Asian journal of Pharmaceutical and biological research 2231-2218
http://www.ajpbr.org/
Volume 10 Issue 3
Sept-Dec 2021
10.5281/zenodo.5571889

Morphogenesis of hyaline cartilage of the knee joint against the background of intra-articular injection of platelet-rich autologous plasma

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Abstract. *The objective of the work* was to evaluate the morphological changes in the structure of hyaline cartilage in experimental osteoarthritis after intra-articular injection of PRP and/or HA. *Material and methods.* The authors used 50 adult rats of Wistar line, weighing 250±2,2 g., distributed into five groups of 10 animals (two control and three experimental groups). An experimental gonarthosis was simulated on four groups of animals. Animals of the first experimental group received intra-articular injection of PRP, the second group – HA, the third – both PRP and HA. *Results.* No morphological signs of degenerative and inflammatory changes in the first control group were identified. Following osteoarthritis simulation the articular cartilage thinned to 121±20,4 microns ($p<0,05$) and the volume fraction of chondrocyte decreased to 1,2±0,6% ($p<0,05$).

Keywords: autologous platelet-rich plasma, articular cartilage, inflammation.

Introduction

Introduction.

Osteoarthritis (OA) is a chronic progressive degenerative joint disease characterized by degradation of the articular cartilage followed by changes in the subchondral bone and the development of marginal osteophytes. These changes lead to the loss of cartilage and concomitant damage to other components of the joint (synovium, ligaments). OA is the most common form of joint pathology. X-ray signs of the disease are observed in the majority of people over 65 years old and in more than 80% of people over the age of 75 years [2, 4, 6, 8, 9, 18, 21].

Hyaline cartilage contains a relatively small number of cells surrounded by a large amount of extracellular matrix. Chondrocytes are involved in the regulation of the synthesis and degradation of the components of the cartilage matrix, and normally

these processes are in equilibrium [22, 23, 25, 26]. Under the influence of many factors, the balance of degradation and repair processes is disturbed, which subsequently causes the development of osteoarthritis, manifested by degenerative-dystrophic changes in the structure of hyaline cartilage and subchondral bone, inflammation in the surrounding soft tissues, disruption of the physicochemical properties of synovial fluid [28, 30, 32, 33, 34, 35, 38, 42, 46, 48, 51, 53, 57, 60].

Deforming osteoarthritis is a heterogeneous group of joint diseases of various etiologies, but with identical biological, morphological and clinical signs and outcomes associated with the loss of hyaline cartilage and concomitant damage to other anatomical structures and tissues of the joint (subchondral bone, synovium, ligaments, joint capsule, periarticular and muscles) [1, 3, 5, 7, 10, 16, 17, 20, 24, 27, 29, 31, 36].

Exogenous hyaluronic acid promotes the formation of its own hyaluronic acid, acts on the CD44 receptors and stimulates the synthesis of proteoglycans by chondrocytes. It has been shown experimentally that blocking CD44 receptors in normal cartilage leads to irreparable loss of proteoglycans by the articular cartilage [13, 14, 44, 45, 47, 49, 50, 52]. It is assumed that medium-molecular forms of hyaluronates stimulate the production of their own hyaluronic acid to a greater extent [19, 54, 55, 60]. However, in a number of recent studies, significant differences in the chondroprotective effect of HA, depending on its molecular weight, have not been identified [11, 56, 58, 59]. Among the few successfully implemented modern approaches to the treatment of osteoarthritis, intra-articular administration of hyaluronic acid (HA) preparations should be noted, which help to reduce dystrophic changes in cartilage tissue, manifestations of the inflammatory process in the joint and normalize its synovial environment [11, 15, 29, 31, 36, 37, 39, 40, 41, 43, 61].

The aim of the study was to assess morphological changes in the structure of the hyaline cartilage of the knee joint in experimental osteoarthritis after intra-articular administration of PRP and / or GC.

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Material and methods

The material for the experimental study was 50 sexually mature Wistar rats weighing 250 ± 2.2 g.

