SCHOLASTIC:
Journal of Natural and Medical Education
Volume 2 Issue 5, Year 2023 ISSN: 2835-303X
https://univerpubl.com/index.php/scholastic

Cervicogenic Headache: Pathophysiology, Clinic, Approaches to Therapy

Pardayeva Zilola Suvonkulovna
Assistant of Pathophysiology Department of the Samarkand State University

Article Information

Received: March 11, 2023
Accepted: April 12, 2023
Published: May 13, 2023

Keywords: *muscle relaxants, antidepressants, anticonvulsants.*

ABSTRACT

Cervicogenic headache (CGB) is one of the most common forms of secondary cephalgia. Despite the progress in understanding the mechanisms of CGB, the clinical diagnosis and effective therapy of this suffering present significant difficulties. Data on the prevalence of CGB are contradictory and depend on the sample and the age of patients.

According to a systematic review by P. Martelletti and H. van Suijlekom (2004), devoted to the epidemiology of CGB, its prevalence in the population ranges from 0.7-13.8% [4]. The prevalence of CGB increases with age and reaches a maximum in 40-60 years. Women suffer 4 times more often than men [5]. According to S. Haldeman [6], the average age of patients with CGB is 42.9 years, while in specialized pain clinics, the frequency of CGB among chronic daily headache reaches 20%. Numerous studies have shown that CGB significantly reduces the quality of life of patients, comparable to chronic migraine and chronic tension headache (GBN), while significantly more disturbing the general physical condition [7]. G. Josey [8] for the first time described headache associated with pathology of the cervical spine, in In 1949, the term CGB, as well as diagnostic criteria were proposed by O. Sjaastad et al. in 1983 [9].

The basis of CGB neuroanatomy is pathological changes in the upper cervical segments of the spine. It is clear that the C1 spinal nerve is involved in the innervation of the short muscles of the suboccipital triangle. Afference from the medial and lateral atlanto- axial joints, some neck muscles (prevertebral, sternoclavicular- mastoid, trapezoidal, peninsular), the dura mater of the posterior cranial fossa enters the posterior horn of the spinal cord along the fibers emanating from the ganglia C2 segment [10-13]. As a result of ascending projections, nociceptive impulses from the upper three cervical segments converge with the nuclear complex of the trigeminal nerve. The functional connection of neurons of the posterior horns C1-3 with the caudal nucleus of the V pair is the basis for the formation of the trigeminal-cervical complex (TCC) [14-18]. The initial steps in the study of CSB are associated with the classical works of Kerr (1961).

Involvement of TCC neurons in the mechanism of formation of CGB was shown, which made it possible to explain the possibility of headache in pathology of the cervical spine [19, 20]. This

assumption was confirmed in subsequent studies: when the occipital nerve was stimulated, an increase in neural activity in the TCC was noted with the activation of neurons of the caudal nucleus of the trigeminal nerve [17, 18]. Currently , it is believed that changes in the structures receiving innervation from the first three cervical segments are the basis of CGB. Thus, the source of headache can be: — atlanto-axial joints, ligaments, tendons; — atlanto-occipital joints, ligaments, tendons; — SI/SIII and SIII/CIV faceted joints; — III/III intervertebral disc; — muscles: suboccipital, lower posterior cervical , lower prevertebral cervical, trapezoidal, sternocleidomastoid; — vertebral arteries. It should be noted once again that nociceptive information from these structures is primarily transmitted along the wires emanating from the ganglia of the posterior roots of segments C1-3. W. Pllman [21] shows the involvement of the large and small occipital nerves, as well as, possibly, the large auricular nerve in CGB. Some authors have hypothesized the role of neurovascular conflict in the pathogenesis of CGB. In particular, the possibility of compression of the C2 root by the ventral part of the upper cervical segment of the vertebral artery was considered, which was confirmed by neuroimaging data and observations during microsurgical decompression [22]. The concept of osteogenic compression of the roots of the upper cervical segments as a possible etiological factor of CGB has now been refuted on the basis of numerous MRI and CT studies. At the same time, a variant of possible compression of the venous plexus of the root and ganglion C2 is considered [23].

