral administration of vitamin K in a jaundice patient, difficulties in correcting hemostatic disorders in these patients may remain [5]. Episodes of bleeding or thrombotic manifestations can aggravate the clinical condition of a patient with jaundice. These manifestations require a careful clinical and laboratory approach to make an accurate diagnosis and provide effective treatment [6].

Abnormal vitamin K-dependent factors are produced when vitamin K is deficient. Such factors lack the residues of gamma-carboxyglutamic acid in the NH2-terminal part of their molecules, in addition to surgery on the liver, leads to serious changes in clotting [7-9].

Cholemia due to MJ leads to the development of endotoxicosis, leads to a violation of the antitoxic function of hepatocytes and reduces the function of the nephron. Renal-hepatic insufficiency develops. Most blood clotting factors and natural anticoagulants are synthesized in hepatocytes. Prolonged obstruction of the biliary tract or hepatocyte disease is accompanied by abnormal clotting. Thrombohemorrhagic changes develop, leading to the development of DIC-syndrome leading to a fatal outcome.

According to the literature, the most common coagulopathies in diseases of the biliary tract include thrombocytopenia, thrombocytopathies and DIC syndrome, hemodilution coagulopathy, overdose with anticoagulants, hepatic coagulopathy.

All these diseases, under certain conditions, lead to biliary hypertension and mechanical jaundice, a frequent complication of which is purulent cholangitis, which contributes to the progression of morphofunctional changes in the liver against the background of increasing intoxication, combined with hemodynamic and hemorheological disorders, lymphodynamic disorders. The degree and speed of changes in the liver depend on the rate of increase of biliary hypertension, microcirculation disorders, tissue hypoxia, the presence of inflammation in the ducts and the duration of jaundice [7,8].

Objectives.

To improve the results of treatment of coagulopathic bleeding during surgery for mechanical jaundice, through proactive therapy.

Materials and Methods.

Before the start of the study, a meeting of the Ethics Committee of the Non-Commercial Joint-Stock Company «Semey Medical University» (NCJSC «SMU»), Semey, Kazakhstan, "Protocol No. 2" dated 10/28/2020, was held, at which the protocol of the study, forms of informed consent, deadlines for the start and completion of scientific research were approved and the approval of the Ethics Committee was obtained. The study was conducted in accordance with the institutional guidelines for human research and the principles of the Helsinki Declaration. The protocols of the study were approved by the Ethics Committee of Semey Medical University and the University Hospital of the Non-Commercial Joint-Stock Company «Semey Medical University», Semey, Kazakhstan. All patients participating in the study are familiar with the informed consent. They also signed a consent to participate in scientific work. A prospective randomized clinical-controlled research was conducted according to the study protocol, which was based on the purpose of the study and objectives. Randomization was performed by choosing an envelope. The sample of patients for the study was determined according to the objectives of scientific research and the stages of work according to the developed scheme of research work.

The state of hemostasis was studied depending on the duration of jaundice in 79 patients with mechanical jaundice treated in the clinic of the University Hospital of the «SMU» NCJSC (Semey Medical University, Non-Commercial Joint-Stock Company) between the ages of 18 and 85, the average age was 62 years (95% confidence interval (CI) 59.2/64.6 for average 61.9). The patients were distributed by gender in the following order: males – 30 patients (38%), females - 49 patients (62%). During planning and during the study, respectively, some patients dropped out of the study at various stages (Figure 1).

Inclusion criteria: All male and female patients aged 18 and older with mechanical jaundice requiring surgical treatment both as planned and as an emergency. The exclusion criteria include children and adolescents under 18 years of age, i.e. who have not reached the age of majority and can not independently decide and consent to participate in the study, patients who do not agree to participate in the study for one reason or another, as well as incapacitated patients, pregnant women are excluded from the study because as the increase in the duration of pregnancy can directly affect the results of the study.

The total number of the sample was 79 (100%) patients for the study, the patients were divided into 2 groups: the main group – 35 (44.3%), patients who were treated with L-carnitine and the control group - 44 (55.7%).

By gender in the main group: males - 12 (34.3%), females - 23 (65.7), in the control group of males - 18 (41%), females - 26 (59%).

By nationality, the number of Kazakhs in the main group was 31 (88.6%), Russians - 4 (11.4%), Kazakh controls - 38 (86.4%) and Russian controls - 6 (13.6%).

By place of residence, the patients were distributed as follows: in the main group the city cases - 27 (77.2%), the village cases - 8 (22.8%), in the control group the city controls - 29 (66%), the village controls - 15 (34%).