Laboratory animals were divided into 5 groups of 10 animals each (2 experimental and 3 basic) (Table 1). All manipulations were performed under general anesthesia using the "Rometar" preparation according to the method described by the manufacturer.

In the second experimental and three main groups, osteoarthritis was modeled by intra-articular injection of 0.2 ml of 10% suspension of sterile talc [2].

Thirty days after modeling of osteoarthritis, the animals of the first main group underwent two intra-articular injection of 0.2 ml of PRP with a frequency of once every 21 days [8]. The animals of the second main group were injected three times intra-articularly with 0.2 ml of HA (1.6% sodium hyaluronate with an average molecular weight of 3600 kDa) with a frequency of once every 7 days [19]. The animals of the third main group were sequentially injected with PRP and HA: first, 0.2 ml of PRP intra-articularly, and after 7, 14 days - 0.2 ml of HA.

The animals of the first experimental group received a single intra-articular injection of 0.2 ml of 0.9% NaCl solution.

All intra-articular injections were performed from a standard anteroposterior approach to the left knee joint. The preparation of PRP began with taking 1.2 ml of whole blood from the femoral vein into a syringe with a pre-drawn 0.4 ml of 5% sodium citrate solution, following a standard access to it. The resulting blood was poured into a hermetically sealed sterile glass semitransparent container and placed in a RotoFix 32 centrifuge (Hettich, Germany) with an appropriate counterweight.

The first centrifugation was carried out for 5 minutes at a speed of 1500 rpm, then 0.8 ml of the supernatant was taken and placed in another similar sterile container.

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After the second centrifugation at 1000 rpm for 5 minutes, 0.6 ml of the supernatant was removed and the precipitated formed elements were dissolved in the remaining plasma. The PRP was removed with a syringe and 0.1 ml of 10% calcium chloride solution was added to it in order to activate platelets. The platelet count was 800 ± 40 × 109 / L.

One month after the last intra-articular injection of the preparations, the animals were withdrawn from the experiment by injecting a lethal dose of Rometar, and the left femur was dissected out for further morphological examination.

Cartilage tissue with subchondral bone was fixed in a 10% solution of neutral buffered formalin (pH 7.4) for 24 hours. An acid-free decalcification was carried out in a solution of sodium ethylenediaminetetraacetate of standard concentration. After complete removal of the mineral component from the bone tissue, standard histological tracing was performed using alcohols of increasing concentrations and the preparations were embedded in paraffin, after which sections with a thickness of 6–8 microns were cut, stained with hematoxylin-eosin and Mallory's method.

Photorecording of microscopic changes was performed using a complex including an Axio Scope microscope (Carl Zeiss, Germany) and a Power Shot digital camera (Canon, Japan). Morphometric analysis was performed using the Video TestMorfo-4 computer program (Microsoft, USA). To assess morphological parameters, the thickness of the articular cartilage (L, μm) and the volume fraction of chondrocytes in relation to the matrix (OD,%) were determined.

The experimental results were processed by methods of basic statistical analysis using the Video TestMorfo-4 (Microsoft, USA) and Statistica 6.0 (Stat Soft Inc., USA) programs. The analysis of parameters with a normal distribution of values was carried out using the Student's t test, the analysis of nonparametric quantitative features - using the Mann - Whitney test. The $\chi 2$ and Fisher tests were used to compare qualitative features. Differences were considered significant if the error probability did not exceed $p < 0.05$.

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Results

The study showed that in the experimental group of animals No. 1 (without arthrosis), the articular hyaline cartilage had a thickness of 330 ± 17.3 μm and a characteristic histological structure. Superficial chondrocytes were characterized by a flattened shape and were located singly in the cartilaginous matrix. Chondrocytes of the transitional and basal zones had a rounded shape and were located in isogenic groups in rows oriented perpendicular to the articular surface. The volume fraction of chondrocytes was 13.7 ± 1.1%. Morphological signs of degenerative-dystrophic processes were not visualized. Mallory's histochemical reaction revealed a uniform arrangement of collagen fibers, the absence of foci of ossification.