The role of musculoskeletal changes in the pathophysiology of CGB is currently being actively discussed. It was found that electromyographic (EMG) activity is significantly higher in the trapezius muscle on the headache side. At the same time, there were no differences between EMG readings in the temporal muscles in the case of unilateral CSB, which can be explained by the involvement of the mechanisms of reflected pain. It was revealed that after correction of both articular and muscular dysfunction in CGB, there was an extension of previously shortened latent periods of the blinking reflex [3, 24]. O. Sjaastad et al. [25, 26] suggest the presence of secondary somatosensory dysfunction in the segments C2—3 on the ipsilateral side with CGB.

There was a significant decrease in pain thresholds in patients with CGB in the occipital zone and on the ipsilateral side. In GBN and migraine, there were no significant differences in the level of the pain threshold in comparison with the control group [27]. CGB can often be the result of a traumatic brain injury or damage to the cervical spine. The first description of a headache after a whiplash injury of the cervical spine was given by H. Crowe in 1928. [28]. This type of traumatic injury is widespread, in the USA there are about 1 million cases per year [29]. The prevalence of CGB after cervical injury , according to various sources, ranges from 37 to 82% [30, 31]. It is emphasized that posttraumatic CGB is primarily associated with muscle spasm and is often associated with BZN neuralgia [29]. Posttraumatic headache is observed for several weeks, while in 30% of cases it tends to be chronic [32]. In addition, the transformation of vascular pain is possible.

When examining a patient with CGB , segmental hypomobility in the cervical spine is often detected . On the basis of CT and MRI studies, a decrease in mobility in the cervical region, mainly at the level of CV-VI, as well as pronounced hypomobility of craniocervical joints C0-II were established [33]. According to J. Meloeh et al. [34], cervical segmental dysfunction may underlie the development of pain with an irritable dermatome. According to the observations of G. Jull [35], dysfunction of the III-III segments of the cervical spine is most often noted. When studying the state of the cervical spine in patients with posttraumatic CSB reveals a reduction in the volume of movements both during stretching and flexion. According to the results of numerous studies, no structures have been revealed that could lead to compression of the BZN. Assumptions about the role of trapezius muscle spasm are not confirmed. It was found that with a spasm of the trapezius muscles, the diameter of the can- la BZN increases. Thus, the contribution of BZN compression to the development of CGB is extremely unlikely [37, 38].

The other most likely cause of CGB is damage to the arch- process joints CII—III. Despite the fact that the cervical spine is a single anatomical and functional system with other departments, it has a number of features, one of which is the possibility of the formation of uncovertebral arthrosis.

In a clinical and experimental study by A. Dwyer et al. [39] provoked a typical pattern of unilateral headache in healthy subjects with irritation of the capsule of the CII- III arch-process joints. R. Dreytus [40], using a similar study design , showed the possibility of provoking unilateral pain in the upper neck and occipital region with stimulation of atlanto-axial and atlanto-occipital joints. The involvement of arch-process joints in CGB is proved by the effectiveness of local blockades in 50-53% of cases. Currently, it has been proven that the combination of segmental dysfunction of the cervical spine and muscle spasm is the neuroanatomic basis for the development of CGB.

Clinical diagnosis of CGB in neurological practice presents certain difficulties. Pain in the cervical region, as well as muscle tension, are common symptoms during a migraine attack and are combined with GBN. In a study by J. Blau et al. [41] it is indicated that 67% of patients with migraine experience pain and/or tension in the neck, while in 31% these symptoms are noted in the prodromal period, in 93% — during the attack and in 31% of cases in the postdromal phase. Myofascial syndrome is equally common in migraine and GBN, which complicates the differential diagnosis of headaches [42-44]. Currently, diagnostic criteria of the International Scientific Group for the Study of Cervical Headache are applied, as well as the criteria of the International

