UDC: 616.716.4 - 001.5: 616.71 - 003.84: 546.41 + 661.746.5: 618.36: 616 - 073.75

***Goltsev A.M., *Lykhytskyi O.O.***
Institute for Problems of Cryobiology and Cryomedicine of the National Academy of Sciences of Ukraine (23, Pereyaslavskaya str., Kharkov, 61015, Ukraine); *National Pirogov Memorial Medical University, Vinnytsya (Pirogov str. 56, Vinnytsya, 21018, Ukraine)

# RENGENOLOGICAL FEATURES OF MORPHOGENESIS OF REGENERATE IN RATS WITH OPEN FRACTURE OF LOWER JAW WITH OSTEOPOROSIS WHICH RECEPTED THE CALCIUM CITRATE WITH IMPROVEMENT OF CRYOPLACENTA

**Summary.** *In the experiment, 210 male rats of the Wistar population with an open fracture of the mandible on the background of osteoporosis, with a separate subplantation of the fragments of the placenta, as well as in combination with calcium preparations, established the dynamics of the radiographic features of the regenerate morphogenesis. By X-ray in rats with fracture of the mandible on the background of osteoporosis, the phenomena of the primary tissue reaction on day 7 after the fracture transcend on 14 and 21 days in a pronounced inflammatory and destructive process, which decreases by 30 days and stops only up to 45 days. In the fracture of the mandible on the background of osteoporosis, when the drug was administered cryoplacenta, the destructive-resorptive and inflammatory reaction was less pronounced than in the control group of rats and subsided until 21-30 days, and until the 45th day, processes of consolidation of jaw fractures predominated. In the group, with the co-administration of cryoplacenta and calcium, the primary tissue reaction was manifested by weakly inflamed inflammation only for 7 days, and by 14 days there were phenomena of consolidation, which, while increasing, led to the formation of dense bony callus up to 45 days.*

**Key words:** *X-ray features, fracture of the mandible, osteoporosis, cryoplacenta, calcium citrate, rats.*

## Introduction

The problem of treatment of patients with fractures of the mandible is not only medical, but also social significance. Most patients in this group are persons of working age, whose long-term residence on a disability or incomplete rehabilitation with temporary disability cannot satisfy neither the patient nor the doctor.

Existing methods for treatment of fractures of the mandible, despite the constant development and improvement of approaches and methods of rendering assistance to the victims, do not allow to fully carry out an adequate, qualitative repositioning and fixation of the chips and to avoid post-traumatic and postoperative complications (osteomyelitis, delayed consolidation of debris, fusion of debris in the wrong position, false joints, etc.) [4, 10]. Actually, for modern traumatology and orthopedics, reconstruction of bone tissue is possible with the help of substitute material that would not cause inflammation, distortion and immunological complications [8, 11].

The high content of cytokines and chemokines in the placenta extract serves as the optimum medium for the cultivation of fibroblast cells in tissue engineering of bone tissue [9]. High osmotic activity of cryoplacenta causes its necrolytic action, it allows it to be used to purify the hearth of inflammation from tissue destruction products. Compared to the bone marrow of the placenta, it is more accessible and does not require any invasive manipulation [3].

Given the fact of local osteopenic syndrome in the bone fracture to optimize osteoporosis, it is advisable to use osteotropic drugs (calcium D-3 nicomed, myocalcic, etc.) [1, 7].

*Aim* of work - to establish the radiological features of the regenerate morphogenesis in rats with an open fracture of the mandible on the background of osteoporosis, which received the preparation of $Ca^{2+}$ with the implantation of cryoplacenta.

## Materials and methods

The study of the individual action of cryopreserved xeno drug of human placenta and calcium-citrate compatible with the processes of repairing bone tissue of the mandible on the background of the modified osteoporosis was performed on 210 male rats of the Vistar population with a body weight of 180-200 g.