After modeling osteoarthritis, the thickness of the articular cartilage decreased to 121 ± 20.4 μm ($p < 0.05$) and the volume fraction of chondrocytes decreased to 1.2 ± 0.6% ($p < 0.05$). In all zones, multiple "empty gaps" and chondrocytes with karyopycnosis were noted, extensive areas of destruction of the articular surface with proliferation of connective tissue, in the thickness of which granulomatous inflammation was determined with pronounced histiomacrophage infiltration and giant multinucleated cells of the type of foreign bodies, plethora of glacial blood substances

After the introduction of PRP against the background of experimental osteoarthritis, an increase in the thickness of the articular cartilage to 275 ± 18.9 μm ($p < 0.05$) and the volume fraction of chondrocytes to 18.4 ± 2.0% ($p < 0.05$) was found morphometrically. As well as after HA administration, three zones delimited from each other were distinguished with degenerative changes typical for osteoatrosis, but less pronounced. In the superficial zone, the contours of the articular surface looked even. Despite the presence of "empty" lacunae and chondrocytes with signs of decay and the formation of apoptotic bodies, an increase in the number of both separately located chondrocytes and their isogenic groups in all zones was determined. In the intermediate zone, focal ossification of the intercellular substance

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occurred, which was especially noticeable when staining according to Mallory. The uniformity of the distribution of collagen fibers and the tinctorial properties of the cartilage matrix were preserved in all zones.

After sequential administration of PRP and GC against the background of experimental osteoarthritis, an increase in the thickness of cartilage to 268 ± 15.3 μm ($p < 0.05$) and the volume fraction of chondrocytes to 12.7 ± 0.9% ($p < 0.05$) were noted. In the surface zone of the preparations, attention was drawn to areas of destruction of the articular surface, in all zones - signs of disorganization and dissociation of collagen fibers of cartilaginous tissue. The interbeam spaces of the subchondral bone were filled with vascular-rich fibrous connective tissue. Deposits of osteoid, newly formed, but not yet mineralized, bone tissue, were determined on the surface of the bone beams surrounded by connective tissue and in the interbeam spaces. In the intermediate zone, focal ossification of the intercellular substance took place. The tinctorial properties of the cartilage matrix were completely preserved, only the basal zone was characterized by focal uneven coloration of collagen fibers.

Conclusions

When modeling osteoarthritis in the knee joint in sexually mature Wistar rats, gross structural changes in the articular cartilage occur, up to its complete destruction, accompanied by vascular proliferation and granulomatous inflammation. The introduction of PRP, GC, and also PRP in combination with GC against the background of developed osteoarthritis is accompanied by a decrease in the severity of degenerative-dystrophic changes, an improvement in the indicators of tinctorial properties of the articular cartilage matrix. The use of PRP alone or the sequential administration of PRP and HA to a greater extent has a positive effect on the reparative process in the cartilaginous tissue as compared with the intra-articular administration of HA.

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References

1. Akhmedov Sh.Sh., Khamraev À.Sh., Vazina G.P., Akramov V.R., Khamraev B.U., Tugizov B.E., THE Peculiarities of prophylaxis of pulmonary thromboembolism after total hip endoprosthesis in dysplastic coxarthrosis // “New day in medicine” Uzbekistan.Tashkent, №2 (30) 2020, pp. 53-56

2. Mirzamurodov Habibjon Halimovich, Nurulloev Sukhrob Ozodovich. Improvement of surgical treatment of patients with combined degenerativedystrophic pathology of the hip joint and spine with prevalence of manifestations of coxarthrosis // British Medical Journal Volume-1, No 2., 2021. P.180-187.

