GEORGIAN MEDICAL NEWS

ISSN 1512-0112

No 5 (326) Январь 2022

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

No 5 (326) 2022

Published in cooperation with and under the patronage
of the Tbilisi State Medical University

Издается в сотрудничестве и под патронажем
Тбилисского государственного медицинского университета

გამოიცემა თბილისის სახელმწიფო სამედიცინო უნივერსიტეტთან
თანამშრომლობითა და მისი პატრონაჟით

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

ТБИЛИСИ - НЬЮ-ЙОРК

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 and The International Academy of Sciences, Education, Industry and Arts (U.S.A.) 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 и Международной академией наук, образования, искусств и естествознания (IASEIA) США 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.

МЕДИЦИНСКИЕ НОВОСТИ ГРУЗИИ

Ежемесячный совместный грузино-американский научный электронно-печатный журнал
Агентства медицинской информации Ассоциации деловой прессы Грузии,
Международной академии наук, индустрии, образования и искусств США.
Издается с 1994 г., распространяется в СНГ, ЕС и США

Website:
www.geomednews.org

The International Academy of Sciences, Education, Industry & Arts. P.O.Box 390177,
Mountain View, CA, 94039-0177, USA. Tel/Fax: (650) 967-4733

Версия: печатная. **Цена:** свободная.
Условия подписки: подписка принимается на 6 и 12 месяцев.
По вопросам подписки обращаться по тел.: 293 66 78.
Контактный адрес: Грузия, 0177, Тбилиси, ул. Асатиани 7, IV этаж, комната 408
тел.: 995(32) 254 24 91, 5(55) 75 65 99
Fax: +995(32) 253 70 58, e-mail: ninomikaber@geomednews.com; nikopir@geomednews.com

По вопросам размещения рекламы обращаться по тел.: 5(99) 97 95 93

GEORGIAN MEDICAL NEWS
Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press; International Academy of Sciences, Education, Industry and Arts (USA).
Published since 1994. Distributed in NIS, EU and USA.

CONTACT ADDRESS IN TBILISI

GMN Editorial Board
7 Asatiani Street, 4th Floor
Tbilisi, Georgia 0177

Phone: 995 (32) 254-24-91
995 (32) 253-70-58
Fax: 995 (32) 253-70-58

CONTACT ADDRESS IN NEW YORK

NINITEX INTERNATIONAL, INC.
3 PINE DRIVE SOUTH
ROSLYN, NY 11576 U.S.A.

Phone: +1 (917) 327-7732

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.

GEORGIAN MEDICAL NEWS
No 5 (326) 2022

Содержание:

GEORGIAN MEDICAL NEWS
No 5 (326) 2022

THE USE OF THROMBOLYSIS THERAPY IN ACUTE STROKE IN THE REPUBLIC OF KAZAKHSTAN, THE COUNTRIES OF NEAR AND FAR ABROAD.

Abdrakhmanova M.G[1], Kasenova A.S[1], Omarova Sh[2], Shinalieva K.A[1], Baltabayeva A.S[1], Bakirova K.T[1].

[1]NJSC Astana Medical University, Ministry of Health of the Republic of Kazakhstan, Nur-Sultan, Kazakhstan; [2]NJSC "Medical University of Karaganda".

Today, stroke has been declared a global epidemic threatening the life and health of the world population. In the world 5.6-6 million people a year suffer from stroke. It is predicted that deaths from stroke will rise to 6.7 million in 2015 and 7.8 million in 2030, if no active global measures have been taken to combat the epidemic. Stroke has been declared a disease-catastrophe in India, South Africa, Spain and all Latin American countries. It is the number one killer of people over the age of 50 in South Africa. In most developed countries stroke is the third most frequent killer after heart disease and cancer [1,2]. The annual mortality rate from stroke in Russia is one of the highest in the world (175 per 100,000 population). Stroke morbidity and mortality rates among people of working age in Russia have increased over the last 10 years by more than 30% (mortality - 41 per 100 thousand people). The early 30-day mortality rate after stroke is 34.6%, and about half of those who fall ill die within a year. Stroke is the leading cause of disability worldwide and imposes special obligations on the family members of the patient, significantly reducing their labor potential, putting a heavy socio-economic burden on society [3,4].