Experimental osteoporosis in rats was induced by administration of 2.5% hydrocortisone acetate solution over a period of 60 days in a dose of 5 mg/kg body weight [2]. Subsequently, the drug was discontinued and traumatic damage to the lower jaw was restored: the rat was fixed on the back of the machine; under light hexanal (0.1 ml of 10% solution per 100 g of body weight) anesthesia in the right submandibular zone was performed damage on the skin parallel to the lower edge of the mandible in the medial direction of 10-12 mm in length; the muscles dissected and skeletoned the lower jaw; separating the external cortical plate with a separating disk, and then a full bone fracture with a bit on the line was applied, connecting the site of the fusion of the body and the branches of the jaw in the retro-molar region with a location 0.9 cm from the medial angle of the mandible. The surgical wound was connected with the oral cavity, the muscles and the skin were sutured with a catgut. All stages of experimental research have been performed in accordance with the International Humane Animal Health Practices Directive in accordance with the rules of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986) and approved by the Committee on Bioethics of the Vinnitsa National Medical University named after Pirogov (Minutes No. 14 of 25.11.2010).

Animals that were in the same conditions of containment

were distributed into the following groups: group 1 - control, animals with combined pathology: rats under the background of the simulated osteoporosis were performed traumatic damage to the mandible (fracture of the mandible); group 2 - study of the effect of cryoplacenta on the repair of bone tissue in animals that had a combined pathology: 24 hours after the manipulation, transplant of the placenta fragments was carried out. The implantation of the drug was performed surgically one day after the fracture of lower jaws. For this purpose, in rats on the back, in the area of the shoulder blade, underneath the local novocaine anesthesia, made a subcutaneous pocket in which a sterile fragment of the placenta weighing 200 mg per animal was fed. The incision was sewn and treated with antiseptics. Human placenta fragments weighing from 1500 to 1800 mg with observance the rules of asepsis and antiseptics were stored in sterile disposable containers of the company "Nunc" for low temperature preservation at a temperature of -196°C. Cryopreservation and storage of containers was carried out according to the technology developed at the Institute for the problem of cryobiology and cryomedicine of the National Academy of Sciences of Ukraine [14]; group 3 - study of the effect of cryoplacenta in combination with calcium (calcium citrate) in animals that had a combined pathology. The drug calcium citrate was administered to animals once a day in a therapeutic dose of 26 mg/kg, taking into account the coefficient of species sensitivity.

X-ray examination was performed using the X-ray and fluoroscopic system "Opera T90 cex" (Italy). X-ray of the lower jaw was carried out in fixed animals, turned to the table with a fracture of the lower jaw. The free edge of the lower jaw was lifted and underneath a dense pillow was placed, a cassette was placed between the lower jaw and the pillow [6].

The research was carried out at 7, 14, 21, 30 and 45 days after fracture simulation.

## Results. Discussion

Comparison of the data of X-ray studies conducted in the dynamics revealed the existence of general patterns in the course of the reparative process. They were the primary tissue reaction in the form of osteoporosis, secondary inflammation in the form of destructive changes, more often in the distal fracture of the jaw and at the lower edge of the cortical plate of the cutter bed, resorption of the alveolar process with the outgrowth of the roots of the teeth and periostitis. Observation was also made of the separation of the place of destruction in the jaw fractures and resection sites of the alveolar appendix. This is evidenced by the appearance of clarity of the edges and an increase in the plane of the bone on the verge of destructive areas, signs of osteosclerosis, as well as the delimitation of sequester and reduction of periostitis.

Following this, signs of consolidation of the jaw fractures appeared in the form of increasing bone density, reducing the intensity of illumination and the width of the fracture,

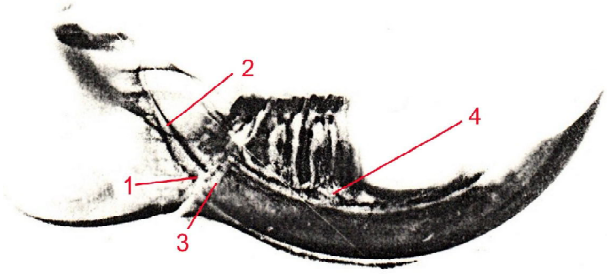


**Fig. 1.** Photo of X-ray of the mandible on the right of the rats with a model of open fracture of the mandible on the background of osteoporosis after implantation of cryoplacenta for 7 days. Signs: 1 - oblique fracture of the body of the jaw between the 3rd and 4th teeth; 2 - phenomena of osteoporosis in the finite parts of the chips; 3 - clearly separated areas of resorption of the alveolar appendix; 4 - weak periosteal reaction at the lower edge of the cutter bed.