Classification of Headaches (ICGB) of the 2nd revision (2004) The revised diagnostic criteria emphasize the importance of the presence of signs of cervical involvement, the presence of headache attacks caused by mechanical action, as well as the positive effect of anesthetic blockade. The absence of clause 1.1 significantly reduces the reliability of the diagnosis. It is proposed, in the presence of criteria 1.2 and 1.3, as well as 2 and 3, to make a temporary or preliminary diagnosis of CGB. In the latest version of the ICGB of the International Headache Society (2004), CGB belongs to subtype 11.2.1, which is included in the heading 11.2 — headache associated with pathology in the neck [46, 47]. Diagnostic criteria and clinical features of CGB according to the ICGB are presented in Table 2. It should be noted that in most cases , a carefully collected medical history of the disease and a properly conducted examination of the patient suggest a diagnosis of CGB without performing therapeutic and diagnostic blockades.

During examination, patients with CGB have limited mobility in the cervical region. Headache can be provoked by active movements in the neck, when performing functional tests with extension and especially with extension and rotation in the direction of pain, as well as when palpating the exit points of BZN on the ipsilateral side [49]. Myofascial trigger points are detected in the neck muscles and suboccipital muscles. Palpation of trigger points provokes a typical headache pattern. Paresthesia and dysesthesia can often be observed in the occipital zone and in the upper part of the cervical region, at the same time , no signs of radiculopathy are detected during examination [43].

Neuroimaging methods (radiography, MRI and CT studies) can be useful in the course of diagnosis of CGB, but none of them can confirm the diagnosis with a high probability. According to the data of a comparative MRI examination of the cervical spine, there were no significant differences between patients with CGB and the control group. At the same time, it is indicated that the frequency of intervertebral disc protrusions at the upper cervical level in both groups was the same (45.5% — CGB, 45% — control group) [50]. In the differential diagnosis of CGB, it is necessary to pay primary attention to the collection of anamnesis, somatic, neurological examination and neuropsychiatric examination. Taking into account the clinical

picture and potential sources of CGB, a differential diagnosis should be carried out with tumors of the posterior cranial fossa,

Laboratory diagnostics should be aimed at excluding somatic pathology with combined damage to muscles and/or bone and joint structures (rheumatoid arthritis, systemic lupus erythematosus, diseases thyroid and parathyroid glands, primary muscle lesions). In the diagnosis of CGB, the role of medical and diagnostic blockades seems to be important. According to O. Sjaastad [45], two clinical criteria are of the greatest importance in the diagnosis of CGB: a unilateral headache without changing sides, the initiation of pain in the cervical region and the temporal zone with irradiation into the frontal-orbital region. The presence of the above simple clinical criteria is an indication for therapeutic and diagnostic blockades [53]. It is most often recommended to carry out blockages of the large and small occipital nerves.

However, G. Bovim et al. [55] on the basis of their own numerous observations, it is recommended to carry out a blockade of BZN on the side of pain, and only in the absence of an effect - a blockade of C2. Taking into account the complexity of clinical diagnosis and differential diagnosis of CGB, most authors share the opinion that it is necessary to conduct a blockade at probable CGB. Lehenie.

Effective therapy of CGB is possible with an integrated approach and the combined use of pharmacological and non-drug methods, including blockades with local anesthetics. Based on the results of individual reviews, antidepressants and anticonvulsants may be recommended for chronic CGB as part of complex therapy. Therapeutic blockades with local anesthetics temporarily reduce the intensity of pain and significantly increase the effect of drug therapy. In each situation, the tactics and methods of therapy are selected individually, depending on the accompanying symptoms and the data of additional examination methods. In the treatment of CGB, drugs of various groups are used (nonsteroidal anti-inflammatory drugs — NSAIDs, muscle relaxants, antidepressants, anticonvulsants), which are successfully used for migraine, GBN, as well as neuropathic pain syndromes. At the same time, none of these groups of medicines is recommended by the FDA as a means of choice for CGB. This fact is due to the lack of correct clinical studies of the effectiveness and safety of drugs in the therapy of CGB. Thus, at present, the pharmaceutical therapy of CGB is based on individual clinical studies and reviews, as well as recommendations of specialists studying this problem.