3. Akramov V.R. Features of hip arthroplasty in case of anatomical disorders of the acetabulum // "Bulletin of the association of doctors of Uzbekistan" Uzbekistan, Tashkent № 3 - 2011, Pages 94-97. [in Russian]

4. Akhmedov Sh.Sh., Khamraev A.Sh., Akramov V.R., Tugizov B.E., Khamraev B.U. Prophylactic features of pulmonary artery thromboembolism after hip arthroplasty in dysplastic coxarthrosis // “Bulletin of the association of doctors of Uzbekistan” Uzbekistan Tashkent № 1 (98) - 2020, pp. 42-47, pp. 42-47. [in Uzbek]

5. Akramov V.R. Some problems of hip joint replacement previously operated on. // “Bulletin of the association of doctors of Uzbekistan” Uzbekistan Tashkent № 2 - 2011, pp. 110-113. [in Russian]

6. Akramov V.R.,Akhmedov Sh.SH., Khamraev B.U.- (Hip replacement in femoral neck fractures) // "Problems of biology and medicine" Uzbekistan, Samarkand No. 3 - 2017 (96), pp.23-26 [in Russian]

7. Akramov V.R., Sh.Sh., Khamraev A.Sh., Khamraev B.U. – (Total hip replacement and prevention of possible complications) // "A new day in medicine” Uzbekistan. Tashkent, No.4 (20) 2017, pp.56-58. [in Russian]

8. Akramov V.R., Akhmedov Sh.SH., Khamraev A.SH., Khamraev B.U. - (Hip replacement in degenerative-dystrophic diseases in adults) // "Bulletin of the

association of doctors of Uzbekistan" Uzbekistan, Tashkent No. 2 - 2018, pp.42-44. [in Russian]

9. SH.SH.Akhmedov, A.SH.Khamraev, V.R.Akramov,B.U.Khamraev, A.A.Teshaev, A.U. Gaffarov The arthroplasty of the hip at fracture of a neck of a femur // "A new day in medicine "Uzbekistan.Tashkent, No. 1 (25) 2019, pp. 5-7.

10. V.R.Akramov,B. A.SH.Khamraev, SH.SH.Akhmedov, B.U.Khamraev The Arthroplasty Of The Hip At Fracture Of A Neck Of A Femur // European Journal of Business & Social Sciences., ISSN: 2235-767X.,Volume 07 Issue 05.,May 2019.

11. V.R.Akramov, B.A.SH.Khamraev, SH.SH.Akhmedov, B.U.Khamraev // Prevention Of Possible Complications Before And After Total Endoprotesization Of The Combin) European Journal of Business & Social Sciences., ISSN: 2235-767X.,Volume 07 Issue 05.,May 2019.

12. Akhmedov Sh.Sh., Khamraev À.Sh., Vazina G.P., Akramov V.R., Khamraev B.U., Tugizov B.E., THE Peculiarities of prophylaxis of pulmonary thromboembolism after total hip endoprosthesis in dysplastic coxarthrosis // "New day in medicine" Uzbekistan.Tashkent, №2 (30) 2020, pp. 53-56.

13. Nurullaev S.O; Akhmedov Sh.Sh; Akramov V.R; KhamraevA.Sh; Khamraev B.U; Mirzamurodov Kh.Kh Our experience in the treatment of grade I-II gonarthroa with hyaluronic acid preparations // Academicia An International Multidisciplinary Research Journal,Vol. 10 Issue 12, December 2020.

14. Asilova Saodat Ubayevna., Akramov Voxid Rustamovich., Akhmedov Shamshod Shavkatovich., Mirzamurodov Khabibjon Khalimovich (Tashkent, Uzbekistan). // Polish science journal., Issue 12 (33) Part 2. Warsaw, Poland Wydawnictwo Naukowe "iScience" 2020. [in Russian]

15. Yuldashev R.M., Mardanov J.J. Vertebroplasty in the surgical treatment of spinal tumors - evaluation of treatment results. Scientific and practical journal // "Doctor-graduate student" No. 4 (53). 2012.S. 9-13. [in Russian]

16. Yuldashev R.M., Mardanov Zh.Zh. Our experience in the treatment of patients with extradural tumors of the spinal cord. // Journal of Theoretical and Clinical Medicine. 2013. - No. 3.- P.100-102. [in Russian]

