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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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EFFECTIVENESS OF PLASMA EXCHANGE IN THE THERAPY OF DRUG-INDUCED HEPATITIS IN PATIENTS WITH PULMONARY TUBERCULOSIS AND CHRONIC VIRAL HEPATITIS B AND C

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Abstract.

Background: This study evaluated the effectiveness of plasma exchange for the management of drug-induced hepatitis in patients with drug-resistant pulmonary tuberculosis, including those with concomitant chronic viral hepatitis. Along with standard conservative therapy, increasing attention is being paid to extracorporeal hemocorrection methods in the treatment of acute hepatitis.

Materials and methods: The study included 127 patients with drug-resistant pulmonary tuberculosis treated at the City Center for Phthisiology and Internal Medicine in Astana from 2024 to February 2026. Chronic viral hepatitis was diagnosed in 65 of 127 patients: hepatitis B in 9 (13.8%), hepatitis C in 51 (78.5%), and mixed hepatitis B + C in 5 (7.7%). During anti-tuberculosis chemotherapy, 53 of 127 patients (41.7%) developed drug-induced hepatitis. This complication occurred significantly more often in patients with chronic viral hepatitis than in those without it: 39 of 65 (60.0%) versus 14 of 62 (22.6%), respectively ($p < 0.001$). Patients were divided into two groups, one of which received plasma exchange for the correction of drug-induced hepatitis.

Results: The use of plasma exchange in the study group made it possible to control manifestations of drug-induced hepatitis without discontinuing specific anti-tuberculosis therapy. In the control group, where plasma exchange was not used, temporary interruption of specific therapy was required.

Conclusion: The inclusion of plasma exchange in the comprehensive treatment of drug-induced hepatitis in patients with drug-resistant pulmonary tuberculosis made it possible to control hepatotoxicity without interrupting anti-tuberculosis chemotherapy, which is especially important in patients with concomitant chronic viral hepatitis.

Key words. Drug-induced hepatitis, pulmonary tuberculosis, drug resistance, chronic viral hepatitis, therapeutic plasma exchange.

Introduction.

Drug-induced liver injury (DILI) associated with anti-tuberculosis drugs has been reported in 5.4-85.7% of treated patients [1-3]. According to recent studies, the frequency of drug-induced hepatitis ranges from 1.0% to 89.9%, whereas the hepatotoxic effect of anti-tuberculosis drugs (ATDs) usually develops during the first month of chemotherapy, which is associated with a cumulative effect [4,5]. Liver damage caused by ATDs is one of the leading reasons for treatment failure in patients with tuberculosis, even in those with high adherence and adequate drug supply [6-8].

Among liver disorders observed in patients with tuberculosis, drug-induced hepatitis ranks first, with a reported frequency ranging from 4.3% to 76.2%. DILI most often develops in the presence of concomitant digestive diseases, particularly liver pathology [9,10]. According to several authors, chronic viral hepatitis C predominates in the structure of comorbidity in patients with tuberculosis, with a frequency of up to 63.7%. Chronic viral hepatitis B occurs 2.0–2.8 times less often, accounting for 27.8% [11-13].

The diagnosis of DILI is an indication for temporary discontinuation of all ATDs. Failure to comply with this recommendation is associated with a risk of acute liver failure. If the severity of the tuberculosis process does not allow interruption of specific therapy, an equivalent treatment regimen or detoxification methods are recommended [14-17]. To prevent or reduce hepatotoxicity, various approaches have been proposed, including alternative routes of administration for chemotherapy drugs (intravenous, lymphotropic, inhalational, and rectal), intermittent chemotherapy regimens, and individualized selection of drug combinations [18,19]. A number of authors also recommend combining ATDs with hepatoprotective agents, antioxidants, vitamins, and phospholipids [20-22].

According to the literature, efferent therapies represent a cost-effective approach to the treatment of liver diseases, and plasma exchange occupies one of the leading positions among extracorporeal hemocorrection procedures [23-26]. Compared with other methods, plasma exchange provides effective removal of macromolecules and protein-bound toxins. The physiological response to plasma exchange depends on the volume of pathological substrates removed during one procedure, the severity of the drainage effect, the volume and frequency of procedures, and the characteristics of plasma exchange volume during and immediately after the session [27-30].

Unlike other extracorporeal hemocorrection methods, the specificity of plasma exchange is largely determined by the volume and quality of plasma exchange. Thus, plasma exchange exerts primarily detoxifying and immunocorrective effects and is a pathogenetically justified component of comprehensive treatment for liver diseases [31-35].

Aim. The aim of this study was to determine the effectiveness of therapeutic plasma exchange in controlling manifestations of drug-induced hepatitis that developed during chemotherapy in patients with drug-resistant pulmonary tuberculosis, including those with concomitant chronic viral hepatitis.

Materials and Methods.

The retrospective study included 127 patients with drug-resistant pulmonary tuberculosis who were treated at the City

Center for Phthisiology and Internal Medicine in Astana from 2024 to February 2026. Inpatient and outpatient medical records were entered into a Microsoft Excel 2017 database.

The patients were 18 to 60 years old, with a mean age of 39.0 ± 0.94 years. Men accounted for 59% (75/127) and women for 41% (52/127). The GeneXpert MTB/RIF molecular assay was used to examine sputum and confirm the diagnosis. More than half of the patients, 53.5% (68/127), had previously received two or more ineffective chemotherapy courses, including regimens containing reserve anti-tuberculosis drugs.

Inclusion criteria were age 18-60 years, completed treatment for pulmonary tuberculosis, and the presence of chronic viral hepatitis. The exclusion criterion was any comorbidity other than chronic viral hepatitis. Of the 127 patients included in the study, 65 were diagnosed with chronic viral hepatitis: chronic hepatitis B was identified in 5/65 patients (7.7%), chronic hepatitis C in 51/65 patients (78.5%), and mixed hepatitis B and C infection in 9/65 patients (13.8%).

All patients underwent a comprehensive examination during hospitalization and follow-up, including biochemical blood tests (total protein, total and direct bilirubin, ALT, AST, GGT, alkaline phosphatase, creatinine, urea, and a coagulation panel) as well as abdominal ultrasound, electrocardiography, fibrogastroduodenoscopy, and chest computed tomography.

Chronic viral hepatitis was diagnosed by serological testing using enzyme-linked immunosorbent assay (HBsAg, anti-HCV), as well as polymerase chain reaction with qualitative and quantitative detection of hepatitis C virus RNA and hepatitis B virus DNA.

All patients received comprehensive treatment, including either a short-course or individualized chemotherapy regimen depending on the drug-resistance profile of Mycobacterium tuberculosis, in accordance with Clinical Guideline of the Ministry of Health of the Republic of Kazakhstan, as well as concomitant therapy. During specific anti-tuberculosis therapy, 53 of 127 patients (41.7%) developed drug-induced hepatitis. Depending on the type of corrective treatment, the patients were divided into a study group and a control group. The study group received infusion detoxification therapy, hepatoprotectors, and sessions of automated plasma exchange, whereas the control group received only infusion detoxification therapy and hepatoprotectors.