In Russia the cost of treatment of one patient who has had a stroke, including in-patient treatment, medical and social rehabilitation and secondary prevention (direct costs) is 127 thousand rubles a year, i.e. the total direct costs of stroke (from 499 thousand cases a year) is 63.4 billion rubles. Indirect costs of stroke, estimated by the loss of GDP due to premature mortality, disability, and temporary incapacity for work of the population, are about 304 billion rubles per year in Russia. According to WHO, in the period from 2005 to 2015 the loss of GDP in Russia because of premature deaths from vascular causes could make 8,2 trillion rubles. Thus, the estimations based only on the economically accountable data, testify to extremely high "price" of stroke [4,5]. In the USA direct and indirect social and economic losses in connection with strokes make approximately 41 billion US dollars. An alarming trend is the rejuvenation of stroke. And therefore, the World Health Organization and World Stroke Organization have developed the Global Stroke Initiative program to create a global information database on stroke and to coordinate countries' stroke prevention and treatment activities [1,6,7].

The Republic of Kazakhstan is in second place after Moldova in terms of cardiovascular disease mortality among the CIS countries. There are 2 million people registered in Kazakhstan who suffer from cardiovascular diseases, which is 12% of the economically active population of the country. At the same time domestic scientists argue that the official statistics are understated [8,32].

According to the official data of the Republican Center of e-health of MH RK the hospitalized morbidity of acute on-cerebral circulation disorder (CCAD) in 2015 was 220.2 per 100 thousand population, 226.9 in 2016, 229.2 in 2017 and 229.7 in 2018 [9].

The number of patients receiving disability benefits nationally due to stroke exceeds 200,000. Incidence of stroke in different regions of Kazakhstan is 2.5 - 3.7 cases per 1000 people, mortality from 1.0 to 1.8 cases per 1000 per year. In comparison with Russia: from 2.5 up to 7.43 cases of stroke per 1,000 persons a year, the mortality rate from stroke fluctuates from 0.7 up to 3.31 cases per 1,000 persons a year [10]. The available official data on the problem of stroke in Kazakhstan do not give a complete and adequate real picture, since the "Stroke Register" was carried out only in some cities of the country.

The number of patients with stroke in Kazakhstan is increasing, and the annual increase in hospitalized morbidity due to stroke is from 1 to 3%.

In-hospital mortality rates for stroke (hemorrhagic + ischemic strokes) in RK for the period from 2015 to 2018 varied from minimal 12,6 to maximal 13,3 %, on the average being 13,0 %. Stroke mortality decreased from 7.5 per 100,000 population in 2015 to 5.9 in 2018 [9].

The provision of specific therapy for stroke patients in the form of thrombolytic therapy and neurosurgery is a recognized international standard in the provision of medical care and indicates a high level of organization in the country as a whole. The number of thrombolysis performed for ischemic stroke increased by 3% (by 123) (from 4,336 in 2015 to 4,459 in 2016). The percentage of thrombolysis performed in patients with ischemic stroke increased from 1.0 to 3.3, respectively, from 2015 to 2018. The percentage of neurosurgical activity also increased from 2.1% in 2015 to 6.2% in 2018 [11]. A stroke is a disorder of brain function caused by a disruption of its blood supply that occurs suddenly. The nature of the disorders of higher nervous activity in stroke depends on the localization of the lesion focus. The cerebral circulation disorders of ischemic type are the consequence of a decrease in the diameter of blood vessels or their complete occlusion [12]. The main causative factor is the occlusion of brachycephalic vessels by a parietal or occluding thrombus [13]. In the final stages of this pathology, preceding the development of brain infarction, there is a transformation of soluble fibrinogen into insoluble fibrin. The fibrin network is filled with blood components, thus creating the basis for future thrombus formation [14]. Modern strategy of ischemic stroke treatment implies timely application of reperfusion therapy combined with the use of modern neuroimaging methods based on CT and MRI technologies, which allows assessing the state of cerebral perfusion both at the time of hospitalization and in dynamics [15]. The tactics of treatment measures in acute circulatory disorders bears the imprint of the influence of the so-called concept of "ischemic penumbra and window of therapeutic possibilities". Within this