17. Kariev G.M., Mardanov J.J., Norov A.U. Pathogenesis of metastasis in the spine. // Scientific and Practical Journal of Neurology 2014.-№4.- P. 37-39. [in Russian]

18. Mardanov J.J., Zikriyaev N.N., Rakhmatov K.R., Rajabov M.M. Quality of life in patients with extradural tumors of the spinal cord. // Journal of Surgery of Uzbekistan 2016.-№4-C-25-27. [in Russian]

19. Mardanov J.J. Surgical treatment of spinal hemangiomas. // Russian neurosurgical journal named after professor A.L. Polenov. 2014 volume-№4. –S.-343-345. [in Russian]

20. Mardanov J.J.The result of surgical treatment of pathological pathological fracture during extradural tumor of spinal cord. // European Sciences Review 2014.-№3-4 - S.-21-24.

21. Mardanov J.J. Back - side access during surgical treatment of extradural tumors of the spinal cord. // Questions of science and education. 2021. - № 22 C. - 147. [in Russian]

22. Mardanov J.J. Surgical treatment of extradural tumors of the spinal cord. // Questions of science and education. 2021. - № 26 S. - 157. [in Russian]

23. Khamraev B.U., Akhmedov Sh.Sh. Two-stage revision hip replacement patiens with severe acetabulum defect (case report) // Asian journal of Pharmaceutical and biological research. Volume 10 Issue 2 MAY-AUG 2021 P. 35-41.

24. Khamraev B.U., Akhmedov Sh.Sh., Our experience of treatment of femor fractures by the method of intramedular locking osteosynthesis.// Asian journal of Pharmaceutical and biological research. Volume 10 Issue 2 may-aug 2021. P. 42-46.

25. BU Khamraev, BP Akramov. Program for expressing the method of treatment by the method of blocking intramedullary osteosynthesis for a fracture of the femur // Certificate of official registration of a computer program. Agency for Intellectual Property of the Republic of Uzbekistan. 2019. [in Russian]

26. Nematov Dilshod Amrilloevich. Features of the application of external osteosynthesis in gonarthrosis // Asian journal of Pharmaceutical and biological research. Volume 10 Issue 2 MAY-AUG 2021. P. 26-30.

27. Ziyadullaev Abdusalom Khabibulla oglu. Evaluation of the future results of application of arthro-medullary bypassing in gonarthrosis // Asian journal of Pharmaceutical and biological research. Volume 10 Issue 2 MAY-AUG 2021. P. 31-34.

28. Mirzamurodov Habibjon Halimovich, Nurulloev Sukhrob Ozodovich. Improvement of surgical treatment of patients with combined degenerative-dystrophic pathology of the hip joint and spine with prevalence of manifestations of coxarthrosis // British Medical Journal Volume-1, No 2., 2021. P.180-187.

29. Nurulloyev S.O., Mirzamuradov H.H. Morphological Changes In Bone Tissue In Chronic Osteomyelitis On The Background Of Application Of Plate Concentrate // The American Journal of Medical Sciences and Pharmaceutical Research Volume 3 Issue 04, 2021. P. 160-164.

30. Mirzamurodov H.H. New approaches to treatment of patients with coxovertebral syndrome // Asian journal of Pharmaceutical and biological research. Volume 10 Issue 2 MAY-AUG 2021. P. 9-19

31. Mirzamurodov Kh.Kh., Akhmedov Sh.Sh., Nuruloev S.O., Ziyadullaev A.Kh., Nematov D.A. Optimization of total hip arthroplasty in dysplastic coxarthrosis // New day in medicine. 4 (32) 2020 P. 667-672. [in Russian]

32. Mirzamurodov H. Kh., Khodzhanov I. Yu., Nurulloev S.O. Complex conservative therapy for hip-spine syndrome // International Scientific and

Educational electronic journal "Education and science in the xxi century" 2021. Issue No. 12 (volume 2). P. 1438-1439. [in Russian]