During anti-tuberculosis therapy, hepatotoxic reactions were recorded in accordance with the recommendations of the American Thoracic Society [36] and were defined as follows: aminotransferase levels exceeding five times the upper limit of normal (ULN) in the absence of symptoms of hepatitis, including nausea, weakness, right upper quadrant pain, anorexia, and jaundice; or aminotransferase levels exceeding three to five times the ULN in the presence of symptoms of hepatitis, including nausea, weakness, right upper quadrant pain, anorexia, and jaundice.

Therapeutic plasmapheresis was indicated in patients with aminotransferase levels exceeding five times the ULN and jaundice. Infusion detoxification and hepatoprotective therapy were indicated in patients with aminotransferase levels exceeding five times the ULN in the absence of jaundice.

The study group consisted of 26 patients, including 20 with concomitant chronic viral hepatitis and 6 without chronic viral hepatitis. The control group consisted of 27 patients, including 19 with concomitant chronic viral hepatitis and 8 without chronic viral hepatitis. The groups were comparable in terms of clinical forms of pulmonary tuberculosis and the presence of chronic viral hepatitis. Fibrous-cavernous and infiltrative pulmonary tuberculosis predominated in both groups (Table 1).

From the beginning of chemotherapy, all patients in both groups received ursodeoxycholic acid prophylactically as a hepatoprotector. After the development of drug-induced hepatitis, hepatoprotective therapy was intensified with silymarin- and glycyrrhizic acid-based drugs in standard therapeutic doses, as well as Essentiale 10.0 mL mixed with autoblood administered intravenously followed by oral therapy. A 5% glucose solution, Reamberin, and Sterofundin ISO were used for detoxification.

The comparison of factors associated with hepatotoxicity and the duration of inpatient treatment between groups of patients with ALT and AST levels exceeding five times the upper limit of normal is presented in Table 2. The two groups were comparable in terms of sex, age, and concomitant chronic viral hepatitis. Most patients had a history of previous ineffective treatment courses. The total duration of hospitalization was significantly longer in the control group than in the intervention group ($p = 0.01$).

Therapeutic plasma exchange was performed using the Haemonetics MCS+ device (USA). The treatment course consisted of 2 to 5 procedures at 3-day intervals. Plasma was removed in a volume corresponding to 20–25% of the calculated individual circulating plasma volume. Advantages of this method include return of cellular blood components, minimal platelet loss due to their low content in the removed plasma, and the possibility of compensating for the removed plasma volume with normal saline during the return cycle.

Pearson's chi-squared test (χ^2), Student's t-test and Fisher's exact test were used to compare parameters between the study and control groups. Differences were considered statistically significant at $p < 0.05$.

Results.

During specific anti-tuberculosis therapy, drug-induced hepatitis developed in 53 of 127 patients (41.7%). In patients with chronic viral hepatitis, this complication was recorded significantly more often than in patients without chronic viral hepatitis: 39 of 65 (60.0%) versus 14 of 62 (22.6%), respectively (Fisher's exact test, $p < 0.001$). ALT levels exceeded five times the ULN in this patient subgroup ($p < 0.001$). No significant increases in other biochemical parameters above the upper limit of normal were observed.

The blood biochemical parameters of patients in both groups before the initiation of corrective therapy are presented in Table 3. As shown in the table, total bilirubin and direct bilirubin levels were significantly higher in patients in the main group than in the control group (Student's t-test, $p < 0.040$ and $p < 0.032$, respectively). The remaining liver function test parameters and total protein levels did not differ significantly between the groups.

Table 1. *Characteristics of pulmonary tuberculosis and chronic viral hepatitis in the study and control groups.*

Characteristics	**Study group (n = 26)**	**Control group (n = 27)**	**P (χ^2 or FET)**
Infiltrative tuberculosis	14	13	0.67*
Fibrous-cavernous tuberculosis	12	14	0.67*
MTB+	26	27	1.000**
Drug-resistant MTB	26	27	1.000**
Chronic viral hepatitis B	3	2	0.669**
Chronic viral hepatitis C	12	13	0.88*
Mixed chronic viral hepatitis B + C	5	4	0.73**

Note: ** – Pearson's chi-squared test (χ2), ** – Fisher's exact test (FET).*

Table 2. *Baseline characteristics of patients in the main and control groups who developed drug-induced hepatitis.*

Variables	**Main group (n = 26)**	**Control group (n = 27)**	**p-value**
	M ± m	M ± m	
Age, years	39.0 ± 0.95	38.0 ± 0.99	0.827***
Male, n (%)	15 (57.7%)	17 (62.9%)	0.695*
Female, n (%)	11 (42.3%)	10 (37.0%)	0.695*
Previous ineffective therapy with anti-tuberculosis drugs, n (%)	20 (76.9%)	21 (77.7%)	0.941*
Total duration of hospitalization, days	153.0 ± 9.5	191.0 ± 10.7	0.01***
Concomitant diseases, n (%)			
Chronic viral hepatitis B, n (%)	3 (11.5%)	2 (7.4%)	0.669**
Chronic viral hepatitis C, n (%)	12 (46.2%)	13 (48.1%)	0.884*
Chronic viral hepatitis B and C, n (%)	5 (19.2%)	4 (14.8%)	0.728**
Death, n (%)	—	—	—

Note: ** - Pearson's chi-square test (χ^2) was used; ** - Fisher's exact test was used; *** - Student's t-test.*

Table 3. *Comparison of blood biochemical parameters in the two groups before the initiation of corrective therapy.*

Parameter	**Main group (n = 26)**	**Control group (n = 27)**	**p-value**
	M ± m	M ± m	
ALT, U/L	285.67 ± 5.44	297.12 ± 6.73	0.192
AST, U/L	273.89 ± 3.50	282.70 ± 4.20	0.113
Total bilirubin, μmol/L	41.03 ± 8.75	17.90 ± 6.70	0.040
Direct bilirubin, μmol/L	32.10 ± 7.91	5.10 ± 9.39	0.032
Total protein, g/L	72.80 ± 0.38	73.42 ± 0.21	0.159
ALP, U/L	145.24 ± 1.15	142.35 ± 1.73	0.170
GGTP, U/L	93.61 ± 2.73	88.70 ± 2.55	0.195

Note: *Student's t-test was used.*

Table 4. *Timing of onset of drug-induced hepatitis in the groups during chemotherapy.*

Timing of onset of drug-induced hepatitis	**Study group (n = 26)**	**Control group (n = 27)**	**P (χ^2 or FET)**
1st month of chemotherapy	17 (65.4%)	15 (55.6%)	0.47*
2nd month of chemotherapy	5 (19.3%)	6 (22.3%)	0.78*
3rd month of chemotherapy	2 (7.7%)	3 (11.1%)	0.58*
4th month of chemotherapy	2 (7.7%)	1 (3.7%)	0.55*
5th month of chemotherapy	0	2 (7.4%)	0.491**