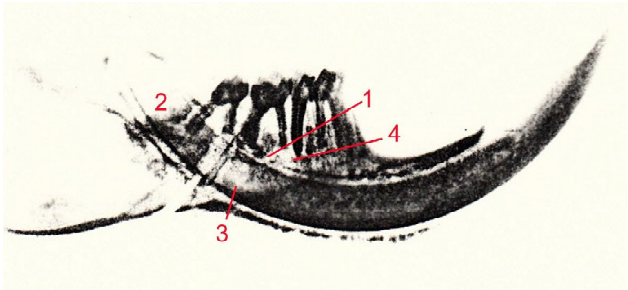


**Fig. 2.** Photo of the X-ray of the lower jaw on the right after an open fracture on an osteoporosis background for 7 days. Signs: 1 - oblique fracture of the body of the jaw between the 3rd and 4th teeth; 2 - osteoporosis in the distal chest of the mandible; 3 - resorption of the alveolar appendix; 4 - pronounced periosteal reaction at the lower edge of the cortical plate of the cutter bed.

clarity of the image of the contours of the chips, as well as the presence of periosteal layers, connecting chips in the area of damage. The process of consolidation of jaw fractures was completed by the disappearance of the fracture line and the formation of bone callus.

The described patterns of X-ray manifestations of osteogenesis in each series of experiments were observed in different terms and had different degrees of severity.

The primary tissue reaction of bone in *all three series* appeared on *day 7* in the form of osteoporosis in the finite parts of the chips (fig. 1).

Characteristic radiological signs of purulent inflammation, destruction and necrosis of the bone are non-ribbed areas, the blurriness of its edges with small bone sequesters in the center, thickening of the periosteum (periosteal reaction) with the formation of inflammatory exostoses. Osteoporosis rapidly and sharply increases, the crack of the fracture in the dynamics more and more expands. These pathological processes in a way slow down the restoration of bone formation [12].

In our study, inflammatory changes in the form of phenomena of destruction and sequestration, as well as pronounced periosteal reaction were noted only in the *control* series (fig. 2).

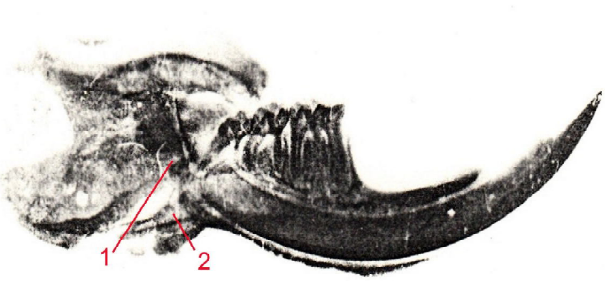


**Fig. 3.** Photo of the X-ray of the lower jaw on the right of the rats with a model of open fracture of the mandible on the background of osteoporosis after 21 days of implantation of cryoplascene. Signs: 1 - clearly separated areas of destruction in the distal chest of the jaw; 2 - a cavity in the bone in the region of fracture with the presence of delimited sequester of a long form.

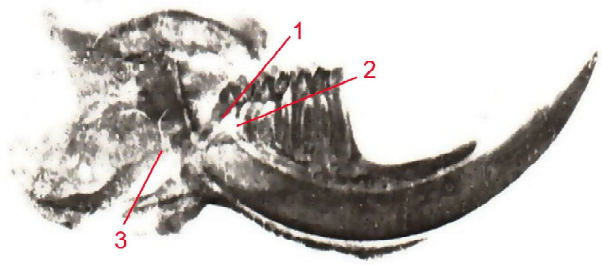


**Fig. 4.** Photo of the X-ray of the lower jaw on the right of the rats with a model of open fracture of the mandible on the background of osteoporosis, after implantation of cryoplacenta and administration of Ca2+ 45 days after the fracture. Sign: 1 - fracture line; 2 - dense bony callus; 3 - complete consolidation of jaw fractures.