Social status in the main group: there were 10 (28.6%) employees, 7 (20%) unemployed, retired patients 18 (51.4%), in the control group: 14 (31.8%) employees, 6 (13.6%) unemployed, retired patients 24 (54.5%).

The average age of main group patients and controls is 61.9 years (M:64, Q1-15, Q3-85). In the main group, the average age of cases was 59.8 years (M:64, Q1-15, Q3-85), the average age of controls was 63.6 years (M:60, Q1-48, Q3-80).

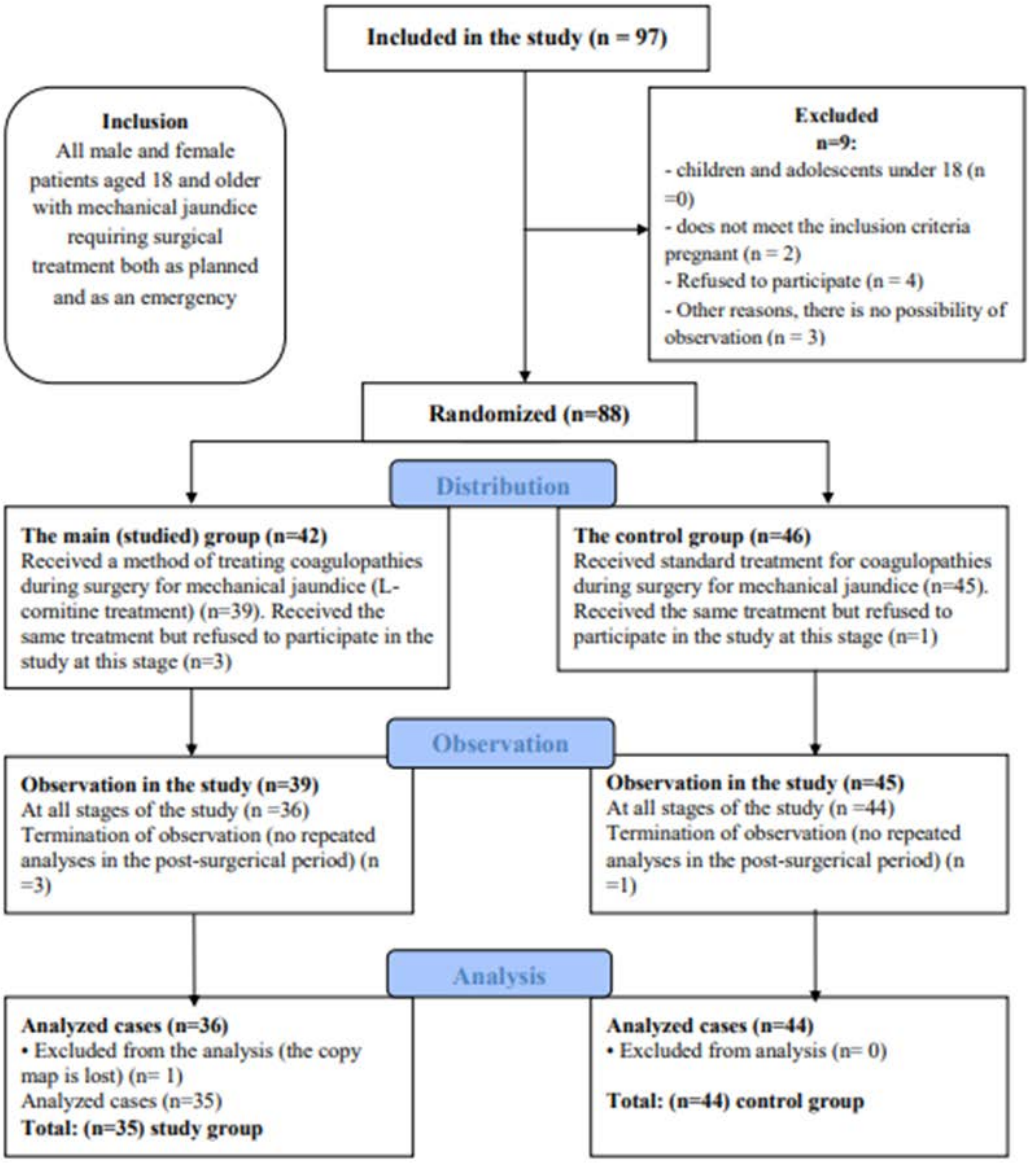

Figure 1. *A scheme reflecting the inclusion and stages of withdrawal of patients from the study.*

The average duration of the underlying disease in the main group was 67.4 days (M:7, Q1-1, Q3-730), in the control group it was 134 days (M:4, Q1-1, Q3-730).