Note: ** – Pearson's chi-squared test (χ2), ** – Fisher's exact test (FET).*

Table 5. *Time to resolution of drug-induced hepatitis in the groups during therapy.*

Time to resolution after initiation of correction	**Number of plasma exchange sessions in the study group**	**Study group (n = 26)**	**Control group (n = 27)**	**P (χ^2 or FET)**
10 days or less	2	9	10 (CDT-4)	0.854*
11-15 days	3	11	7 (CDT-3)	0.208*
16-20 days	4	4	6 (CDT-3)	0.728**
21-29 days	5	2	4 (CDT-0)	0.669**
Chemotherapy discontinuation	0%	0	10 (37%)	0.001**

Note: *CDT - chemotherapy discontinuation; * Pearson's chi-squared test (χ^2); ** Fisher's exact test (FET).*

Drug-induced hepatitis most often developed during the early phase of anti-tuberculosis drug administration, predominantly within the first 2 months of therapy. In both groups, the number of cases during the first month exceeded that in the second and subsequent months (Table 4). This may be related to the fact that most patients had a history of previous ineffective treatment courses.

As shown in Table 5, manifestations of drug-induced hepatitis were resolved in patients of both groups. In the study group, chemotherapy discontinuation was not required in any case.

By day 10 of corrective therapy, patients in the study group had undergone two plasma exchange sessions, which were sufficient to eliminate manifestations of drug-induced hepatitis in 9 patients. The remaining patients required an extended course. Between days 11 and 15, an additional session was performed in 17 patients, which resulted in resolution of drug-induced hepatitis in 11 patients. The remaining 6 patients required further continuation of plasma exchange: 4 patients received up to 4 sessions within 20 days, and 2 patients received up to 5 sessions within 29 days.

In the control group, chemotherapy was temporarily suspended in 10 of 27 patients (37.0%) for 8 to 20 days, with a mean duration of 14 days. Resolution of drug-induced hepatitis within 10 days was achieved in 10 patients, of whom 4 required interruptions of chemotherapy. In 7 patients, resolution required 11–15 days, including 3 patients in whom chemotherapy was interrupted. In the remaining 10 patients, a longer period was required.

The rate of resolution of drug-induced hepatitis within the predefined time frames did not differ significantly between the groups. However, the need for temporary chemotherapy discontinuation arose significantly more often in the control group. The rate of chemotherapy discontinuation was statistically significantly higher in the control group ($p < 0.001$).

Clinical Cases.

This study presents two clinical cases of treatment of patients with chronic viral hepatitis C. Two clinical cases were selected as representative examples of decision-making in patients with drug-resistant pulmonary tuberculosis and concomitant chronic hepatitis C who developed drug-induced hepatitis despite normal baseline liver function tests. They illustrate how the choice of management was guided by biochemical severity and treatment response: therapeutic plasma exchange allowed continuation of chemotherapy in one patient, whereas insufficient response to standard corrective therapy required temporary chemotherapy discontinuation in the other.

Clinical Case 1.

Patient I. was treated for cavitary infiltrative pulmonary tuberculosis with dissemination, sputum-positive disease, and drug-resistant Mycobacterium tuberculosis. The concomitant diagnosis was chronic hepatitis C with minimal biochemical activity.

According to the medical history, the patient developed hemoptysis, which prompted an emergency medical call. He was transported to the hospital and evaluated in the emergency department.

Chest computed tomography (CT) at admission (Figure 1) revealed extensive irregular areas of infiltrative consolidation in the upper lobe of the right lung and in the upper and lower lobes of the left lung. Cavitary lesions measuring up to 35 × 10 mm were visualized within the right-sided infiltrates. Multiple nodular foci of varying size were detected in all lobes of both lungs, with partial confluence into small infiltrates. The trachea and main bronchi were patent to the segmental level; the bronchial walls appeared infiltrated, and tractional bronchial dilatation was noted. The heart, pericardium, thoracic aorta, pulmonary trunk, and its branches were clearly visualized. The major mediastinal vessels were of normal caliber. Calcified atherosclerotic plaques were identified in the thoracic aorta and coronary arteries. Mediastinal lymph nodes were moderately enlarged, measuring up to 12 mm. Overall, the CT findings were consistent with cavitary infiltrative pulmonary tuberculosis with dissemination, mediastinal lymphadenopathy, and aortic and coronary atherosclerosis.

The patient was referred to a specialized tuberculosis center. In the admission department, sputum testing using the GeneXpert MTB/RIF assay was positive for M. tuberculosis and demonstrated rifampin resistance. Sputum smear microscopy for M. tuberculosis was also positive.

Given the hemoptysis, medical history, examination findings, and disease severity, the patient was hospitalized in the therapeutic department. A short-course chemotherapy regimen was prescribed, consisting of cycloserine 250 mg, three capsules once daily, clofazimine 100 mg, one capsule once daily, amisolid 600 mg, one tablet once daily, bedaquiline 100 mg, two tablets once daily, and levosin 500 mg, two tablets once daily.

Before chemotherapy, liver biochemical parameters were within the reference ranges: total bilirubin, 12.60 μmol/L; direct bilirubin, 3.80 μmol/L; thymol turbidity test, 1.6 units; ALT, 10.40 U/L; AST, 31.3 U/L; alkaline phosphatase, 45 U/L; GGT, 17 U/L; and total protein, 68.90 g/L. One month after treatment initiation, elevated liver biochemical markers were observed: total bilirubin, 38 μmol/L; ALT, 310 U/L; AST, 280 U/L; alkaline phosphatase, 142 U/L; and GGT, 95 U/L. The patient therefore received hepatoprotective therapy, supportive infusion therapy, and a course of therapeutic plasma exchange consisting of four sessions. After two plasma exchange sessions, liver biochemical parameters decreased to total bilirubin, 17 μmol/L; ALT, 117 U/L; AST, 93 U/L; alkaline phosphatase, 101 U/L; and GGT, 84 U/L. After two additional sessions, all parameters returned to the reference ranges.

Thereafter, liver biochemical parameters remained normal throughout the remainder of treatment, and chemotherapy was continued without interruption. After 2 months of therapy, sputum smear conversion was achieved, constitutional symptoms resolved, and body weight increased by 10 kg.