In CGB, simple analgesics and NSAIDs are most often used. At the same time, according to the majority of experts, based on practical experience , the use of NSAIDs (ketorolac, diclofenac, nimesulide) is more preferable. The use of NSAIDs is possible both for the relief of acute pain and as part of complex therapy for chronic CGB. It is advisable to prescribe drugs with a pronounced anti-inflammatory and analgesic effect, taking into account the concomitant somatic pathology. One of the modern NSAIDs with a powerful analgesic effect is ketorolac (Ketorol) — arylacetic acid derivative, non- selective COX inhibitor. The results of a prospective multicenter study by J. Forrest et al. ketorolac has been shown to be highly effective in relieving acute pain syndromes. A comparative analysis of the efficacy and safety of ketorolac with diclofenac and ketoprofen included the results of treatment of 11,245 patients. It was found that the frequency of adverse drug reactions (NLR) when taking ketorolac (scheme 90 mg / day parenterally for 2 days, after 40 mg / day for 7 days) did not differ in comparison with the use of diclofenac (scheme 150 mg / day parenterally for 2 days , after 150 mg / day 7 days) or ketoprof- na (scheme 200 mg / day 2 days parenterally, after 200 mg / day 7 days).

At the same time, the risk of gastrointestinal bleeding and allergic reactions was significantly ($p=0.05$) is lower in patients taking ketorolac, relative to the comparison group (diclofenac, ketoprofen). G. Jelinek [58] in his systemic review emphasizes the significant analgesic effect of ketorolac, comparable to that of narcotic analgesics, with a significantly lower incidence of

serious adverse drug reactions. reactions, which together significantly reduces the cost of pharmacotherapy. Russian authors , according to their own research, also note the powerful analgesic result of ketorolac (Ketorol) and recommend it as a first-choice remedy for the relief of acute pain syndromes, including musculoskeletal pain syndromes and pain at the prehospital stage [59]. In neurological practice, the use of ketorolac (Ketorol) for no more than 5 days in the form of intramuscular injections at a dose of up to 90 mg / day or in tablet form of 20-40 mg / day is recommended for the treatment of CGB. If it is necessary to prolong therapy, it is possible to switch to nimesulide (Naiz) 200 mg/day, 7-10 days [1]. It should be noted that the use of narcotic analgesics is not indicated for CGB. Given the high frequency of CGB and the tendency to chronicity, the use of narcotic painkillers significantly increases the risk of developing an acute headache and multiple NLR [60]. Antimigrenous drugs (triptans and ergotamines) have poor efficacy in CGB. The positive effect of taking these medications may be due to the combination of CGB with migraine [60]. A mandatory addition to NSAID therapy is the use of muscle relaxants, especially with a central mechanism of action (tizanidine, baclofen). At present, convincing data have been obtained on the effectiveness of injections of botulinum toxin type A into the pericranial and cervical muscles [56, 61, 62]. It should be remembered that if there is no regression of the left syndrome within 2 weeks, it is necessary to conduct an additional examination in order to clarify the possible etiology of CGB. The tactics of pharmacotherapy for chronic CGB with the use of antidepressants and anticonvulsants do not differ from those for other pain syndromes. The most significant positive results were obtained with the use of tricyclic antidepressants (amitriptilin), as well as serotonin and epinephrine reuptake inhibitors (venlafaxine, duloxetine). Selective serotonin reuptake inhibitors in chronic CSBS are ineffective. From the group of anticonvulsants recommended for use: gabapentin, topiramate, valproic acid, pregabalin, and carbamazepine [56]. Non-pharmacological methods are of great importance in the therapy of CGB . Controlled clinical studies have shown reliable effectiveness of manual therapy in CGB. In the manual on CBT, D. Biondi (2005) points to the high importance of soft manual therapy techniques, including PIR, massage and BOS, as part of the complex treatment [48, 63-65].