In the main group, the average duration of jaundice at admission was 9.3±2.3. In the control group, the average indicators were 11.8±4.6.

All patients were examined as pre-surgical preparation, from the generally accepted parameters of blood tests, the following were taken into account: leukocytosis, from the leukoformula – the number of rod-shaped, segmented leukocytes, the rate of erythrocyte sedimentation.

The following biochemical parameters were determined: bilirubin (total bilirubin, direct bilirubin and indirect bilirubin), blood diastase, AlT, AsT at admission and after completion of treatment at discharge. A blood test was conducted for the parameters of the coagulogram of APTT, Claus fibrinogen, INR and PT at admission on the 1st, 3rd, 5th day after treatment and at discharge. All patients underwent ultrasound examination of the abdominal organs.

The prevention was based on a previously developed method of treating coagulopathies during surgery for mechanical jaundice, which includes a systemic effect on hemostasis and low invasiveness, which increases the effectiveness and safety of the treatment method developed based on the use of a combination of levocarnitine with standard methods of treating hemostasiopathies in surgery, depending on their stages.

Any massive bleeding during surgery on the biliary tract is highly likely to be associated with disorders in the hemostasis system, which must be identified or excluded in a timely manner and appropriate targeted hemostatic therapy should be initiated.

One of the important factors in the cascade mechanism of coagulopathy development is hypoxia and tissue ischemia. Therefore, the use of antihypoxants along with standard hemostatic therapy is appropriate.

Hemostasis disorders, as the cause of pathological bleeding during surgery, and as a consequence, vascular damage can be compensated, subcompensated and decompensated.

The key point in the correction of any acquired coagulopathy are measures aimed at preventing and eliminating factors that provoke the development of hemostasis disorders. Any coagulopathy has a laboratory and clinical stage of the process.

At the laboratory stage, correction is proactive, priority is given to measures aimed at eliminating violations of the organism homeostasis that led to the development of coagulopathy; specific hemostasiological correction is required in case of violation of the compensatory capabilities of the hemostasis system. At the clinical stage of coagulopathy, immediate hemostasiological correction is necessary, aimed at eliminating the consequences of thrombosis or stopping bleeding. In addition, any coagulopathy may be accompanied by a compensated, subcompensated or decompensated state of the hemostasis system.

In the compensated stage of coagulopathy, measures will be aimed at stopping bleeding using surgical hemostasis and antioxidants. The most applicable and effective antioxidants in influencing the coagulation system include levocarnitine in a dose of 5 ml intravenously slowly over 2-3 minutes, or drip in 100-200 ml of 0.9% sodium chloride.

The principle of proactive therapy based on continuous intra- and post-surgerical hemostasiological monitoring is primarily applicable to patients with initially sub- or decompensated functional state of the organism. This approach will increase the efficiency and speed of correction of hemostatic disorders and reduce the material costs of this correction.

The principles of additional specific therapy aimed at preventing hemostasis disorders in patients with sub- and decompensated functional state are formulated.

Subcompensated functional state:

1. Normovolemic hemodilution.
2. Prolonged epidural analgesia.
3. Thromboprophylaxis with low molecular weight heparins (enoxaparin sodium 0.5 mg/kg) (in patients with a high risk of thromboembolic complications - starting from the pre-surgical stage).
4. Levocarnitine 5 ml intravenously slowly for 2-3 minutes, or drip in 100-200 ml 0.9% sodium chloride.

Decompensated functional state:

1. The choice for blood substitutes infusions with minimal effect on the hemostasis system (modified gelatin, Hydroxyethylamylum).
2. Limitation of the volume of infusion of crystalloids.
3. Adequate proactive compensation for the loss of coagulation factors and platelets in blood loss.
4. The use of aprotinin preparations, membrane stabilizers (dicinone), antifibrinolytics under the control of thromboelastogram (TEG) in the intra-surgical and early post-surgical period.
5. Levocarnitine 5 ml intravenously slowly for 2-3 minutes, or drip in 100-200ml 0.9% sodium chloride.

To compare the effectiveness of this method, two groups were taken: control and main. After treatment with and without the use of a method for the treatment of coagulopathies during surgery for mechanical jaundice, blood clotting parameters were compared.