concept, the "core of the infarction" is the area where there are irreversible structural changes, and the area where the changes are functional, marked as hypoperfusion, but in general the level of energy metabolism is sufficient, is called the "penumbra" or ischemic penumbra [16]. Disruption of cerebral blood supply is accompanied by activation of oxygen-free glucose oxidation pathway, development of metabolic acidosis, impaired ion pump function and eventually cytotoxic edema - all this leads to activation of apoptosis mechanism and further expansion of destruction site [17]. The time of formation of the brain "infarct core" is 5-8 minutes from the onset of the signs of neurological deficit. The increase of infarct zone volume occurs due to the destruction of "penumbra" cells [16]. The formation of 50% of the infarct volume occurs in the first 1.5 hours from the onset of symptoms and 70-80% - in the next 6 hours [18]. The time up to 6 hours from the development of the disease is called the "therapeutic window". It is during this period that measures to restore perfusion in the "penumbra" zone are characterized by the greatest effectiveness [19]. Reperfusion therapy in ischemic stroke should be performed as early as possible, there is a concept of "door to needle", which implies that care should be provided as early as possible. According to recent studies, timely thrombolytic therapy allows expanding the "therapeutic window" - the sooner thrombolysis is performed, the higher the rates of patients' recovery [20,21].

The history of development of thrombolytic therapy (THT) originates from 1958, when the first report on THT in stroke was published (Sussman B.J.et al., 1958). The advent of computed tomography (CT) in the early 1980s made further study of TLT possible. J.A. Zivin et al. [22] found out that rtPA application in rabbits immediately after cerebral vessel occlusion with embolus (obtained from autoblood and injected into the neck artery) leads to radical reduction of brain infarct size. In fact, they showed for the first time that thrombolysis with rtPA performed in the first hours of acute ischemic stroke (AIS) can significantly improve neurological functions [23].

In 2014, Joanna M WardlawVeronic, MurrayEivind, Berge Gregory, J del Zoppo searched the Cochrane Registry of Clinical Trials for Stroke (last conducted November 2013), MEDLINE (from 1966 to November 2013), and EMBASE (from 1980 to November 2013). Conference and journal proceedings and reference materials were also reviewed. The selection criteria were randomized trials of any thrombolytic agent versus control in people with diagnosed ischemic stroke.

This review included 27 studies with 10,187 participants, testing preparations of urokinase, streptokinase, rt-PA, recombinant prourokinase, or desmoteplase. Four studies used intraarterial administration and the rest used intravenous administration. Most of the data are from trials that started treatment six hours after the stroke. About 44% of the trials (about 70% of participants) tested intravenous rt-PA administration. In the study, 16% of the participants were over 80 years of age. More than 50% of the trials met the criteria for complete concealment.

Thrombolytic therapy, mostly given within six hours of ischemic stroke, significantly reduced the proportion of participants who were dead or disabled (modified Rankin 3 through 6) three to six months after stroke (odds ratio (OR) 0.85, 95% confidence interval (CI) 0.78 to 0.93). Thrombolytic therapy increases the risk of symptomatic intracranial hemorrhage (OR 3.75, 95% CI 3.11 to 4.51), early death (OR 1.69, 95% CI 1.44 to 1.98; 13 trials, 7458 participants), and death three to six months after stroke (OR 1.18, 95% CI 1.06 to 1.30). Early death after thrombolysis was mostly related to intracranial hemorrhage. Treatment within three hours of stroke was more effective in reducing mortality or disability (OR 0.66, 95% CI 0.56 to 0.79) without increasing mortality (OR 0.99, 95% CI 0.82 to 1.21; 11 trials, 2187 participants). There was heterogeneity between trials. Current antithrombotic drugs increased the risk of death. Trials testing rt-PA showed a significant reduction in mortality or dependence on treatment before six hours (OR 0.84, 95% CI 0.77 to 0.93, P = 0.0006; 8 trials, 6729 participants) with significant heterogeneity; treatment at three hours was more beneficial (OR 0.65, 95% CI 0.54 to 0.80, P < 0.0001; 6 trials, 1779 participants) without heterogeneity. Participants over 80 years of age benefited equally from participants under 80 years of age, particularly if they were treated within 3 hours of stroke. 6729 participants) with significant heterogeneity; treatment within three hours was more beneficial (OR 0.65, 95% CI 0.54 to 0.80, P < 0.0001; 6 trials, 1779 participants) without heterogeneity.