An integral component of CGB therapy is blockades with local anesthetics. Recommended for the use of blockade of the large / small occipital nerves, roots C2—3. It is also possible to block trigger points and areas of soreness/tension in the muscles, as well as arch-process joints [66, 67]. In chronic CGB, it is necessary to additionally use psychotherapy methods: cognitive and behavioral psychotherapy, BOS, training of patients in the ways of muscle relaxation. In case of refractory to therapy or compression of C2-3 joints, surgical treatment is indicated. It is possible to conduct neurolysis of the occipital nerve or decompression of the roots of C2-3. In recent years, data have been obtained on the effectiveness of BZN stimulation [68]. It should be emphasized that early diagnosis of CGB, as well as the use of a multidisciplinary approach to the treatment of this suffering, in most cases leads to a reduction of pain syndrome, a significant reduction in the cost of examination and treatment, improvement of the quality of life and normalization of social adaptation of the patient.

References:

1. Шодиев А. и др. К особенностям клинического течения и лечения нетравматических внутримозговых кровоизлияний у детей //Журнал проблемы биологии и медицины. – 2018. – №. 2.1 (101). – С. 128-131.
2. Vladimirovna S. V., Anvarovna S. L., Vladimirovna M. E. Menorrhagia-One of the Formidable Complications in Gynecology //Scholastic: Journal of Natural and Medical Education. – 2023. – Т. 2. – №. 4. – С. 72-79.

3. Абдувалиев Ш. И., Шодиев А. Ш., Пардаева З. С. НЕКОТОРЫЕ ОСОБЕННОСТИ КЛИНИЧЕСКОГО ПРОЯВЛЕНИЯ НЕТРАВМАТИЧЕСКИХ ВНУТРИМОЗГОВЫХ КРОВОИЗЛИЯНИЙ У ДЕТЕЙ //XX ДАВИДЕНКОВСКИЕ ЧТЕНИЯ. – 2018. – С. 9-10.
4. Vladimirovna S. V. et al. PREGNANCY WITH CONGENITAL HEART DISEASE //Science and innovation. – 2023. – Т. 2. – №. D4. – С. 127-136.
5. Suvonkulovna P. Z. ORTHOSTATIC HYPOTENSION: DEFINITION, PATHOPHYSIOLOGY, CLASSIFICATION, PROGNOSTIC ASPECTS, DIAGNOSIS AND TREATMENT //Science and innovation. – 2023. – Т. 2. – №. D4. – С. 107-112.
6. Vladimirovna S. V. ABOUT THE CAUSES OF ENDOMETRIAL HYPERPLASIA AND FORMS OF ENDOMETRIAL HYPERPLASIA //ResearchJet Journal of Analysis and Inventions. – 2022. – Т. 3. – №. 11. – С. 66-72.
7. Khidirovna L. Z. HYPERTROPHIC CARDIOMYOPATHY: GENETIC CHANGES, PATHOGENESIS AND PATHOPHYSIOLOGY //Science and innovation. – 2023. – Т. 2. – №. D4. – С. 120-126.
8. Sarkisova V. et al. UTERINE ARTERY EMBOLIZATION AS A METHOD OF TREATMENT OF UTERINE FIBROIDS //Science and innovation. – 2023. – Т. 2. – №. D3. – С. 115-121.
9. Khidirovna L. Z. The Structure of Cardiovascular Pathology in Childhood //Scholastic: Journal of Natural and Medical Education. – 2023. – Т. 2. – №. 5. – С. 91-98.
10. Vladimirovna S. V. et al. Menstrual Cycle Disturbances in the Reproductive Period //Central Asian Journal of Medical and Natural Science. – 2023. – Т. 4. – №. 2. – С. 389-397.
11. Aslamovna K. G. Clinical Pathophysiology and Anatomy of Acute Pain //Scholastic: Journal of Natural and Medical Education. – 2023. – Т. 2. – №. 5. – С. 66-73.
12. Vladimirovna S. V. et al. Ovarian Apoplexy and its Impact on Reproductive Health //Central Asian Journal of Medical and Natural Science. – 2023. – Т. 4. – №. 2. – С. 381-388.
13. Khidirovna L. Z. Primary and Secondary Hyperalgesia //Scholastic: Journal of Natural and Medical Education. – 2023. – Т. 2. – №. 5. – С. 99-104.
14. Sarkisova V., Numonova A., Xegay R. АСПЕКТЫ СОСТОЯНИЯ ВЕГЕТАТИВНОЙ НЕРВНОЙ СИСТЕМЫ ПРИ ГИПОКСИИ //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 228-231.
15. Aslamovna K. G. Clinical Pathophysiology and Anatomy of Acute Pain //Scholastic: Journal of Natural and Medical Education. – 2023. – Т. 2. – №. 5. – С. 66-73.
16. Vladimirovna S. V. Epidemiology, Theories Of The Development, Conservative And Operative Treatment Of The Endometriosis //The Peerian Journal. – 2023. – Т. 15. – С. 84-93.
17. Vladimirovna S. V. Epidemiology, Theories Of The Development, Conservative And Operative Treatment Of The Endometriosis //The Peerian Journal. – 2023. – Т. 15. – С. 84-93.
18. Лапасова З. Х. и др. Юрак қонтомир касалликларивожланишигаолибкелувчихавфомилларииўрганиш Биология ва тиббиёт муаммолари //Халкаро илмий журнал. – 2019. – С. 213-215.