33. Nurulloev S.O., Mirzamuradov Kh.Kh. Our experience in the treatment of degree I-II gonarthrosis with drugs hyalouranic acid // Innovation in the modern education system. 2021. Part 5, Issue 1. P. 546-548. [in Russian]

34. Sulaymanova Gulnoza Tulkindzanovna, Amonov Muhammad Komilovich. Regional Causes Of Iron Deficiency Anemia, Pathogenesis And Use Of Antianemic Drugs. // The American Journal of Medical Sciences and Pharmaceutical Research (ISSN – 2689-1026) Published: April 30, 2021. P. 165-170.

35. Sulaymonova Gulnoza Tulkinjanovna, Raufov Alisher Anvarovich. The influence of defiency of microelements in children with bronchial hyperreactivity // ACADEMICIA: An International Multidisciplinary Research Journal (ISSN: 2249-7137) Published: Vol. 10, Issue 4, April 2020 | Pages: 846-853

36. Sulaimonova G.T., Amonov M.K., Rakhmonova K.E. The frequency of detection of risk factors for chronic kidney disease in the rural population. // Bulletin of Science and Education № 24 (102). Part 2. 2020. pp. 79-85. [in Russian]

37. Orziev Zavkidin Mansurovich, Suleimanova Gulnoza Tulkinzhanovna. Regional causes of iron deficiency anemia in women of fertile age. // Electronic scientific journal "Biology and Integrative Medicine" №4 – April (21) 2018. Pp. 74-82. [in Russian]

38. Z.M. Orziev, GT Sulaimonova. Analysis of modern ideas on the formation of critical periods in the event of iron deficiency anemias (review) // Bulletin of the Council of Young Scientists and Specialists of the Chelyabinsk Region Volume 5, No. 4, 2017. P. 17-25 [in Russian]

39. Abdullaeva U.K. Predicting the risk of atrophic transformation in chronic gastritis using serum pepsinogen // World journal of pharmaceutical research, Faculty of Pharmacy Medical University, Bulgaria, Vol. 8, Iss. 13, 2019, P. 219-228.

40. Abdullaeva U.K., Sobirova G.N., Karimov M.M., Aslonova I.J. The prevalence and possibilities of prevention of noncardial gastric cancer in the Bukhara region // American journal of medicine and medical sciences, 2020, 10(9), P. 679-681.

41. Sobirova G.N., Abdullaeva U.K., Nosirova M.S., Aslonova I.J. Evaluation of the gastrointestinal mucosa by the OLGA system in chronic atrophic gastritis // Journal of critical reviews, Kuala Lumpur, Malaysia, Vol. 7, Iss. 2, 2020, P. 409-413.

42. Karimov M.M., Sobirova G.N., Abdullaeva U.K., Aslonova I.Zh., Tulyaganova F.M. Possibilities of serological diagnosis of atrophic processes of the gastric mucosa // European Journal of Molecular & Clinical Medicine Vol. 7, Iss. 11, 2020, P. 2955-2960.

43. Karimov M.M., Sobirova G.N., Abdullaeva U.K. Chronic gastritis and carcinogenesis issues // Herald of Pancreatic Club, 2019. Iss. 45 (4). P. 65-70. [in Russian]

44. Sobirova G.N., Abdullaeva U.K. Immunopatogenesis of chronic gastritis and its role in carcinogenesis // Journal of Biomedicine and Practice, 1 (4). P. 40-44.

45. Karimov M.M., Sobirova G.N., Abdullaeva U.K., Aslonova I.Zh., Tulyaganova F.M. Possibilities of Serological Diagnosis of Atrophic Processes of the Gastric Mucosa // Annals of the Romanian Society for Cell Biology, , Vol. 25, Issue 1, 2021, Pages. 6168 – 6174.

46. Abdullaeva U.K., Shadjanova N.S. Using the OLGA system in chronic atrophic gastritis // New day in medicine, 2020, №2, P. 9-12.