Thus, thrombolytic therapy given within six hours of stroke reduces the proportion of death or disability. Those treated within the first three hours received significantly more benefit than those treated later. This overall benefit was evident despite an increase in symptomatic intracranial hemorrhage, mortality after 7-10 days, and mortality at follow-up (except in trials with rt-PA testing, which had no effect on death at follow-up).

The NINDS trial was the first multicenter, randomized, placebo-controlled trial to prove the safety and efficacy of systemic TLT using rt-PA in the first three hours of onset [24,25]. The following randomized placebo-controlled trials ECASS I and II [22,23] evaluated the safety and efficacy of different doses of rt-PA (ECASS I - 1.1 mg/kg, ECASS II - 0.9 mg/kg) in the first six hours from stroke onset. The results of the ECASS I and II studies regarding the safety of the drug were comparable with those of the NINDS study. There were no significant differences between the main group and the placebo group with regard to efficacy.

Two parts of the ATLANTIS study (A and B) evaluated the safety and efficacy of rt-PA at a dose of 0.9 mg/kg up to five hours from onset. No significant positive effect of rt-PA compared with placebo was observed [26].

The ECASS III study [27] demonstrated the safety and efficacy of systemic thrombolysis in the first 4.5 hours after the onset of symptoms. The results of this work served as a reason for the revision of European and American recommendations on the treatment of ischemic stroke. It was proposed to increase the therapeutic window for systemic TLT to 4.5 hours [28,29]. In the Russian Federation, the relevant changes in the instructions for alteplase drug were made on May 25, 2011.

The largest study IST III [28] evaluated the safety and efficacy of rt-PA systemic TLT in ischemic stroke within the first six hours of its onset. The results were considered neutral, because the primary endpoint - the prevalence of persons with good

recovery of impaired functions according to the Oxford Scale in the TLT group - was not achieved.

Thus, the current positive evidence base for alteplase comes from only two large studies, NINDS and ECASS III.

The dependence of the effectiveness and safety of fibrinolytic therapy on the time of its initiation has been demonstrated in several large studies. Combined analysis of the results of the NINDS, ECASS I and II, ATLANTIS studies (n = 2775) showed that the odds ratio (OR) of a favorable outcome was 2.81 (95% confidence interval (CI) 1.75-4.5) if thrombolysis was started within the first 90 minutes of stroke and 1.55 (95% CI 1.12-2.15) from 90 to 180 minutes. When TLT was initiated between 181 and 270 minutes, the OR of favorable outcome was 1.40 (95% CI 1.05-1.85), and after 271-360 minutes it was 1.15 (95% CI 0.90-1.47) [29]. Thus, time is the most important condition for the effectiveness of TLT . For this reason, in all recommendations on treatment of patients with stroke the necessity of reduction of all delays with the beginning of therapy is emphasized [30].

In addition to the timing factor, the age of patients is also important to consider when administering TLT. According to the instructions on the use of alteplase preparation and the recommendations of European Stroke Organization, patients under 18 years old should not undergo TLT and patients over 80 years old - with special care [30].

F. Mateen et al. analyzed data from the Canadian TLT registry for patients aged 80 to 89 years and from 90 to 99 years [31,32]. Both age groups were characterized by a preponderance of female patients (61% in the 80–89-year-old group and 77% in the 90–99-year-old group) and baseline stroke severity (greater than 15 points on the National Institutes of Health Stroke Scale, in 52 and 58%, respectively). Both groups had similar rates of symptomatic hemorrhagic transformation (4 and 7%, respectively), three-month mortality (33 and 52%, respectively), and good recovery of impaired neurological functions (26 and 30%, respectively).

Thus, thrombolysis in patients of different age groups, including those aged 80 to 89 years and older, is equally safe and effective.