Follow-up chest CT (Figure 2) demonstrated irregular areas of pulmonary consolidation with predominantly smooth, focally slightly irregular, well-defined margins in the upper and lower lobes of both lungs, along with fibrotic changes in the surrounding parenchyma. Cylindrical dilatation of the subsegmental bronchi was visualized in the upper lobe of the right lung. Multiple nodular opacities of varying size were

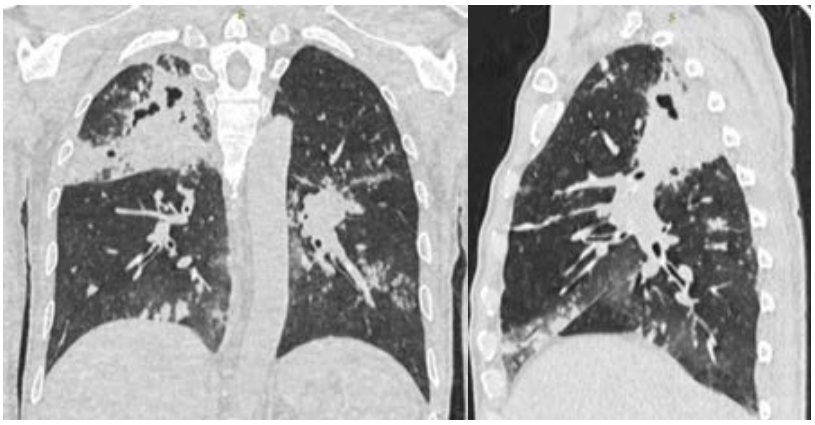

Figure 1. *Chest computed tomography (reconstruction in frontal and lateral views) of patient I. on admission, dated 24.07.2025.*

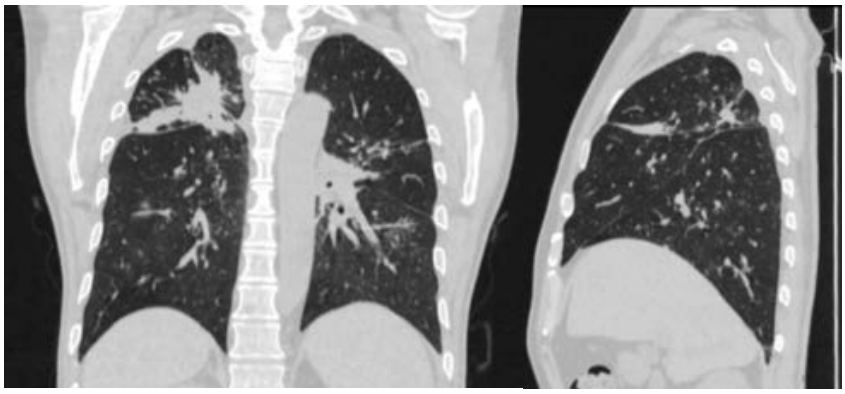

Figure 2. *Chest computed tomography (reconstruction in frontal and lateral views) of patient I. at discharge, dated 26.02.2026.*

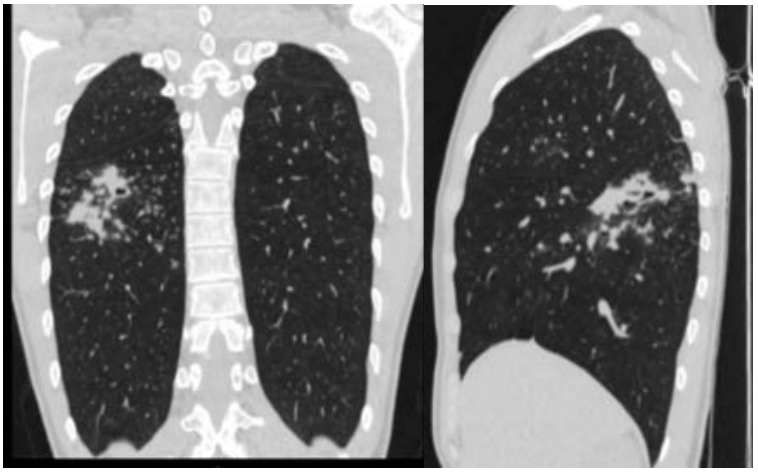

Figure 3. *Chest computed tomography (reconstruction in frontal and lateral views) of patient R., dated 11.07.2025.*

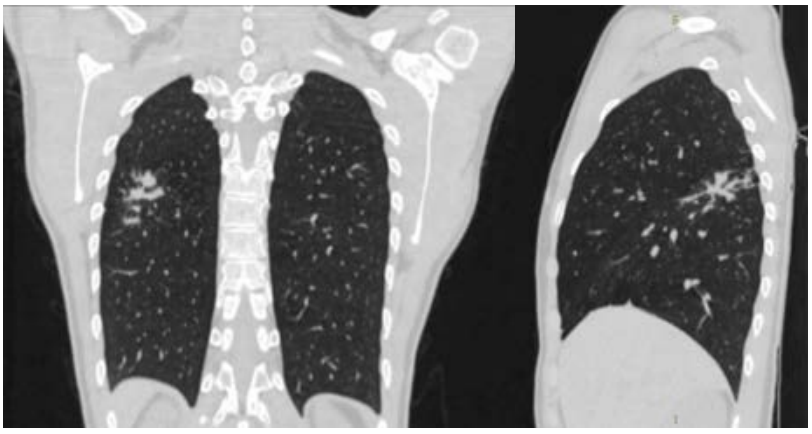

Figure 4. *Chest computed tomography (reconstruction in frontal and lateral views) of patient R. at discharge, dated 06.01.2026.*

present bilaterally. A solitary calcified focus was noted in the lower lobe of the left lung. The trachea and main bronchi remained patent to the segmental level; the bronchial walls were thickened, with focal calcifications. Calcified plaques were also observed along the thoracic aorta and in the region of the left coronary artery. No enlargement of intrathoracic lymph nodes was observed. Overall, the CT findings were consistent with infiltrative pulmonary tuberculosis in the phase of resorption and consolidation, with scarring of the cavitary lesion in the right lung. Compared with baseline CT performed at admission, the infiltrates had decreased in size, and the right-sided cavitary lesion had scarred.

The patient was discharged in satisfactory condition. Outpatient follow-up with a tuberculosis specialist at the place of residence was recommended, including monthly sputum monitoring, routine clinical laboratory testing, electrocardiography, chest radiography every 3 months, and additional investigations as clinically indicated.

Clinical Case 2.

Patient R. was admitted with cavitary infiltrative pulmonary tuberculosis with bronchogenic dissemination, microbiologically confirmed Mycobacterium tuberculosis, and documented drug resistance. The concomitant diagnosis was chronic hepatitis C with minimal biochemical activity.

The patient had been symptomatic for 10 days and sought medical care on the third day after symptom onset. Initial chest radiography suggested right-sided pneumonia. The patient received ceftriaxone 1.0 g twice daily for 10 days, dexamethasone 8 mg, and intravenous ascorbic acid 8.0 mL. Subsequent chest computed tomography (CT) revealed inflammatory changes in the right lung and the lower lobe of the left lung, destructive changes in the lower lobe of the right lung, and mediastinal lymphadenopathy.

The patient was referred to a specialized tuberculosis center for further evaluation. Sputum testing using the GeneXpert MTB/RIF assay was positive for M. tuberculosis and demonstrated rifampin resistance. Sputum microscopy for acid-fast bacilli was positive on two occasions.

