ISSN 1817-7883 eISSN 2522-9354

НАУКОВІ ОГЛЯДИ

DOI: 10.31393/reports-vnmedical-2019-23(2)-24
UDC: (611.018.4+599.323.4):616.716.4

MODERN VIEWS ON ETIOPATHOGENESIS OF TRAUMATIC INJURIES OF THE LOWER JAW AGAINST THE BACKGROUND OF OSTEOPOROSIS AND THE USE OF DRUGS FOR CORRECTION OF THE PROCESSES OF REPARATIVE OSTEOGENESIS

Lykhytskyi O. O.
National Pirogov Memorial Medical University, Vinnytsia (Pyrogov Str., 56, Vinnytsia, Ukraine, 21018)

Responsible for correspondence:
e-mail: *oleksiilikhitskyi@gmail.com*

Received: 11 March 2019; Accepted: 18 April 2019

Annotation. *The purpose of the work is to analyze contemporary views on the etiopathogenesis of traumatic injuries of the lower jaw against the background of osteoporosis and the use of drugs to correct the processes of reparative osteogenesis. The analysis is based on a review of domestic and foreign articles and studies for 2006-2018, using the scientometric databases PubMed, eLIBRARY.RU, Web of Science. Damage to the lower jaw, namely its fractures, is a fairly common pathology both in Ukraine and in other countries of the world, and is associated with a violation of many key functions, in particular, nutrition and communication, and in case of complications, even a violation of aesthetic function. One of the factors that increase the likelihood of fracture formation is osteoporosis, a systemic disease of bone tissue characterized by a decrease in bone mass per unit volume and a violation of its microarchitecture. And if the problem of fractures of the lower jaw is sufficiently disclosed, then the features of the formation of fractures of this bone against the background of diseases, including against the background of osteoporosis, are not adequately addressed in both Ukrainian and foreign sources. This article presents modern works on the etiology and pathogenesis of traumatic injuries of the lower jaw against the background of osteoporosis and modern methods of correction of reparative osteogenesis.*
Keywords: *reparative osteogenesis, damage to the lower jaw, osteoporosis, etiology and pathogenesis.*

The problem of treating patients with mandibular fractures has not only medical but also social significance [28]. The vast majority of patients in this group are persons of working age, whose long stay in disability or incomplete rehabilitation with temporary disability cannot satisfy either the patient or the doctor. The main task of treating this category of patients is to restore the anatomical integrity of the mandible and, as a result, to restore the ability to perform many functions: speech, laughter, chewing, swallowing, fixing the teeth on the alveolar process of the mandible [7, 40, 45].

Existing surgical methods of treatment of fractures of the lower jaw, despite the constant development and improvement of approaches and techniques of providing assistance to the victims, do not allow to carry out completely adequate, qualitative reposition and fixation of fragments and to avoid post-traumatic and postoperative complications (osteomyelitis, slow consolidation of debris, splicing in the wrong position, etc.) [7, 20, 42]. This is due to the fact that they are mainly calculated and applied to fractures that occurred on the bone without osteoporosis. However, fractures of the mandible caused by impaired repair and low calcium are widespread and are reflected in the inconsistent statistics of morbidity, disability in patients of both sexes, middle and elderly age [5, 23, 40].

The purpose of our study is to analyze the current views on the etiopathogenesis of traumatic injuries of the mandible against osteoporosis and the use of drugs to correct the processes of reparative osteogenesis.

Currently, maxillofacial surgery is considered to be one of the most complexes and popular areas of modern medicine. After all, a person's face primarily determines his personality and appearance, participates in the provision of such vital functions as breathing and eating, allows communication through language and facial expressions [17].

Among the lesions of the facial skeleton are the most common fractures of the mandible, which according to domestic and foreign authors account for from 70% to 85% of all bone fractures of the maxillofacial region [1, 5, 40]. The lower jaw is the only bone in the facial skull that breaks not only from direct but also indirect injuries. If direct injury is combined with indirect injury, multiple fractures usually occur [5].