REFERENCES

1. Kulebras A. Stroke is an acute disease that can be prevented. Journal of Neurology and Psychiatry named after S.S. Korsakov. S.S. Korsakov. 2007; special issue:74-76.
2. Hakim A.M. Changes in Stroke Care: Canadian Experience. Journal of Neurology and Psychiatry. S.S. Korsakov. 2007; special issue:129-132.
3. Gusev E.I. The problem of stroke in Russia. Journal of neurology and psychiatry. S.S. Korsakov. 2003; 9:3-5.
4. Skvortsova V.I. Reduction of morbidity, mortality and disability from strokes in the Russian Federation. Journal of Neurology and Psychiatry. S.S. Korsakov. 2007; special issue:25-28.
5. Federal program. Complex of measures for the prevention, diagnosis and treatment of patients with cardiovascular disease in the Russian Federation. Journal of Neurology and Psychiatry. S.S. Korsakov. 2007; special issue:7-19.
6. Rudd E.G. National strategy to improve hospital care for patients with acute stroke by the example of Great Britain. Journal of neurology and psychiatry. S.S. Korsakov.2007; special issue:347-151.
7. Grady B.O. Development and Implementation of a Comprehensive System of Care for Stroke. Journal of Neurology and Psychiatry named after S.S. Korsakov. S.S. Korsakov.2007; special issue:133-136.
8. Abseitova S.R. Modern state of the problem of cardiovascular diseases in South Kazakhstan region.2008. www. cardio center.
9. Health of the population of the Republic of Kazakhstan and the activities of health care organizations in 2017 (statistical compendium). Ministry of Health RK. Astana. 2018;C.1-354.
10. Zhusupova A.S. Stroke - a global problem of domestic neurology. Journal of Man and Medicine - Kazakhstan. 2017;3:C.6-9.
11. Akhmetzhanova, S.G. Medukhanova, G.K. Zhumabaeva, E.B. Adilbekov. Stroke in Kazakhstan. Neurochemistry and neurology of Kazakhstan. 2018; 2:C.8-44.
12. Konstantinova E.V. Modern possibilities of reperfusion therapy of myocardial infarction and ischemic stroke. E.V. Konstantinova, N.A. Shostak, M.Yu. Gilyarov. The clinician. 2015;1:C. 5-6.
13. Savello A.V. Clinical guidelines: intravascular treatment of ischemic stroke in the acute period. A.V. Savello, I.A. Vozniuk, D.V. Svistov. Plenum of the Board of the Russian Association of Neurosurgeons. 2015;C.35.
14. Maksimenko A.V. Thrombolysis by plasminogen activators: application and study of serine proteinases, prospects and realities. Biomedical Chemistry.2014;6:677-682.
15. Verzakova I.V. Modern methods of neuroimaging in diagnostics of acute ischemic stroke. I.V. Verzakova, L.B. Novikova, E.I. Sayfullina. Medical Imaging. 2007;1:104-111.
16. Trofimenko A.I. Dynamics of cytokine status and β-endorphin level in patients with ischemic stroke at application of TES-therapy. A.I. Trofimenko, F.A. Nekhai, A.H. Kade et al. Kubanskiy nauchn. med. vest. 2015;6:147-150.
17. Gusev E.I. Ischemic stroke. Current state of the problem. E.I. Gusev, M.Y. Martynov, P.R. Kamchatnov. Doktor.ru. 2013;5:7-8.
18. Kadyrova I.A. Systematic review of methods for predicting the outcome of brain stroke. I.A. Kadyrova, F.A. Mindubaeva, A.M. Grzhibovsky. Human Ecology. 2015;10:55-64.
19. Shcheglov D.V. Evolution of invasive and noninvasive interventions in acute cerebral ischemia. D.V. Shcheglov, S.V. Konotopchik, S.V. Chebanyuk et al. Endovascular neuroventricular neurosurgery. 2015;2:74-82.
20. Kutashov V.A. Systemic thrombolysis as the main method for treatment of ischemic stroke. V.A. Kutashov, I.E. Sazonov, A.A. Kudrinov et al. Applied information aspects of medicine. 2015;2:68-72.
21. Groot A.E. Association between i.v. thrombolysis volume and door-to-needle times in acute ischemic stroke. A.E. Groot, I.N. Van Schaik, M.C. Visser et al. J. of neurology. 2016;263:807-813.
22. Adams H.P., Adams R.J., Brott T.G. et al. Guidelines for the early management of patients with ischemic stroke. A scientific statement from the stroke council of the American Stroke