Based on the clinical history, laboratory findings, imaging data, and confirmed sputum positivity, the patient was hospitalized and started on an individualized anti-tuberculosis regimen consisting of pretomanid 200 mg once daily, linezolid 600 mg once daily, moxifloxacin 400 mg once daily, and bedaquiline 200 mg, administered as two 100-mg tablets, three times weekly.

Chest CT at treatment initiation (Figure 3) demonstrated irregular areas of infiltrative consolidation with air bronchograms and slit-like cavitary lesions measuring up to 7 × 20 mm in segment 6 of the right lung. Clustered, medium-sized foci of bronchogenic dissemination were identified in the surrounding parenchyma, as well as in segment 3 of the right lung and segment 8 of the left lung. The trachea and main bronchi were patent to the segmental level; however, the bronchial walls in the lower lobe of the right lung appeared infiltrated. The heart, pericardium, thoracic aorta, pulmonary trunk, and its branches were clearly visualized. No enlargement of intrathoracic lymph nodes was observed. Overall, the CT findings were consistent with infiltrative tuberculosis involving segment 6 of the right lower lobe, with cavitation and dissemination.

Compared with the previous chest CT scan, a mildly positive radiologic response was observed, with partial resolution and consolidation of infiltrative changes and foci in the right lung; however, the cavitary lesions persisted.

At admission, liver biochemical parameters were within the reference ranges: total protein, 74.60 g/L; total bilirubin, 12.50 μmol/L; direct bilirubin, 5.20 μmol/L; AST, 27.00 U/L; ALT, 15 U/L; alkaline phosphatase, 76 U/L; and GGT, 35 U/L. Two and a half months after the start of chemotherapy, liver biochemical abnormalities developed: total bilirubin, 18 μmol/L; ALT, 290 U/L; AST, 270 U/L; alkaline phosphatase, 151 U/L; and GGT, 72 U/L.

Infusion detoxification therapy and hepatoprotective treatment did not result in a sufficient clinical and biochemical response; therefore, chemotherapy was temporarily discontinued. The criterion for discontinuation was a grade 3 severe adverse reaction to anti-tuberculosis drugs, defined as an ALT increase to 5-20 times the upper limit of normal, in accordance with Clinical Guidelines of the Ministry of Health of the Republic of Kazakhstan. During subsequent treatment, liver biochemical parameters gradually improved, and chemotherapy was resumed according to the treatment plan 2 weeks later, after normalization of liver function tests.

Follow-up chest CT (Figure 4) showed irregular, limited areas of residual infiltration with air-containing bronchi and fibrotic strands in segment 6 of the right lung. Clustered small foci were visualized in the surrounding parenchyma, as well as in segment 3 of the right lung and segment 8 of the left lung. The trachea and main bronchi remained patent to the segmental level, while the bronchial walls in the lower lobe of the right lung remained infiltrated. Overall, the CT findings were consistent with infiltrative tuberculosis of segment 6 of the right lower lobe in the phase of resolution and consolidation, with scarring of the cavitary lesion in the right lung.

Sputum smear and culture conversion were achieved after 3 months of treatment, and cavity healing was observed after 8 months. The patient was discharged in satisfactory condition. Recommendations included dispensary registration and follow-up with a pulmonologist at the place of residence, monthly sputum monitoring, routine clinical laboratory testing and electrocardiography, and chest radiography every 3 months.

Discussion.

The present study demonstrates that chronic viral hepatitis is an important risk factor for drug-induced hepatitis during anti-tuberculosis chemotherapy in patients with drug-resistant pulmonary tuberculosis. Drug-induced hepatitis developed significantly more often in patients with chronic viral hepatitis than in those without viral hepatitis, indicating reduced hepatic tolerance to prolonged multidrug chemotherapy. This finding is consistent with recent meta-analyses showing that chronic hepatitis C and chronic hepatitis B increase susceptibility to anti-tuberculosis drug-induced liver injury [37-40]. In a recent meta-analysis, the pooled prevalence of DILI was 15.54% in patients with HCV-TB co-infection compared with 8.54% in patients without HCV, with an overall odds ratio of 3.50; when a strict definition of DILI was applied, namely ALT >5 × ULN, the risk remained increased, with an odds ratio of 4.13 [37].

Similarly, chronic hepatitis C was associated with increased DILI risk in an earlier meta-analysis of 14 studies, while chronic hepatitis B was also associated with increased risk, with pooled estimates ranging from approximately twofold to nearly threefold depending on study design [38-40].

The predominance of chronic hepatitis C in our cohort is clinically relevant. HCV-related liver disease may remain biochemically mild before chemotherapy; however, persistent necroinflammatory activity, oxidative stress, mitochondrial dysfunction, and reduced hepatocellular reserve may increase vulnerability to drug-induced injury. In patients with drug-resistant tuberculosis, this risk may be further amplified by previous ineffective treatment courses, repeated exposure to anti-tuberculosis drugs, and the cumulative metabolic burden of prolonged chemotherapy.

Drug-induced hepatitis developed predominantly during the first two months of chemotherapy, which is consistent with evidence that DILI usually occurs early after treatment initiation and may range from asymptomatic aminotransferase elevation to severe hepatitis and acute liver failure [41]. This early onset is particularly important in drug-resistant tuberculosis, where interruption of chemotherapy may compromise treatment continuity, delay sputum conversion, and increase the risk of unfavorable outcomes.

The most clinically significant finding of this study was that therapeutic plasma exchange allowed continuation of anti-tuberculosis chemotherapy in all patients in the plasma exchange group, whereas chemotherapy was temporarily discontinued in more than one-third of patients in the control group. Although time to biochemical resolution did not differ significantly between groups, the need for chemotherapy discontinuation was significantly lower in the plasma exchange group. Thus, the main value of plasma exchange in our study appears to be preservation of treatment continuity rather than merely acceleration of biochemical recovery.

This finding is supported by broader evidence on plasma exchange in severe liver injury, although direct evidence in anti-tuberculosis DILI with concomitant chronic viral hepatitis remains limited. Liu et al. reported two cases of DILI-related acute liver failure successfully treated with high-volume plasma exchange without liver transplantation; one case involved a 94-year-old man with newly diagnosed pulmonary tuberculosis who developed DILI and acute liver failure five days after starting anti-tuberculosis treatment, with grade 4 hepatic encephalopathy, followed by recovery after plasma exchange [42]. In a randomized trial of 182 patients with acute liver failure, high-volume plasma exchange improved hospital survival compared with standard medical therapy alone, 58.7% versus 47.8%, respectively [43-45]. Standard-volume plasma exchange has also been associated with improved outcomes in acute liver failure, while systematic reviews support a potential survival benefit, although optimal indications, timing, and exchange volume remain uncertain [46-48].