Repeated control studies give an opportunity to judge the specific weight of inflammatory and reparative phenomena in the process of healing. The presence of destructive lesions and sequesters, especially their number and location, is determined with certainty only on the basis of the data of the X-ray examination, therefore, the latter in the fracture of the mandible becomes particularly important [13].

Up to *14 days in the control* series of animals, the phenomena of inflammation in the form of osteoporosis, destruction, sequestration and periosteum increased. In the same terms in the *second* series of the experiment, the same phenomena were expressed to a lesser degree, and in the *third* series - by this time there were signs of consolidation in the form of sealing of the finite sections of the fractures. The phenomena of sequestration and destruction in the third series of experiments did not manifest.

Up to *21 days in the control* series of the experiment, along with the growing inflammatory reaction in the form of large destruction, sequestration and pronounced periostitis, osteosclerosis sites appeared in the finite sections of the fractures, indicating a weakening of the inflammatory process. In the *second* series of experiments, in the same period the phenomena of periostitis were expressed slightly, and the destruction sites and sequester were already clearly delimited due to osteosclerosis (fig. 3). In the *third* series, up to 21 days, an increase in the density of the finite sections of the fractures were determined; the fracture line was determined only in the lower jaw sections. The periosteal layers connecting the chips appeared. Osteoporosis was detected only in the form of foci in the final parts of the fractures. All this testifies to the effective influence on the consolidation of jaw fractures of the complex of therapeutic measures applied in the third series of the experiment.

Up to *30 days in the control* series due to the sites of progressive osteosclerosis, the fields of destruction and sequestering were distinguished. The periodic reaction was moderate. In the *second* series, in the same period, the phenomenon of sealing of the bone predominated, the periosteal reaction was slightly expressed. There was no sequestration. All this indicated the beginning of the consolidation of the chippings of the mandible in animals of the *second* experimental group. In the *third* series of experiments, up to 30 days, phenomena of consolidation of chips in the form of bone densification, blurring of contours, and periosteal layers, connecting chips, were expressed. The line of fracture was not traced.

Up to *45 days in the control* series, the density of sequester decreased, there was a limit on them due to severe osteosclerosis in the final parts of the fractures. In the *second* series, in the same terms, the phenomena of consolidation of the chips were determined, the consolidation in the final departments increased, the intensity of illumination and the width of the fracture line diminished. The periodic reaction was moderate. In the *third* series up to 45 days, a dense bony callus was determined in place of the fracture line (fig. 4).

It is known that in the absence or suppression of purulent necrotic processes, the processes of forming granulation tissue are activated, leukocyte infiltration is reduced, immature bone tissue is replaced by mature, destroyed cells secrete osteoid (extracellular matrix), which is mineralized with the formation of bone trabecula (beams). When forming a new bone tissue in the area of bony callus, there are osteoclasts. During the healing and differentiation of osteoclast fragments of bones are replaced by mature lumbar bone, and the trabeculae of the cerebrospinal fluid expand [5].

The results of our studies indicate that the achievement of the most optimal ratio between the rate of proliferative processes, the differentiation of osteogenic cellular elements in osteoblasts and fibrin formation can be obtained with the combined application of biological preparations of cryoplacenta and calcium preparations.

## Conclusions and perspectives of further development

1. X-ray in the *control* group of rats (fracture of the mandible in the background of osteoporosis), the phenomena of the primary tissue reaction at 7 days after the fracture (osteoporosis in the extremities of the fractures

and secondary inflammation) transcend at 14 and 21 days in the expressed inflammatory and destructive process (destruction, sequestration and pronounced periostitis), which decreases by 30 days (delimitation of the fields of destruction and sequester by the sites of progressive osteosclerosis) and is stopped only up to 45 days (decrease in the density of sequester by the expressive osteosclerosis).

2. In the *second* group (fracture of the mandible in the background of osteoporosis when the preparation of cryoplacenta was administered), the destructive-resorptive and inflammatory reaction was less pronounced than in the control, subsided to 21-30 days, and by the 45th day the processes of consolidation of the jaw fragments were already prevailing.

3. In the *third* group (fracture of the mandible in the background of osteoporosis with the co-administration of preparations of cryoplacenta and calcium), the primary tissue reaction was manifested by weakly inflamed inflammation only for 7 days, and by 14 days there were phenomena of consolidation, which, by increasing, led to the formation of a dense bony callus to 45 day.