19. Sarkisova V., Numonova A., Xegay R. АСПЕКТЫ СОСТОЯНИЯ ВЕГЕТАТИВНОЙ НЕРВНОЙ СИСТЕМЫ ПРИ ГИПОКСИИ //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 228-231.
20. Sarkisova V., Numonova A., Xegay R. АНТИБИОТИКОРЕЗИСТЕНТНОСТЬ ИЛИ БОРЬБА С ГЛОБАЛЬНОЙ УГРОЗОЙ XXI ВЕКА //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 232-241.
21. Нарзуллаева У. Р., Самиева Г. У., Пардаева З. С. Pathogenetic aspects of verified risk factors such as arterial hypertension and dyslipidemia in the development of chronic heart failure //American Journal of Medicine and Medical Sciences. – 2020. – Т. 10. – №. 10. – С. 776-779.
22. Sarkisova V., Regina X. РОЛЬ БРАДИКИНИНА В ПРОТЕКАНИИ ОСНОВНЫХ ЖИЗНЕННЫХ ПРОЦЕССОВ //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 587-593.
23. Vladimirovna S. V. PATHOGENETIC RELATIONSHIPS OF ARTERIAL HYPERTENSION AND INSULIN RESISTANCE //IQRO JURNALI. – 2023. – Т. 2. – №. 1. – С. 685-691.
24. Zilola Suvankulovna Pardayeva Samarqand viloyati Narpay tumani aholisining fertil yoshidagi ayollarda hayz sikli buzilishlarining uchrash darajasini o'rganish // Science and Education. 2023. №2. URL: https://cyberleninka.ru/article/n/samarqand-viloyati-narpay-tumani-aholisining-fertil-yoshidagi-ayollarda-hayz-sikli-buzilishlarining-uchrash-darajasini-o-rganish (дата обращения: 10.05.2023).
25. Саркисова В. В. Патогенетические отношения артериальной гипертензии и сопротивления инсулина //IQRO JURNALI. – 2023. – Т. 2. – №. 1. – С. 727-731.
26. Sarkisova V., Xegay R., Numonova A. ENDOCRINE CONTROL OF THE DIGESTION PROCESS. GASTROINTESTINAL ENDOCRINE CELLS //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 582-586.
27. Sarkisova V. ASPECTS OF THE STATE OF THE AUTONOMIC NERVOUS SYSTEM IN HYPOXIA //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 977-982.
28. Sarkisova V. et al. ESSENTIAL ROLE OF BRADIKININ IN THE COURSE OF BASIC LIFE PROCESSES //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 576-581.
29. Vladimirovna S. V. et al. Analysis of Women's Reproductive and Somatic Health, Hospitalized for Endometrial Hyperplasia and Uterine Bleeding //Eurasian Medical Research Periodical. – 2023. – Т. 17. – С. 91-96.
30. Нарзуллаева У., Самиева Г., Пардаева З. МИОКАРД РЕПЕРФУЗИОН ШИКАСТЛАНИШИ СИНДРОМИ ПАТОФИЗИОЛОГИЯСИ //Журнал вестник врача. – 2020. – Т. 1. – №. 2. – С. 155-158.
31. Vladimirovna S. V. About the Causes of Endometrial Hyperplasia and Forms of Endometrial Hyperplasia //Global Scientific Review. – 2023. – Т. 12. – С. 25-32.
32. Niyazov N. K., Nabidjanova D., Valiyeva M. INDICATIONS OF MORPHOLOGICAL CHANGES OF THE PANCREAS IN EXPERIMENTAL HYPOTHYROISIS //INTERNATIONAL SCIENTIFIC CONFERENCE" INNOVATIVE TRENDS IN SCIENCE, PRACTICE AND EDUCATION". – 2022. – Т. 1. – №. 4. – С. 16-19.
33. Muhamadovna A. S. et al. Indicators of Fetometry of the Fetus in Pregnant Women in a State of Hypothyroidism //Texas Journal of Medical Science. – 2023. – Т. 16. – С. 75-78.