Normally, bone repair occurs in several stages: inflammation, proliferation, differentiation, formation of tissue-specific structures, mineralization, remodeling of the regenerate and complete restoration of bone structures. Thus, both the processes of catabolism and anabolism take place in the formation of regenerate [4].

Consider the work concerning the study of the effectiveness of drugs for the correction of the processes of reparative osteogenesis in fractures of the mandible with and without osteopenia.

Studies by B. V. Trifonov [19] and A. A. Chernichenko [21] found that the use of nanosized hydroxyapatite with the addition of a binder resorbable polymer, anti-inflammatory and antiseptic drugs activates the processes of bone regeneration of the mandible of laboratory animals.

To accelerate bone regeneration, granular hydroxyapatite preparations and various biodegraded materials are introduced into defects, which are the basis for bone

formation. However, it has been found that hydroxyapatite is destroyed by macrophages, which often form multinucleate forms that do not lyse locally hydroxyapatite, and together with this substance migrate to other tissues and organs in lysosomes [16].

In the experiment on rabbits with fracture of the mandible, the use of the drug "Tizol" stimulated pronounced and accelerated regeneration of the microcirculatory bed for 3-5 days and the formation of collagen-reticulin framework for 6-8 days, which was ahead of the normal process for 5 days [12].

In rats, the use of osteoplastic material "TIOPROST" and material "KollapAn-M" conducted a comparative study of the speed and efficiency of regeneration of the bone tissue of the mandible. It was determined that when using "TIOPROST" the rate of filling the volume of bone defect is more than 1 month ahead of bone tissue regeneration compared to the use of the "KollapAn-M" material. After filling the bone defect with material "TIOPROST" a porous three-dimensional structure is formed, which is a tissue-engineering matrix and performs a supporting function [18].

Studies conducted by K. V. Barsukova and O. M. Gorshkova [2] have shown that the use of the titanium glycerosolvate aquacomplex in the treatment regimens of patients with mandibular fractures accelerates the regeneration process. In comparison with the use of standard treatment regimens, the processes of osteointegration have been observed for 2-3 days of using "Tizol".

Finish result of osteoreparation is the joint of bone fragments, but very often there is no cleft of fracture, which in most cases is caused by osteoporosis of the mandible - one of the variants of the disease of the human bone system, whose degenerative-dystrophic changes is manifested by dysfunction and pain [13].

Recent large-scale studies have shown that fractures of the lower jaw bone structures due to osteoporosis in people of all ages and genders are occurring more and more frequently [3, 36]. Defects of the lower jaw caused by tissue dysplasia, atrophy, post-radiation necrosis, benign or malignant neoplasms are less common [45].

There are two main forms of osteoporosis: primary and secondary. Primary osteoporosis more often develops in women during menopause, and in men in the elderly. Secondary osteoporosis is a complication of endocrine, inflammatory, hematologic, gastroenterological diseases, or drug therapy (eg, with steroids) [43].

The direct influence of systemic osteoporosis on the bone tissue of the alveolar ridge, which is highly sensitive to hormonal regulating and controlling mechanisms of the organism, has been established [6]. Osteoporosis is characterized by a long period of recovery after fracture and often the treatment of fracture in osteoporosis requires additional surgery. Fractures in people with osteoporosis are more often accompanied by complications and disability during the rehabilitation period [7].

In fractures resulting from osteoporosis, there is a potential risk of local and systemic side effects, which are most noticeable in terms of the completion of reparative osteogenesis of damaged bone tissue, which is explained by imbalance in bone metabolism caused by local and local factors [29, 38]. All this affects bone strength, which reflects the integration of two basic characteristics: bone mineral density and bone quality (exchange, architectonics, damage accumulation and mineralization) [8].