Chronic viral hepatitis represents a state of pre-existing hepatic vulnerability, and DILI may act as an acute hepatic insult superimposed on chronic liver disease. Evidence from acute-on-chronic liver failure suggests that plasma exchange may reduce systemic inflammation and improve short-term outcomes in selected patients [49]. However, current evidence does not support routine use of plasma exchange in all cases of DILI. Rather, it supports individualized use in selected patients with severe biochemical hepatitis, hyperbilirubinemia or jaundice, and a strong clinical need to avoid interruption of essential anti-tuberculosis therapy.

Existing studies support plasma exchange in acute liver failure, acute-on-chronic liver failure, severe toxic hepatitis, and selected cases of DILI-related acute liver failure [42-49]. However, data specifically addressing therapeutic plasma exchange for anti-tuberculosis drug-induced hepatitis in patients with concomitant chronic viral hepatitis remain limited. In this context, our findings suggest that plasma exchange may be a clinically useful adjunctive intervention that allows continuation of chemotherapy and may reduce hospitalization duration in carefully selected patients. This conclusion is consistent with the American Society for Apheresis framework, which emphasizes disease-specific indications, severity assessment, and individualized decision-making when therapeutic apheresis is considered [50].

Several limitations should be acknowledged. The retrospective design limits causal interpretation, and the relatively small sample size may have reduced the statistical power to detect differences in time to biochemical resolution. In addition, patients were not randomized to plasma exchange, and the indication for the procedure was based on clinical severity, including jaundice and marked aminotransferase elevation, introducing potential confounding by indication. Finally, long-term outcomes after discharge, including recurrence of hepatotoxicity, sustained tuberculosis treatment success, and viral hepatitis activity, were not fully evaluated.

Conclusion.

Chronic viral hepatitis significantly increased the risk of drug-induced hepatitis during anti-tuberculosis chemotherapy in patients with drug-resistant pulmonary tuberculosis. Therapeutic plasma exchange, used as part of comprehensive corrective therapy, was associated with preservation of chemotherapy continuity and shorter hospitalization, despite more pronounced bilirubin elevation before the initiation of corrective treatment.

These findings suggest that therapeutic plasma exchange may be considered as an adjunctive strategy in selected high-risk patients with anti-tuberculosis drug-induced hepatitis and concomitant chronic viral hepatitis. A course of plasma exchange consisting of 2-5 sessions at 3-day intervals may improve chemotherapy tolerance and alleviate manifestations of drug-induced hepatitis in patients with drug-resistant pulmonary tuberculosis, including those with chronic viral hepatitis.

Prospective controlled studies are required to confirm these results, define optimal indications and timing, and evaluate the long-term impact of this approach on tuberculosis treatment outcomes and hepatic safety.

REFERENCES

1. Avdeeva MG, Kulbuzheva MI, Kolodko EI, et al. Problemy lecheniya toksicheskogo gepatita na fone khronicheskogo virusnogo porazheniya pecheni HCV-etiologii. Klinicheskiy primer uspeshnoy terapii. Epidemiologiya i infektsionnye bolezni. 2018;23:50-56.
2. Maev IV, Polunina TE. Lekarstvennye povrezhdeniya pecheni: diagnoz isklyucheniya. Terapevticheskii arkhiv. 2023;95:611-620.
3. Klyaritskaya IL, Maksimova EV, Stilidi EI, et al. Lekarstvennye porazheniya pecheni: sovremennyy vzglyad na problemu (chast 1). Krymskiy terapevticheskiy zhurnal. 2024;4:65-73.
4. Sukhanov DS, Timofeev EV, Alekseeva YuS, et al. Lekarstvennye porazheniya pecheni pri tuberkuleze. Mekhanizmy razvitiya i metody diagnostiki. Juvenis Scientia. 2023;9:24-42.
5. Zakrzewska A, Grzybowska ME, Wydra DG, et al. Plasma exchange for suspected drug-induced liver injury during pregnancy: a multidisciplinary diagnostic and therapeutic challenge. J Clin Med. 2025;14:8385.
6. Saenko SA, Sterlikov SA, Rusakova LI. Prediktory preryvaniya lecheniya bolnymi tuberkulezom s mnozhestvennoy lekarstvennoy ustoychivostyu mikobakteriy tuberkuleza. Tuberkulez i bolezni legkikh. 2021;3:461-474.
7. Dixon EG, Rasool S, Otaalo B, et al. No action is without its side effects: adverse drug reactions and missed doses of antituberculosis therapy, a scoping review. Br J Clin Pharmacol. 2024;90:313-320.
8. Kėvelaitienė K, Davidavičienė VE, Danila E. Tuberculosis treatment failure: what are the risk factors? A comprehensive literature review. Multidiscip Respir Med. 2025;20:1030.
9. Singh KA, Kumar SE, Zachariah UG, et al. Single-centre experience with low-volume plasma exchange and low-dose steroid in patients with idiosyncratic drug-induced acute liver failure. J Clin Exp Hepatol. 2024;14:101303.
10. Vaniev EV, Samoylova AG, Ergeshov AE, et al. Vozmozhnosti apparatnogo plazmafereza pri gepatotoksicheskikh reaktsiyakh na khimioterapiyu u bolnykh tuberkulezom legkikh s mnozhestvennoy lekarstvennoy ustoychivostyu, v tom chisle pri soputstvuyushchikh virusnykh gepatitakh. Tuberkulez i bolezni legkikh. 2018;96:13-19.
11. Baramzina SV. Khronicheskie virusnye gepatity B i C u bolnykh tuberkulezom: udelnyy ves nozoform, dinamicheskie izmeneniya. Zhurnal infektologii. 2015;7:47-53.
12. Olaru ID, Meier MB, Mirzayev F, et al. Global prevalence of hepatitis B or hepatitis C infection among patients with tuberculosis disease: systematic review and meta-analysis. EClinicalMedicine. 2023;58:101938.
13. Feleke BE, Feleke TE, Adane WG, et al. Impacts of hepatitis B and hepatitis C co-infection with tuberculosis: a prospective cohort study. Virol J. 2020;17:113.
14. Belfeki N, Strazzulla A, Isnard P, et al. Successful therapeutic plasma exchange in cold autoimmune hemolytic anemia in patient with disseminated tuberculosis. Reumatismo. 2021;72:247-251.
15. Devarbhavi H, Singh R, Patil M, et al. Outcome and determinants of mortality in 269 patients with combination anti-tuberculosis drug-induced liver injury. J Gastroenterol Hepatol. 2013;28:161-167.
16. Kumar R, Singh A, Patel N, et al. Therapeutic plasma exchange as adjunctive treatment in severe pulmonary tuberculosis. Int J Infect Dis. 2022;116:120-126.
17. Yakut N, Kutlu NO, Kilinc A, et al. A case of immunocompetent tuberculosis-associated immune reconstitution inflammatory syndrome treated with a novel strategy-zipper method plasma exchange. J Paediatr Child Health. 2023;59:389-391.
18. Nyang'wa BT, Berry C, Kazounis E, et al. TB-PRACTECAL team. Short oral regimens for pulmonary rifampicin-resistant tuberculosis (TB-PRACTECAL): an open-label, randomised, controlled, phase 2B-3, multi-arm, multicentre, non-inferiority trial. Lancet Respir Med. 2024;12:117-128.
19. Guglielmetti L, Khan U, Velásquez GE, et al. Oral regimens for rifampin-resistant, fluoroquinolone-susceptible tuberculosis. N Engl J Med. 2025;392:468-482.
20. Okovityy SV, Raykhelson KL, Akhmedov VA, et al. Gepatotropnaya terapiya pri lekarstvennykh porazheniyakh pecheni (soveshchanie ekspertov). Permskiy meditsinskiy zhurnal. 2025;42:58-74.
21. Sukumaran D, Usharani P, Paramjyothi GK, et al. A study to evaluate the hepatoprotective effect of N-acetylcysteine on anti-tuberculosis drug induced hepatotoxicity and quality of life. Indian J Tuberc. 2023;70:303-310.
22. Nasiri MJ, Khoshdel N, Venketaraman V. Glutathione and N-acetylcysteine in TB management. Int J Tuberc Lung Dis. 2025;29:171-177.
23. Agrawal D, Ariga KK, Gupta S, et al. Therapeutic plasma exchange in hepatology: indications, techniques, and practical application. J Clin Exp Hepatol. 2025;15:13-24.
24. Tan EX, Wang MX, Pang J, et al. Plasma exchange in patients with acute and acute-on-chronic liver failure: a systematic review. World J Gastroenterol. 2020;26:219-245.
25. Lyubchak VV, Plaksa VM, Pelo IM, et al. Therapeutic plasma exchange in a complex treatment of patients with chronic hepatitis. Wiad Lek. 2020;73:1454-1458.
26. Abramyan MV, Yarustovskiy MB. Ekstrakorporalnaya gemokorrektsiya v intensivnoy terapii pechenochnoy nedostatochnosti. Anesteziologiya i reanimatologiya. 2025;4:72-80.
27. Chalasani N, Bonkovsky HL, Fontana R, et al. United States Drug Induced Liver Injury Network. Features and outcomes of 899 patients with drug-induced liver injury: the DILIN Prospective Study. Gastroenterology. 2015;148:1340-1352.e7.
28. Berber I, Cagin YF, Erdogan MA, et al. Early therapeutic plasma exchange may improve treatment outcomes in severe acute toxic hepatitis. Transfus Apher Sci. 2021;60:1-6.
29. Che XQ, Li ZQ, Chen Z, et al. Plasma exchange combining with plasma bilirubin adsorption effectively removes toxic substances and improves liver functions of hepatic failure patients. Eur Rev Med Pharmacol Sci. 2018;22:1118-1125.
30. Al-Azzawi H, Patel R, Sood G, et al. Plasma exchange for refractory pruritus due to drug-induced cholestasis. Case Rep Gastroenterol. 2021;15:1-8.
31. Al-Nattah S, Sharma KL, Caldis M, et al. Plasma exchange for pembrolizumab-induced hepatitis in a patient with squamous cell carcinoma and prior orthotopic liver transplantation. Case Rep Hepatol. 2022;2022:5908411.