Statistical analysis: To analyze quantitative variables, we used nonparametric tests. The critical significance level was $p < 0.05$. Statistical analysis of the data was performed using IBM SPSS 20 (SPSS Inc., Chicago, IL, USA).

Results.

Data on the main characteristics of the compared study groups are presented in Table 1.

Table 1. *Sample characteristics.*

	Main group n = 35	**Control group n = 44**
Age (Me, Q1, Q3)	60 (52,69)	65 (55.75, 72)
Duration of the underlying disease (Me, Q1, Q3)	7 (4.5, 21)	4 (1, 90.5)
Duration of inpatient treatment (Me, Q1, Q3)	13 (12,14)	13(10, 14)
m: 1 n(%)	12 (34%)	18 (41%)
f: 2 n(%)	23 (66%)	26 (59%)
Kazakh: 1 n(%)	31 (88,5%)	38 (86,4%)
Russians: 2 n(%)	4 (11,5%)	6 (13,6%)
citizen: 1 n(%)	27 (77%)	29 (66%)
villager: 2 n(%)	8 (23%)	15 (34%)
working: 1 n(%)	10 (28.5%)	14 (31,8%)
unemployed: 2 n(%)	7 (20%)	6 (13,6%)
pensioners: 3 n(%)	18 (51.5%)	24 (54,5%)

Surgical treatment of mechanical jaundice was applied to all patients participating in the study: 56 (71.2%) patients underwent choledochoduodenoanastomosis (CDA) according to Yurash-Vinogradov; in 4 (5.5%) choledocholithotomy was performed with drainage of the choledochus by Keru; in 3 (4.1%) hepaticoejunoanastomosis of the disconnected loop according to Ru; 7 (8.2%) - dissociation of the cholecystoduodenal fistula (Mirizzi syndrome type V, according to Csendens – Beltran 2008 classification) with suturing of the hole in the duodenum with double-row sutures; in 9 (11%) - hepaticoejunostomy with interstitial anastomosis according to Brown and a plug according to Shalimov.

Bilirubinemia was also analyzed in patients of both groups. The following results were obtained during the study: Total bilirubin in the main group was 112.9 micromole/l, 95% CI 75.6-115.29 micromole/l (M:97.5, Q1-50.2; Q3-198.4). In the control group it was 110.4 micromole/l, 95% CI 68.5-152.2 micromole/l (M:92.2, Q1-22.6; Q3-265.9).

Direct bilirubin in the main group was 77.9 micromole/l, 95% CI 52.6-103.2 micromole/l (M:64.7, Q1-40.2; Q3-127.3). In the control group it was 139.7 micromole/l, 95% CI - 20.6-300 micromole/l (M:49.2, Q1-10.8; Q3-1092).

Indirect bilirubin in the main group was 32.8 micromole/l, 95% CI 18.4-47.2 micromole/l (M:32.6, Q1-8,5; Q3-71,1). In the control group, it was 40.8 micromole/l, 95% CI -24.1-57.6 micromole/l (M:30.3, Q1-7.4; Q3-104.6).

Since hyperbilirubinemia was initially observed in both groups - 102.3 micromole/l upon admission, attention was paid to the level of bilirubin on the 5th day after surgery. According to the results, there was no significant shift in bilirubin indicators on day 1. Billirubin decreased on day 5 - 46.7 micromole/l in the main group and 51.4 micromole/l in the controls. This

indicates that the decrease in bilirubin levels is associated with the elimination of the root cause, that caused mechanical jaundice (surgical treatment) and is in no way related to the use of levocarnitine.

As a result of the therapy performed by the method of treating coagulopathies during surgery for mechanical jaundice, which includes systemic effects on hemostasis and low invasiveness, the following results were obtained (Figure 2).

This diagram clearly shows the results of changes in blood clotting parameters in patients with mechanical jaundice upon admission and on the 1st, 3rd and 5th days after treatment with the proposed method, so there is a shift in the indicators of APTT, Claus fibrinogen, INR and PT towards hypercoagulation already on day 1. (because they are specific markers continued bleeding). As a result of the prophylaxis on the 3rd and 5th days, the indicators are within the normal range, which indicates the absence of coagulopathic bleeding. Changes in blood clotting indicators after treatment are shown in the form of a table (Table 2).

The main way to improve the results of treatment of coagulopathic bleeding during surgery for mechanical jaundice, through proactive therapy, which was the most applicable and effective in affecting the coagulation system, was the use of levocarnitine at a dose of 5 ml intravenously slowly for 2-3 minutes, or drip in 100-200 ml of 0.9% sodium chloride.

Discussion.