For studies in the maxillofacial area, animal models are used to study the features of the repair of jaw defects in osteopenia. Most often, experimental studies of fracture consolidation are performed in laboratory rats after ovariectomy [39]. Also, delayed fracture healing is observed, in particular, in an animal model of osteoporosis induced by corticosteroids [26, 35].

In animal models, when fracture was healed, osteoporosis was reduced by a 40% reduction in the area of the corpus callosum and a 23% reduction in bone mineral density in the lesion area. The mechanical properties of the corn are also disturbed and the stability and strength of the fixation of the implants is impaired [11]. For greater persuasion, we will present both preclinical and clinical data.

In the works by E. V. Zhelnina [9], evidence of osteoporosis of alveolar bone that arose under the influence of dexamethasone for two weeks is presented. This revealed shifts in the activity of alkaline phosphatase, the levels of metabolites of nitric oxide with a constant content of Ca and P in the blood [10].

Y. Li et al. [37] found in simulations of rabbit defect a positive correlation between bone repair activity and the expression/activity of calcitonin gene-bound peptide and nitric oxide synthase.

I. V. Mayborodin et al. [15] proved that the introduction to rats into the area of mandible bone damage, a suspension of autologous bone marrow mesenchymal stem cells in the culture medium accelerates the development of bone tissue integrity restoration processes.

After surgery to fill the defect of the mandible bone enriched with platelet fibrin clot in rats, further effective replacement of the defect with bone tissue and bone marrow formation was observed [14].

The effectiveness of the use of autologous and allogeneic adipose tissue stem cells to optimize regeneration of the mandibular bone defect in rabbits was pruved. Bioengineered design based on collagen sponge from hydroxyapatite GAPCOL (GAPCOL, "NGO polystyrene") for transplantation of adipose stem cells into bone tissue defect. Osteogenic stem cells induced by osteogenic differentiation have been shown to stimulate reparative osteogenesis. Moreover, the influence of autologous cells is more pronounced than allogeneic cells (higher rate of bone matrix maturation) [22].

In the domestic and foreign scientific and medical literature there are practically no works devoted to the study of the ability to stimulate regeneration in fractures of the mandible with the help of placental therapy and calcium

preparations [3, 25, 40, 44].

Only the results of the study by Russian colleagues [3] of the effectiveness of implantation of PLATEX-choral (chorionic sheath preparation) into the fracture zone of the mandible to stimulate reparative osteogenesis of bone tissue can be named from the works.

A. G. Guliuk et al. [7] improved the method of complex treatment of patients with mandibular fracture against the background of structural and metabolic changes in bone tissue with the combined use of calcium and zinc.

C. Roux et al. [41] and A. Avenell et al. [24] studied the repair process in osteoporous, osteopenic fractures and evaluated the potential for the use of vitamin D and calcium drugs in slow or insufficient bone healing.

We did not include any studies on drugs capable of influencing different stages of reparative osteogenesis of other body bones without and against osteoporosis.

The analysis of the literature showed the variety of existing methods of treatment of fractures of the mandible, which have a regenerative effect on bone tissue, which is confirmed by morphological methods of research [7, 13, 27, 41].

It should be noted that it is difficult to extrapolate the positive results of administration of the above-mentioned drugs to humans, as there is no evidence of safety or bio-similarity for patients. As a rule, the doses used in animals are several times higher than the therapeutic doses in humans [30].

Evidence of similarity in clinical studies on the model of the mandibular fracture caused by corticosteroids allows us to extrapolate the results of efficacy studies, provided that the investigated drugs have a similar mechanism of action in animals and humans [31, 32]. For preparations of cryopreserved tissue of the placenta and calcium preparations, their bio-analogy (bio-similarity) has been proved in relation to many indications for use [33, 34]. Therefore, with proper scientific justification, it is possible to extrapolate to other indications prior to their use (in our case it is a correction of reparative osteogenesis in osteoporosis).