47. Abdullaeva U.K. The value of interactive teaching methods in improving the level of clinical knowledge of students // Medical education and professional development. 2019, №1 (33), P. 29-32. [in Russian]

48. GN Sobirova, UK Abdullaeva Chronic gastritis and carcinogenesis issues // Central Asian Problems of Modern Science and Education. 2019, Iss. 4, №2, P. 159-172

49. Orziev Zavkiddin Mansurovich, Abdullaeva Umida Kurbanovna, Nurkhanova Nilufar Odiljonovna Study of the effectiveness of cholelitholytic therapy in patients with cholelithiasis, taking into account the type of violation of the contractility of the gallbladder // Science of the Young - Eruditio Juvenium. 2015. №4. P. 50. [in Russian]

50. Karimov M.M., Sobirova G.N., Abdullaeva U.K., Aslonova I.Zh., Tulyaganova F.M. Serological Diagnosis of Atrophic Processes of the Gastric Mucosa // The American Journal of Medical Sciences and Pharmaceutical Research, Vol. 2, Issue 12, 2020, Pages. 118-124

51. DB Mirzaeva, UK Abdullaeva, RR Boboeva The importance of interactive teaching methods in improving the level of clinical knowledge of students // Central Asian Problems of Modern Science and Education Vol. 4, Issue 2, 2019, Pages. 159-166

52. MM Karimov, ST Rustamova, ZhA Ismailova, UK Abdullaeva, ZZ Saatov Diagnostic efficacy of C14 breath test in Helicobacter pyloriosis // Cardiovascular therapy and prevention. 2019. Vol. 18, Issue S1, P. 85-86

53. Abdullaeva U.K., Jalolova V.Z. Study of the effectiveness of cholelitholytic therapy in patients with cholelithiasis, taking into account the type of violation of the contractility of the gallbladder // Bulletin of the Council of Young Scientists and Specialists of the Chelyabinsk Region. 2016. Vol. 5, Issue 4(15), P. 85-86 [in Russian]

54. Orziev Z.M., Abdullaeva U.K. Regional causes of extrahepatic "Subtransaminasemia" // Biology and integrative medicine 2016, №3. P. 28-40. [in Russian]

55. Abdullaeva U.K., Mirzaeva D.B. Regional prospects for metabolic therapy for stable senocardia Summary. // Bulletin of the South Kazakhstan Medical Academyю 2019. P. 74-76 [in Russian]

56. Orziev Z.M., Abdullaeva U.K., Yuldasheva D.H. Method for early prediction of the efficiency of cholelytic therapy based on dynamic control of bild pH indicators in patients with cholelystone disease // Innovative development of modern science. 2014. P.76-79 [in Russian]

57. Orziev Z.M., Abdullaeva U.K. Relationship between the effectiveness of cholelitholytic therapy and the state of contractility of the gallbladder // Bulletin of the Council of Young Scientists and Specialists of the Chelyabinsk Region. 2015. №3(10) [in Russian]

58. Orziev Z.M., Abdullaeva U.K. The effectiveness of cholelitholytic therapy for cholelithiasis // Health is the basis of human potential: problems and ways to solve them. 2015. Iss. 10. №2. P. 610-612. [in Russian]

59. Hamroev Behzod Uktamovich, & Akhmedov Shamshod Shavkatovich. (2021). Optimization of blocking intramedullary osteosynthesis methods for femoral fractures // Asian Journal of Pharmaceutical and Biological Research 2231-2218, Volume 10 (Issue 3 Sept-Dec 2021), P. 29–43.

60. Abdullaeva U.K. Predicting the risk of atrophic transformation in gastritis associated with chronic Helicobacter pylori // abstract of PhD dissertation on medical sciences. Tashkent. 2021. 46-p.

61. Halimova E.M. Obesity as a risk factor for recurrent polycystic ovary disease // Asian Journal of Pharmaceutical and Biological Research 2231-2218, Volume 10 (Issue 3 Sept-Dec 2021), P. 96–114.