32. Zhou M, Jin Y, Mou Y, et al. Impact of artificial liver plasma perfusion combined with plasma exchange therapy on clinical efficacy and short-term prognosis of hepatitis B virus-related acute-on-chronic liver failure with or without HIV infection. BMC Infect Dis. 2025;25:1081.
33. Tölle M, Gökbuget N, Habringer S, et al. Plasma exchange effectively abrogates severe liver toxicity of pegaspargase in a patient with acute lymphoblastic leukemia. Ann Hematol. 2024;103:3269-3271.
34. Ramakrishnan S, Hans R, Duseja A, et al. Therapeutic plasma exchange is a safe and effective bridge therapy in patients with alcohol-associated ACLF not having immediate prospects for liver transplantation: a case-control, pilot study. J Clin Apher. 2022;37:553-562.
35. Gao Y, Zhang B, Yuan D, et al. Successful treatment of severe toxic hepatitis and encephalopathy without respiratory failure caused by paraquat intoxication. Am J Med Sci. 2021;363:267-272.
36. Saukkonen J.J, Cohn D.L, Jasmer R.M, et al. An official ATS Statement: hepatotoxicity of antituberculosis. Am. J. Respir. Crit. Care Med. 2006;174:935-952.
37. Wei X, Cai R, Wu X, et al. Risk of drug-induced liver injury in chronic hepatitis C and tuberculosis co-infection: a systematic review and meta-analysis. BMC Infect Dis. 2025;25:1566.
38. Chang TE, Huang YS, Chang CH, et al. The susceptibility of anti-tuberculosis drug-induced liver injury and chronic hepatitis C infection: A systematic review and meta-analysis. J Chin Med Assoc. 2018;81:111-118.
39. Wang NT, Huang YS, Lin MH, et al. Chronic hepatitis B infection and risk of antituberculosis drug-induced liver injury: Systematic review and meta-analysis. J Chin Med Assoc. 2016;79:368-374.
40. Chou C, Veracruz N, Chitnis AS, et al. Risk of drug-induced liver injury in chronic hepatitis B and tuberculosis co-infection: A systematic review and meta-analysis. J Viral Hepat. 2022;29:1107-1114.
41. Kumar R, Kumar A, Kumar S. Acute liver failure from anti-tuberculosis drug-induced liver injury: An update. World J Hepatol. 2025;17:106618.
42. Liu CT, Chen TH, Cheng CY. Successful treatment of drug-induced acute liver failure with high-volume plasma exchange. J Clin Apher. 2013;28:430-434.
43. Singh KA, Kumar SE, Zachariah UG, et al. Single-centre experience with low-volume plasma exchange and low-dose steroid to treat patients with idiosyncratic drug-induced acute liver failure. J Clin Exp Hepatol. 2024;14:101303.
44. Ostapowicz G, Fontana RJ, Schiødt FV, et al. U.S. Acute Liver Failure Study Group. Results of a prospective study of acute liver failure at 17 tertiary care centers in the United States. Ann Intern Med. 2002;137:947-954.
45. Larsen FS, Schmidt LE, Bernsmeier C, et al. High-volume plasma exchange in patients with acute liver failure: An open randomised controlled trial. J Hepatol. 2016;64:69-78.
46. Maiwall R, Bajpai M, Singh A, et al. Standard-volume plasma exchange improves outcomes in patients with acute liver failure: A randomized controlled trial. Clin Gastroenterol Hepatol. 2022;20:e831-e854.
47. Kumar SE, Sithamparapillai K, Choudhury AK, et al. Therapeutic plasma exchange in patients with acute-on-chronic liver failure improves survival: an updated meta-analysis. Liver Int. 2025;45:e70018.
48. Sithamparapillai K, Zachariah U, Eapen CE, et al. Plasma exchange improves survival in acute liver failure: An updated systematic review and meta-analysis focussed on comparing within single etiology. Indian J Gastroenterol. 2024;43:397-406.
49. Maiwall R, Bajpai M, Choudhury AK, et al. Therapeutic plasma-exchange improves systemic inflammation and survival in acute-on-chronic liver failure: A propensity-score matched study from AARC. Liver Int. 2021;41:1083-1096.
50. Connelly-Smith L, Alquist CR, Aqui NA, et al. Guidelines on the Use of Therapeutic Apheresis in Clinical Practice — Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Ninth Special Issue. J Clin Apher. 2023;38:77-278.