Conclusions and prospects for further development

1. The analysis of the literature indicates that there are numerous reliable (confirmed by morphological studies) methods of treatment of fractures of the mandible, which are aimed specifically at improving the processes of reductive osteogenesis, which in turn indicates the urgency of the topic.

In particular, works that have highlighted the features of healing of the fracture of the mandible in the background of comorbidities, namely, osteoporosis, are of particular scientific and practical value.

Список посилань

1. Афанасьев, В. В. (2010). *Травматология челюстно-лицевой области*. М.: Изд-во "ГЭОТАР - Медиа".
2. Барсукова, К. В., & Горшкова, О. М. (2013). Гистохимическая оценка процесса регенерации костной ткани при использовании препарата "Тизоль". *Журнал анатомии и гистопатологии,* 2 (3), 58-60.
3. Березка, Н. И., Литовченко, В. А., Иванов, А. Н., & Гарячий, Е. В. (2011). Оптимизация репаративного остеогенеза при дисрегенерации костной ткани. *Научные ведомости Белгородского государственного университета. Серия: Медицина. Фармация,* 20 (141), 46-50.
4. Брагина, В. Г., & Горбатова, Л. Н. (2014). Травма челюстно-лицевой области у детей. *Экология человека,* 2, 20-24.
5. Варес, Я. Е., Філіпський, А. В., & Філіпська, Т. А. (2011). Травматогенез і структура переломів нижньої щелепи. *Практична медицина,* 17 (5), 9-14.
6. Гулюк, А. Г., & Желнин, Е. В. (2013). Взаимосвязь маркеров остеогенеза и процессов посттравматической регенерации альвеолярной кости у крыс. *Фундаментальные исследования,* 7, 534-539.
7. Гулюк, А. Г., Тащян, А. Э., & Гулюк, Л. Н. (2012). Профилактика осложнений консолидации при переломах нижней челюсти у больных со структурно-метаболическими изменениями костной ткани. *Вісник стоматології,* 2, 65-71.
8. Деев, Р. В., Бозо, И. Я., Дробышев, А. Ю., & Исаев, А. А. (2013). Эффективность ген-активированного остеопластического материала с плазмидными ДНК, содержащими ген VEGF, в замещении костных дефектов. *Пробл. криобиологии и криомедицины*, 23 (3), 355-358.
9. Желнин, Е. В. (2012). Морфологические особенности посттравматической регенерации альвеолярной кости в эксперименте. *Український морфологічний альманах,* 10 (3), 35-38.
10. Желнин, Е. В. (2013). Биохимические критерии прогнозирования посттравматической регенерации альвеолярной кости в эксперименте. *Фундаментальные исследования,* 9-6, 1006-1010.
11. Корж, Н. А., Дедух, Н. В., & Никольченко, О. А. (2006). Репаративная регенерация кости: современный взгляд на проблему. Системные факторы, влияющие на заживление перелома (сообщение 3). *Ортопедия, травматология и протезирование,* 2, 93-99.
12. Коротких, Н. Г., Лесникова, И. Н., & Барсукова, К. В. (2013). Морфологические критерии регенерации кости нижней челюсти у кроликов при использовании в терапии препарата "Тизоль". *Вестник новых медицинских технологий.* Электронное издание, 1, 60.
13. Котельников, Г. П., Колсанов, А. В., Щербовских, А. Е., Николаенко, А. Н., Приходько, С. А., Попов, Н. В., & Хассан, М. А. (2017). Реконструкция посттравматических и постоперационных дефектов нижней челюсти. *Хирургия,* 7, 69-72. DOI: 10.17116/hirurgia2017769-72.
14. Майбородин, И. В., Колесников, И. С., Шевела, А. И., Шеплев, Б. В., Дровосеков, М. Н., & Тодер, М. С. (2011). Влияние фибринового сгустка при повреждении кости нижней челюсти в эксперименте. *Стоматология,* 4, 9-12.
15. Майбородин, И. В., Матвеева, В. А., Колесников, И. С., Дровосеков, М. Н., Тодер, М. С., & Шевела, А. И. (2012). Влияние аутологичных мезенхимальных стволовых клеток костномозгового происхождения на регенерацию поврежденной кости нижней челюсти крыс. *Стоматология,* 1, 5-8.
16. Майбородин, И. В., Матвеева, В. А., Шевела, А. И., Шеплев, Б. В., Колесников, И. С., Выборнов, М. С., … Шевела, А. А. (2010). Применение биодеградируемых полигидроксиалканоатов после повреждения кости нижней челюсти в эксперименте. *Клиническая стоматология*, 4, 54-57.
17. Оскольский, Г. И., & Юркевич, А. В. (2013). *Челюстно-*