The obtained results allow, in the future, after the clinical approbation, to more correctly solve the questions of diagnosis and treatment of fractures of the mandible.

## List of references


1. Barannik, N.G., Ryabokon, E.N., & Moseyko, A.A. (2010). Lechenie bolnyih s perelomami nizhney chelyusti v predelah zubnogo ryada s pomoschyu kompressionno-distraktsionnogo apparata i osteotropnyih preparatov. *Zaporozhskiy meditsinskiy zhurnal,* 12(3), 5-8. (in Russian)
2. Batura, I.A. (2005). Osteonnyie konstruktsii bedrennoy kosti kryis pri dlitelnom vvedenii gidrokortizona. *Visnyk Bilotserkivs'koho derzhavnoho ahrarnoho universytetu,* 33, 300-304. (in Russian)
3. Fan, Z.X., Lu, Y., Deng, L., Li, X. Q., Zhi, W., Li-Ling, J., ... Xie, H.Q. (2012). Placenta-versus bone-marrow-derived mesenchymal cells for the repair of segmental bone defects in a rabbit model. *FEBS J.*, 279(13), 2455-2465.
4. Furr, A.M., Schweinfurth, J.M., & May, W.L. (2006). Factors associated with long-term complications after repair of mandibular fractures. *Laryngoscope*, 116(3), 427-430.
5. Iryanov, Yu.M., & Silanteva, T.A. (2007). Sovremennyie predstavleniya o gistologicheskih aspektah reparativnoy regeneratsii kostnoy tkani. Kletochnyie istochniki reparativnogo osteogeneza. Geterogennost kletochnoy populyatsii v oblasti travmaticheskogo povrezhdeniya kosti. *Geniy ortopedii,* 2, 111-116. (in Russian)
6. Ivanov, V.P. (2014). Klinicheskaya veterinarnaya rentgenologiya. M.: Lan. (in Russian)
7. Korzh, N.A., Goridova, L.D., Deduh, N.V., & Romanenko, K.K. (2006). Reparativnaya regeneratsiya kosti: sovremennyiy vzglyad na problemu. Medikamentoznyie preparatyi, optimiziruyuschie reparativnyiy osteogenez (soobschenie 2). *Ortopediya, travmatologiya i protezirovanie*, 3, 85-92. (in Russian)
8. Marin-Garcia, J., & Goldenthal, M.J. (2006). Application of Stem Cells in Cardiology: Where we are and where we are Going. *Current Stem Cell Research & Therapy*, 1, 1-11.
9. Oh, E.J., Kim, T.K., Shin, J.H., Choi, J.H., & Chung, H.Y. (2011). Biologic filler using human fibroblasts and placenta extracts. *J. Craniofac. Surg.*, 22(5), 1557-1560.
10. Petrenko, V.A., Klevakin, A.Yu., Tumanov, I.A., & Chekanov, S.A. (2010). Novyie metodyi i ustroystva dlya lecheniya postradavshih s povrezhdeniyami chelyustno-litsevoy oblasti. *Uralskiy meditsinskiy zhurnal*, 6, 99-102. (in Russian)
11. Sanchez-Lara, P.A., & Warburton, D. (2013). Impact of stem cells in craniofacial regenerative medicine. *Front. Physiol.*, 3, 188.
12. Semizorov, A.N. (2007). Rentgenografiya v diagnostike i lechenii perelomov kostey. Posobie dlya vrachey. M.: Vidar. (in Russian)
13. Vasilev, A.Yu., Bulanova, I.M., Malginov, H.H., Kiseleva, E.V., Chernyaev, S.E., Nikulina, O.M., ... Volozhin, A.I. (2008). Vozmozhnosti tsifrovoy mikrofokusnoy rentgenografii pri otsenke reparativnoy regeneratsii kostnoy tkani v eksperimente. *Vestnik rentgenologii i radiologii,* 3, 21-25. (in Russian)
14. Yurchenko, T.N., & Goltsev, A.N. (2013). Platsenta: kriokonservirovanie, klinicheskoe primenenie. Harkov: FOP Brovin A.V. (in Russian)