Эффективность плазмафереза в коррекции лекарственно-индуцированного гепатита у больных туберкулёзом лёгких на фоне хронических вирусных гепатитов В и С

Аннотация

Актуальность. В данной статье представлена оценка эффективности плазмафереза при лечении лекарственно-индуцированного гепатита у больных туберкулёзом лёгких с лекарственной устойчивостью микобактерий туберкулёза, в том числе на фоне хронических вирусных гепатитов. В лечении острого гепатита наряду со стандартной консервативной терапией всё большее внимание уделяется методам экстракорпоральной гемокоррекции.

Материалы и методы. В исследование включены 127 больных туберкулёзом лёгких с лекарственной устойчивостью микобактерий туберкулёза, проходивших лечение в «Городском центре фтизиопульмонологии и внутренних болезней» города Астаны с 2024 по февраль 2026 года включительно. У 65 из 127 пациентов были диагностированы хронические вирусные гепатиты: у 9 (13,8%) – гепатит В, у 51 (78,5%) – гепатит С, у 5 (7,7%) – mixt-гепатит В+С. На фоне противотуберкулёзной химиотерапии у 53 из 127 пациентов (41,7%) развился лекарственно–индуцированный гепатит. У пациентов с хроническими вирусными гепатитами данное осложнение наблюдалось достоверно чаще, чем у больных без хронических вирусных гепатитов: у 39 из 65 (60,0%) против 14 из 62 (22,6%) соответственно (p <0,001). Больные были разделены на две группы, в одной из которых для коррекции лекарственно-индуцированного гепатита применяли плазмаферез.

Результаты. Применение плазмафереза в основной группе способствовало купированию проявлений лекарственно-индуцированного гепатита без отмены специфической противотуберкулёзной терапии. В контрольной группе, где плазмаферез не применялся, потребовалась временная отмена специфической терапии.

Заключение. Использование плазмафереза в комплексной терапии лекарственно-индуцированного гепатита у больных туберкулёзом лёгких с лекарственной устойчивостью микобактерий туберкулёза позволяет купировать проявления гепатотоксичности без прерывания

противотуберкулёзной химиотерапии, что имеет особое значение у пациентов с сопутствующими хроническими вирусными гепатитами.

Ключевые слова:

лекарственно-индуцированный гепатит, туберкулёз лёгких, лекарственная устойчивость, хронические вирусные гепатиты, дискретный аппаратный плазмаферез.

პლაზმაფერეზის ეფექტურობა მედიკამენტებით ინდუცირებული ჰეპატიტის კორექციაში ფილტვის ტუბერკულოზით დაავადებულ პაციენტებში ქრონიკული B და C ვირუსული ჰეპატიტების ფონზე

შესავალი. აღნიშნულმა კვლევამ შეაფასა პლაზმაფერეზის ეფექტიანობა მედიკამენტოზური ჰეპატიტის მართვაში წამალრეზისტენტული ფილტვის ტუბერკულოზის მქონე პაციენტებში, მათ შორის თანმხლები ქრონიკული ვირუსული ჰეპატიტის შემთხვევებშიც. მწვავე ჰეპატიტის მკურნალობაში სტანდარტულ კონსერვატიულ თერაპიასთან ერთად სულ უფრო მეტი ყურადღება ეთმობა ექსტრაკორპორალური ჰემოკორექციის მეთოდებს.

მასალები და მეთოდები. კვლევაში ჩართული იყო წამალრეზისტენტული ფილტვის ტუბერკულოზის მქონე 127 პაციენტი, რომლებიც მკურნალობდნენ სტანას ფთიზიოლოგიისა და შინაგან დაავადებათა საქალაქო ცენტრში 2024 წლიდან 2026 წლის თებერვლამდე. ქრონიკული ვირუსული ჰეპატიტი დიაგნოსტირდა 127-დან 65 პაციენტში: B ჰეპატიტი — 9-ში (13.8%), C ჰეპატიტი — 51-ში (78.5%), ხოლო შერეული B + C ჰეპატიტი — 5-ში (7.7%). ტუბერკულოზის საწინააღმდეგო ქიმიოთერაპიის მიმდინარეობისას 127-დან 53 პაციენტს (41.7%) განუვითარდა მედიკამენტოზური ჰეპატიტი. ეს გართულება მნიშვნელოვნად უფრო ხშირად აღინიშნებოდა ქრონიკული ვირუსული ჰეპატიტის მქონე პაციენტებში, ვიდრე მის გარეშე პაციენტებში: შესაბამისად 65-დან 39 (60.0%) და 62-დან 14 (22.6%) შემთხვევაში ($p < 0.001$). პაციენტები დაიყო ორ ჯგუფად, რომელთაგან ერთ ჯგუფში მედიკამენტოზური ჰეპატიტის კორექციის მიზნით გამოყენებული იყო პლაზმაფერეზი.

შედეგები. საკვლევ ჯგუფში პლაზმაფერეზის გამოყენებამ შესაძლებელი გახადა მედიკამენტოზური ჰეპატიტის გამოვლინებების კონტროლი ტუბერკულოზის საწინააღმდეგო სპეციფიკური თერაპიის შეწყვეტის გარეშე. საკონტროლო ჯგუფში, სადაც პლაზმაფერეზი არ გამოიყენებოდა, საჭირო გახდა სპეციფიკური თერაპიის დროებითი შეწყვეტა.

დასკვნა. პლაზმაფერეზის ჩართვამ მედიკამენტოზური ჰეპატიტის კომპლექსურ მკურნალობაში წამალრეზისტენტული ფილტვის ტუბერკულოზის მქონე პაციენტებში შესაძლებელი გახადა ჰეპატოტოქსიკურობის კონტროლი ტუბერკულოზის საწინააღმდეგო ქიმიოთერაპიის შეწყვეტის გარეშე, რაც განსაკუთრებით მნიშვნელოვანია თანმხლები ქრონიკული ვირუსული ჰეპატიტის მქონე პაციენტებში.

საკვანძო სიტყვები: მედიკამენტოზური ჰეპატიტი, ფილტვის ტუბერკულოზი, წამალრეზისტენტობა, ქრონიკული ვირუსული ჰეპატიტი, თერაპიული პლაზმაფერეზი.