Despite the fact that the predominant moment of the hypocoagulated condition associated with mechanical jaundice is a violation of the absorption of vitamin K in the intestine, the pathogenesis includes many factors.

Coagulopathy usually develops with mechanical jaundice as an adverse reaction of the organism to the disease, which can lead to disseminated intravascular coagulation syndrome (DIC syndrome) with a high risk of mortality. In addition, cases of mechanical jaundice complicated by sepsis can also lead to the manifestation of disseminated blood clotting syndrome. Recent in vivo and in vitro studies have demonstrated that levocarnitine can prevent oxidative damage, including reduction of lipid peroxidation, removal of hydrogen peroxide and superoxide radicals, chelation of transition metal ions and activation of the endogenous antioxidant defense system. Due to mechanical jaundice, there is an excessive release of a number of pro-inflammatory cytokines, such as TNFa, IL-6 and IL-8. The results of this experimental study showed that levocarnitine reduces liver damage associated with mechanical jaundice and reduces TNFa, IL-6 and IL-8 levels. Further studies are needed to confirm and clarify these results of the clinical treatment of mechanical jaundice using L-carnitine.

Conclusion.

Prevention and treatment with levocarnitine at a dose of 5 ml intravenously slowly for 2-3 minutes, or drip in 100-200 ml of 0.9% sodium chloride, significantly improved blood clotting during surgery and in the post-surgerical period, so the indicator of Clausfibrinogen in the blood on the 5th day was 3.8 g / l, which turned out to be statistically significant U - 412,500 (P = 0.05) and the PT on the 5th day was 12.3 seconds, the statistical significance of U was 208,500 (P = 0.05).

The proposed improved method of preventing coagulopathic bleeding during surgery for mechanical jaundice has significantly reduced the incidence of coagulopathy in these patients, which is especially important, the frequency of their clinical manifestation.

Author Contributions: conceptualization, M.T.O., M.Zh.A., S.T.A.; methodology, M.T.O., M.Zh.A., S.T.A., N.B.O.; software, M.T.O., S.T.A., M.N.A., A.S.O., A.E.M.; validation, M.T.O., M.Zh.A., S.T.A., N.B.O., M.A.A., A.S.O.,