***Гольцев А.М., Ліхіцький О.О.***

**РЕНТГЕНОЛОГІЧНІ ОСОБЛИВОСТІ МОРФОГЕНЕЗУ РЕГЕНЕРАТУ У ЩУРІВ З ВІДКРИТИМ ПЕРЕЛОМОМ НИЖНЬОЇ ЩЕЛЕПИ НА ТЛІ ОСТЕОПОРОЗУ, ЯКІ ОТРИМУВАЛИ ПРЕПАРАТ КАЛЬЦІЮ ЦИТРАТУ З ІМПЛАНТАЦІЄЮ КРІОПЛАЦЕНТИ**

**Резюме.** *В експерименті на 210 самцях щурів популяції Вістар з відкритим переломом нижньої щелепи на тлі остеопорозу, при окремій підсадці фрагментів плаценти, а також у сполученні з препаратами кальцію встановлено динаміку рентгенологічних особливостей морфогенезу регенерату. Рентгенографічно у щурів з переломом нижньої щелепи на тлі остеопорозу, явища первинної тканинної реакції на 7 добу після перелому переростають на 14 та 21 добу у виражений запальний і деструктивний процес, який зменшується на 30 добу та купірується лише до 45 доби. При переломі нижньої щелепи на тлі остеопорозу при введенні препарату кріоплаценти деструктивно-резорбтивна і запальна реакція були менш виражені, ніж у контрольній групі щурів та вщухали до 21-30 діб, а до 45-ї доби превалювали процеси консолідації відламків щелепи. В групі при сумісному введенні препаратів кріоплаценти та кальцію первинна тканинна реакція проявлялась слабовираженим запаленням лише на 7 добу, а вже до 14 доби спостерігалися явища консолідації, які, наростаючи, призводили до утворення щільної кісткової мозолі до 45 доби.*

**Ключові слова:** *рентгенологічні особливості, перелом нижньої щелепи, остеопороз, кріоплацента, кальція цитрат, щури.*

***Гольцев А.Н., Лихицкий А.А.***

**РЕНТГЕНОЛОГИЧЕСКИЕ ОСОБЕННОСТИ МОРФОГЕНЕЗА РЕГЕНЕРАТА У КРЫС С ОТКРЫТЫМ ПЕРЕЛОМОМ НИЖНЕЙ ЧЕЛЮСТИ НА ФОНЕ ОСТЕОПОРОЗА, КОТОРЫЕ ПОЛУЧАЛИ ПРЕПАРАТ КАЛЬЦИЯ ЦИТРАТ С ИМПЛАНТАЦИЕЙ КРИОПЛАЦЕНТЫ**

**Резюме.** *В эксперименте на 210 самцах крыс популяции Вистар с открытым переломом нижней челюсти на фоне остеопороза, при отдельной подсадке фрагментов плаценты, а также совместно с препаратами кальция установлено динамику*

*рентгенологических особенностей морфогенеза регенерата. Рентгенографически у крыс с перелом нижней челюсти на фоне остеопороза, явления первичной тканевой реакции на 7 сутки после перелома перерастают на 14 и 21 сутки в выраженный воспалительный и деструктивный процесс, который уменьшается на 30 сутки и купируется лишь к 45 суткам. При переломе нижней челюсти на фоне остеопороза при введении препарата криоплаценты деструктивно-резорбтивная и воспалительная реакции были менее выражены, нежели в контрольной группе крыс и затихали к 21-30 суткам, а к 45 суткам превалировали процессы консолидации отломков челюсти. В группе при совместном введении препаратов криоплаценты и кальция первичная тканевая реакция проявлялась слабовыраженным воспалением лишь на 7 сутки, а уже к 14 суткам наблюдались явления консолидации, которые, нарастая, приводили к образованию плотной костной мозоли к 45 суткам.*

**Ключевые слова:** *рентгенологические особенности, перелом нижней челюсти, остеопороз, криоплацента, кальция цитрат, крысы.*

***Reviewer - prof. Gunas I.V.***

*Article received on 5.06.2017*

*Goltsev Anatoly Mykolayovych* - academician of the National Academy of Sciences of Ukraine, Professor, DSc (Med), MD, Director of Institute for Problems of Cryobiology and Cryomedicine of the National Academy of Sciences of Ukraine; +38(057)3734143; cryo@online.kharkov.ua