лицевая ортопедия. Учебное пособие. Хабаровск: ГБОУ ВПО ДВГМУ.
18. Сахаров, А. В. (2011). Сравнительное исследование репаративной регенерации костной ткани при использовании тканеинженерной матрицы на основе материала "ТИОПРОСТ" и материала "КОЛЛАПАН-М". *Гены и клетки*, 6 (4), 89-94.
19. Трифонов, Б. В. (2013). Регенерация костной ткани при заполнении ее дефекта композитом "титановое волокно - костнопластический материал". *Композиты и наноструктуры,* 2 (18), 59-64.
20. Фаренюк, О. О. (2014). Розробка методики індивідуального підбору варіанта лікування пацієнтів із переломами нижньої щелепи. *Український стоматологічний альманах,* 1, 51-62.
21. Черниченко, А. А. (2008). Репаративная регенерация костной ткани нижней челюсти при использовании титанового имплантата в эксперименте. *Сибирское медицинское обозрение,* 49 (1), 29-33.
22. Черняев, С. Е., & Киселева, Е. В. (2009). *Возможности использования стволовых клеток у детей с патологией челюстно-лицевой области.* Тезисы представлены в материалах III Всероссийской научно-практической конференции "Врожденная и наследственная патология головы, лица и шеи у детей: актуальные вопросы комплексного лечения", Москва (190-192). М.: [б. и.].
23. Arosarena, O., Ducic, Y., & Tollefson, T. T. (2012). Mandible fractures: discussion and debate. *Facial. Plast. Surg.Clin. North. Am.,* 20 (3), 347-363. DOI: https://doi.org/10.1016/j.fsc.2012.05.001.
24. Avenell, A., Mak, J. C., & O'Connell, D. (2014). Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men. *Cochrane Database Syst. Rev.,* 14 (4), CD000227. https://doi.org/10.1002/14651858.CD000227.pub4.
25. Bauer, D. C. (2013). Clinical practice. Calcium supplements and fracture prevention. *N. Engl. J. Med.*, 369, 1537-1543. DOI: 10.1056/NEJMcp1210380.
26. Caplan, A. I., & Correa, D. (2011). PDGF in bone formation and regeneration: New insights into a novel mechanism involving MSCs. *J. Orthop. Res.*, 29, 1795-1803. https://doi.org/10.1002/jor.21462.
27. Claes, L., Recknagel, S., & Ignatius, A. (2012). Fracture healing under healthy and inflammatory conditions. *Nat. Rev. Rheumatol.,* 8, 133-143. https://doi.org/10.1038/nrrheum.2012.1.
28. Dillon, J. K., Christensen, B., McDonald, T., Huang, S., Gauger, P., & Gomez, P. (2012). The financial burden of mandibular trauma. *J. Oral. Maxillofac. Surg.*, 70 (9), 2124-2134. https://doi.org/10.1016/j.joms.2012.04.048.
29. Feng, J., Liu, S., Ma, S., Zhao, J., Zhang, W., Qi, W., … Lei, W. (2014). Protective effects of resveratrol on postmenopausal osteoporosis: regulation of SIRT1-NF-?B signaling pathway. *Acta Biochim Biophys Sin* (Shanghai), 46 (12), 1024-1033. https://doi.org/10.1093/abbs/gmu103.
30. Garcia, P., Histing, T., Holstein, J. H., Klein, M., Laschke, M. W., Matthys, R., … Menger, M. D. (2013). Rodent animal models of delayed bone healing and non-union formation: A comprehensive review. *European Cells and Materials*, 26, 1-14.