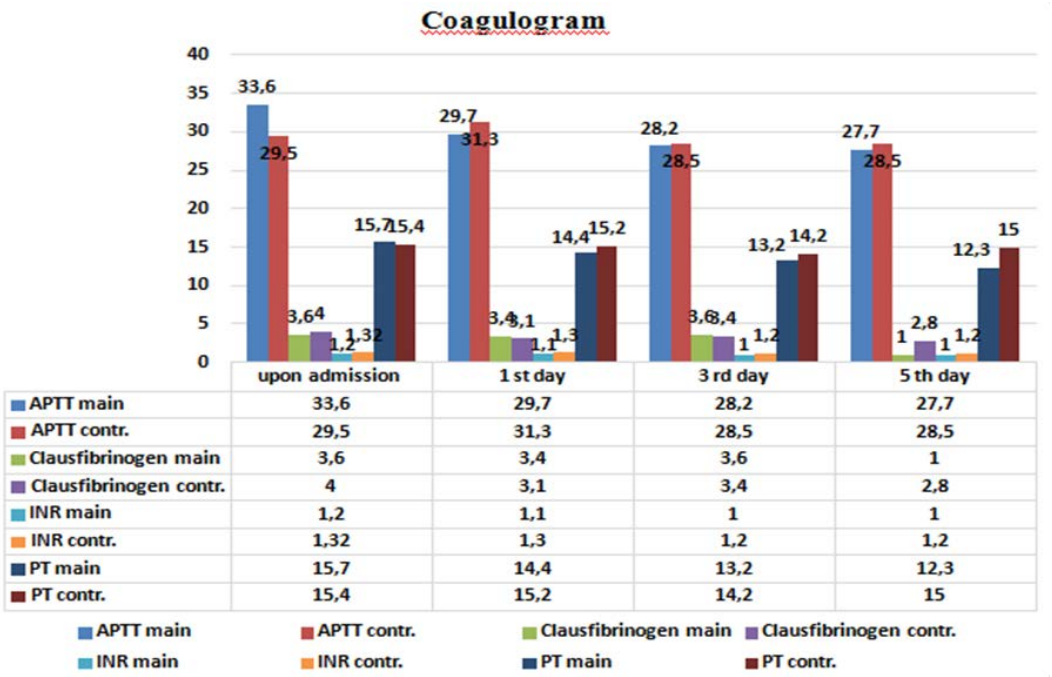

Figure 2. *Dynamics of changes in blood clotting indicators (n=79).*

Table 2. *Indicators of blood clotting after treatment in dynamics (n=79).*

		Upon admission (n=79)				**1st day (n=79)**				**3rd day (n=79)**				**5th day (n=79) *ф**				
№		**Main, sec n=35**	**95% CI**	**Con-trols, sec n=44**	**95% CI**	**Main, sec n=35**	**95% CI**	**Con-trols, sec n=44**	**95% CI**	**Main, sec n=35**	**95% CI**	**Con-trols, sec n=44**	**95% CI**	**Main, sec n=35**	**95% CI**	**Con-trols, sec n=44**	**95% CI**	**P - value**
1	**APTT**	33,6	(M:33,5, Q1-25; Q3-45,6)	29,5	(M:28,3, Q1-22,1; Q3-55,4).	29,7	(M:28,8, Q1-22,6; Q3-38,8)	31,3	(M:31,1, Q1-23,5;Q3-38,1)	28,2	(M:28,1, Q1-20,5; Q3-40)	28,2	(M:28,1, Q1-20,5; Q3-40)	27,7	(M:27,1, Q1-20,2; Q3-37,8)	28,5	(M:29,4, Q1-19; Q3-,38,9)	Fried-man chi-squared = 47.916, df = 3, p < 0.001
2	**Claus fi-brinogen**	3,6	(M:3,6, Q1-1,8; Q3-5,6	4	(M:3,9, Q1-2; Q3-6,5).	3,4	(M:3,4, Q1-2; Q3-5,4)	3,1	(M:3,1, Q1-2; Q3-4,8)	3,6	(M:3,6, Q1-2,0; Q3-5,5)	3,4	(M:3,6, Q1-2; Q3-4,8)	3,8	(M:3,6, Q1-3,0; Q3-5,3)	2,8	(M:3,1, Q1-1; Q3-4,6)	Fried-man chi-squared = 11,753, df = 3, p < 0.001
3	**INR**	1,2	(M:1,1, Q1-0,7; Q3-2,1)	1,32	(M:1,1, Q1-0,8; Q3-3,3).	1,1	(M:1,1, Q1-0,7; Q3-1,5)	1,3	(M:1,2, Q1-0,9; Q3-1,9)	1,0	(M:1,0, Q1-0,8; Q3-1,5)	1,2	(M:1,1, Q1-0,8; Q3-2,4)	1,0	(M:0,9, Q1-0,7; Q3-1,4)	1,2	(M:1,1, Q1-0,8; Q3-1,9)	Fried-man chi-squared = 40.122, df = 3, p < 0.001
4	**PV**	15,7	(M:16,1, Q1-9,5; Q3-29,5)	15,4	(M:14, Q1-11,2; Q3-39,3)	14,4	(M:14,4, Q1-8,9; Q3-26,5)	15,2	(M:14,8, Q1-8,9; Q3-26,5)	13,2	(M:13,6, Q1-8,5; Q3-18,2)	14,2	(M:14,1, Q1-8,5; Q3-18,2)	12,3	(M:12,5, Q1-9; Q3-14,5)	15	(M:14,1, Q1-12; Q3-19,7)	Fried-man chi-squared = 52.719, df = 3, p < 0.001

D.S.B., J.V.O., A.M.U.; formal analysis, M.T.O., M.Zh.A., S.T.A.,M.A.A., A.E.M.; investigation, M.T.O., M.Zh.A., S.T.A., N.B.O., M.A.A., M.N.A., A.S.O.; data curation, M.T.O., M.Zh.A., S.T.A., N.B.O.; writing—original draft preparation, M.T.O., M.Zh.A., S.T.A.; writing—review and editing, M.T.O., M.Zh.A., S.T.A. visualization, M.T.O., M.Zh.A., S.T.A., N.B.O.,A.S.O.; supervision, M.T.O., M.Zh.A., S.T.A.; project administration, M.T.O., M.Zh.A., S.T.A.; funding acquisition, M.T.O.. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted in accordance with the guidelines of the Helsinki Declaration and approved by the Ethics Committee of the Semey State Medical University (Protocol 2 of October 10, 2022, Project Identification Code).

Informed Consent Statement: The datasets created and analyzed in the course of this study are available from the relevant author upon reasonable request.

Data Availability Statement: The data is contained in the article.

Conflicts of Interest: The authors declare that there is no conflict of interest.

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