*Lykhytskyi Oleksiy Oleksiyovych* - assistant of the Department of Surgery №2 with the course of the basis of dentistry of National Pirogov Memorial Medical University, Vinnitsa, +38(067)3964340



**УДК:** 577.112.386:616.61

***Волощук Н.І., Конюх С.А., Мельник А.В.***

Вінницький національний медичний університет імені М.І. Пирогова, кафедра фармакології (вул. Пирогова, 56, м. Вінниця, 21018, Україна)

# УЧАСТЬ СИСТЕМИ ГІДРОГЕН СУЛЬФІДУ В ПАТОГЕНЕЗІ ЕКСПЕРИМЕНТАЛЬНОЇ НИРКОВОЇ НЕДОСТАТНОСТІ

**Резюме.** *В дослідах на щурах встановлено причетність системи гідроген сульфіду до стану видільних органів за гострої міоглобінуричної та хронічної ниркової недостатності. За умов гострого ураження, підвищення рівня гідроген сульфіду в нирках корелювало із погіршенням функціонального стану канальцевого та клубочкового апарату нирок, а зниження його кількості - навпаки, виявляло нефропротекторну дію. За умов хронічної ниркової недостатності виявлена протилежна закономірність, донатори гідроген сульфіду проявляли захисну дію, а інгібітори його синтезу - погіршували показники роботи нирок.*

**Ключові слова:** *гідроген сульфід, гостра ниркова недостатність, хронічна ниркова недостатність.*

## Вступ

Актуальність проблеми уражень нирок весь час зростає, оскільки ця патологія в світі охоплює від 10 до 16% дорослого населення. У 2011 році експерти ООН назвали хвороби нирок найбільш важливими неінфекційними захворюваннями сучасності [5]. У 1990 році хронічна хвороба нирок (ХХН) займала 27 місце серед усіх причин смертності, тоді як у 2010 році займала 18 місце (росла приблизно на 82%), що становило третє місце за швидкістю приросту летальності серед 25 основних причин смерті (після ВІЛ/СНІД - 396%, та діабету - 93%) [8]. В Україні станом на початок 2004 року на обліку перебувало 9647 хворих на ХНН, з яких 1634 були зареєстровані вперше. На кінець 2007 року на обліку перебувало вже 435 468 хворих з діагнозом хронічна хвороба нирок (ХХН), з яких 49 267 були виявлені вперше [3]. Молекулярні механізми ураження нирок є предметом інтенсивних досліджень. На сьогоднішній день не викликає сумнівів залучення таких процесів як прямий безпосередній вплив на певні клітинні мішені, субклітинні структури, ферментні чи транспортні білки, оксидативний та нітрозативний стрес, апоптоз та запалення [10]. Однак, повної ясності в цих питаннях наразі немає. Тому встановлення молекулярних механізмів захисного потенціалу видільних органів набуває особливої ваги з огляду на можливість визначення додаткових маркерів нефротоксичності та розробки патогенетично обґрунтованих підходів до попередження і медикаментозного лікування ураження нирок.

Останні роки все більше уваги привертає така сигнальна молекула як гідроген сульфід ($H_2S$), яка утворюється в організмі в процесі метаболізму сірковмісних амінокислот. Гідроген сульфід приймає участь в регуляції фізіологічних та патологічних процесів в різних органах, в т.ч. і нирках. $H_2S$ утворюється в нирках за умови наявності реакцій, що каталізуються ензимами ЦГЛ (КФ 4.4.1.1), ЦБС (КФ 4.2.1.22), та 3-МСТ (ЕС 2.8.1.2) разом із ЦАТ (ЕС 2.6.1.3) у досить значних кількостях, що є свідченням досить значної ролі, яку відіграє цей газотрансмітер у функціонуванні як канальцевого, так і клубочкового апарату видільних органів [6, 9].

Зміни вмісту $H_2S$ в організмі можуть виникати внаслідок застосування лікарських засобів та наявності у пацієнта патологічних станів та захворювань [10]. На сьогодні до кінця не з'ясована роль гідроген сульфіду