34. Ниёзов Н. и др. CHANGES IN THE PANCREAS AGAINST THE BACKGROUND OF EXPERIMENTAL HYPOTHYROIDISM. – 2023.
35. Рахимова М. О. и др. ФЕТОМЕТРИЧЕСКИЕ ПОКАЗАТЕЛИ ПЛОДОВ У БЕРЕМЕННЫХ В СОСТОЯНИИ ГИПОТИРЕОЗА //Оргкомитет конференции. – 2021. – С. 143.
36. Курбанович НН и соавт. Особенности морфологических изменений поджелудочной железы //Техасский журнал медицинских наук. – 2023. – Т. 16. – С. 79-83.
37. Мухамадовна А.С. и соавт. Показатели фетометрии плода у беременных в состоянии гипотиреоза //Техасский журнал медицинских наук. – 2023. – Т. 16. – С. 75-78.
38. 54-59.

    МЕЛИКУЗИЕВ О., Тургун Д. СИСТЕМА ЭНДОГЕННЫХ АНТИМИКРОБНЫХ ПЕПТИДОВ У ДЕТЕЙ, БОЛЬНЫХ ПНЕВМОКОККОВОЙ ПНЕВМОНИЕЙ //Журнал" Медицина и инновации". – 2022. – №. 3. – С. 405-415.
39. Olimxo‘Jaev F. X., Rahmonov O. R., Xamdamov S. I. Jigar mikroqon tomirlarining postnatal rivojlanishi dinamikasi //Science and Education. – 2021. – Т. 2. – №. 6. – С. 38-47.
40. Шадманова Л. Ш. и др. СТАБИЛИЗАЦИЯ РЕМИССИЙ И ПРОФИЛАКТИКА РЕЦИДИВОВ У БОЛЬНЫХ С АЛКОГОЛЬНОЙ ЗАВИСИМОСТЬЮ //2017 год. – С. 106.
41. Tujchibaeva N. M. Islamova Sh. A., Shigakova LA, Otaeva NT Drugresistant epilepsy. Mechanisms and causes //Infekciya, immunitet i farmakologiya. – 2014. – Т. 4. – С. 123-129.
42. Kurbanov A. K. et al. The study of. – 2022.
43. Халиков П. Х. и др. ЦИТОГЕНЕТИЧЕСКИЙ МЕТОД В ИЗУЧЕНИИ НАСЛЕДСТВЕННОСТИ ЧЕЛОВЕКА //Journal of Integrated Education and Research. – 2023. – Т. 2. – №. 1. – С. 15-18.