Association. Stroke 2003; 34:1056-1083.
23. Zivin J.A., Lyden P.D., DeGirolami U., Tissue plasminogen activator. Reduction of neurologic damage after experimental embolic stroke. Arch Neurol 1988; 45:387-391.
24. Hacke W., Kaste M., Fieschi C. et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Second European-Australasian Acute Stroke Study Investigators. Lancet. 1998;352:1245-1251.
25. Clark W.M., Wissman S., Albers G.W. et al. Recombinant tissue-type plasminogen activator (Alteplase) for ischemic stroke 3 to 5 hours after symptom onset. The ATLANTIS Study: a randomized controlled trial. Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke. JAMA. 1999;282:2019-2026.
26. Hacke W., Kaste M., Bluhmki E. et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N. Engl. J. Med. 2008;359:1317-1329.
27. European Stroke Organisation // www.eso-stroke.org.
28. Jauch E.C., Saver J.L., Adams H.P. Jr. et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association. American Stroke Association. Stroke. 2013; 44:870-947.
29. IST-3 collaborative group, Sandercock P., Wardlaw J.M. et al. The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial. Lancet. 2012; 379:2352-2363.
30. Hacke W., Donnan G., Fieschi C. et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. Lancet. 2004;363:768-774.
31. Mateen F.J., Buchan A.M., Hill M.D. Outcomes of thrombolysis for acute ischemic stroke in octogenarians versus nonagenarians. Stroke. 2010;41:1833-1835.
32. Zhumabayev M., Maltabarova N., Kokoshko A. A Cerebralstroke and the Problem of Inflammatory Complications. Research Journal of Medical Sciences. 2016;10:492-497.

SUMMARY

APPLICATION OF THROMBOLYSIS THERAPY FOR ACUTE CEREBRAL CIRCULATION IN THE REPUBLIC OF KAZAKHSTAN, COUNTRIES OF THE FAR AND NEAR FOREIGN COUNTRIES.

Abdrakhmanova M.G[1]., Kasenova A.S[1]., Omarova Sh[1]., Shinalieva K.A[1]., Baltabaeva A.S[1].
[1]NJSC "Astana Medical University", Ministry of Health of the Republic of Kazakhstan, Nur-Sultan, Kazakhstan.

Abstract. In the world, stroke suffers 5.6-6 million people a year. Stroke deaths are predicted to rise to 6.7 million in 2015 and to 7.8 million in 2030.

Stroke is the leading cause of disability worldwide.

The provision of specific therapy to patients with stroke in the form of thrombolytic therapy and neurosurgical operations are recognized international standards in the provision of medical care. The advent of computed tomography (CT) in the early 1980s made it possible to further study TLT. In 2014 Joanna M WardlawVeronic, MurrayEivind, Berge Gregory, J del Zoppo searched the Cochrane Stroke Trial Registry (Last November 2013), MEDLINE (1966 to November 2013) and at EMBASE (from 1980 to November 2013). We concluded that thrombolytic therapy administered within six hours of a stroke reduces the proportion of deaths or disability. The dependence of the efficacy and safety of fibrinolytic therapy on the time of its initiation has been demonstrated in a number of large studies. A pooled analysis of the results of the NINDS, ECASS I and II, ATLANTIS studies (n = 2775) showed that the odds ratio (OR) of a favorable outcome of the disease when thrombolysis was initiated in the first 90 minutes of a stroke. Thus, time is the most important condition for the effectiveness of TLT.

In addition to the time factor, it is important to take into account the age of patients during TLT. F. Mateen et al. analyzed data from the Canadian TLT registry for patients aged 80 to 89 years and 90 to 99 years. Thus, thrombolysis in patients of various age groups, including those aged 80 to 89 years and older, is equally safe and effective.

Keywords. Ischemic stroke, thrombolytic therapy, NINDS studies, ECASS I, II, III, ATLANTIS (A and B), stroke in the CIS countries.