31. Goldhahn, I., Little, D., Mitchell, P., Fazzalari, N. L., Reid, I. R., Aspenberg, P., & Marsh, D. (2010). Evidence for anti-osteoporosis therapy in acute fracture situations - recommendations of a multidisciplinary workshop of the International Society for Fracture Repaire. *Bone,* 46 (2), 267-271. https://doi.org/10.1016/j.bone.2009.10.004.
32. Govindarajan, P., Bocker, W., El Khassawna, T., Kampschulte, M., Schlewitz, G., Huerter, B., … Heiss, C. (2014). Bone matrix, cellularity, and structural changes in a rat model with high turnover osteoporosis induced by combined ovariectomy and a multiple-deficient diet. *Am. J. Pathol.,* 184 (3), 765-777. https://doi.org/10.1016/j.ajpath.2013.11.011.
33. Han, N. R., Park, C. L., Kim, N. R., Kim, H. Y., Yoou, M. S., Nam, S. Y., … Kim, H. M. (2015). Protective effect of porcine placenta in a menopausal ovariectomized mouse. *Reproduction,* 150 (3), 173-181. DOI: 10.1530/REP-15-0157.
34. Hong, J. W., Lee, W. J., Hahn, S. B., Kim, B. J., & Lew, D. H. (2010). The effect of human placenta extract in a wound healing model. Ann. Plast. Surg., 65 (1), 96-100. DOI: 10.1097/SAP.0b013e3181b0bb67.
35. Ibrahim, N., Mohamad, S., Mohamed, N., & Shuid, A. N. (2013). Experimental fracture protocols in assessments of potential agents for osteoporotic fracture healing using rodent models. *Curr. Drug. Targets,* 14, 1642-1650.
36. Kanis, J. A., Cooper, C., Rizzoli, R., Abrahamsen, B., Al-Daghri, N. M., Brandi, M. L., … & Thomas, J.-Y. T. (2017). Identification and management of patients at increased risk of osteoporotic fracture: outcomes of an ESCEO expert consensus meeting. *Osteoporos Int.,* 28 (7), 2023-2034. https://doi.org/10.1007/s00198-017-4009-0.
37. Li, Y., Tan, Y., Zhang, G., Yang, B., & Zhang, J. (2009). Effects of calcitonin Gene-Related Peptide on the expression and activity of Nitric Oxide Synthase during mandibular bone healing in rabbits: An Experimental study. *J. Oral MaxIIIofac Surg.*, 67, 273-279. https://doi.org/10.1016/j.joms.2008.06.077.
38. Marini, F., Cianferotti, L., & Brandi, M. L. (2016). Epigenetic Mechanisms in Bone Biology and Osteoporosis: Can They Drive Therapeutic Choices? *Int. J. Mol. Sci.,* 17 (8), 13-29. https://doi.org/10.3390/ijms17081329.
39. Naveen Shankar, A., Naveen Shankar, V., Hegde, N., & Sharma, P. R. (2012). The pattern of the maxillofacial fractures - A multicentre retrospective study. *J. Craniomaxillofac Surg.*, 40 (8), 675-679. https://doi.org/10.1016/j.jcms.2011.11.004.
40. Robbins, J. A., Aragaki, A., Crandall, C. J., Manson, J. E., Carbone, L., Jackson, R., … & Wactawski-Wende, J. (2014). Women's Health Initiative clinical trials: interaction of calcium and vitamin D with hormone therapy. *Menopause,* 21, 116-123. https://doi.org/10.18370/2309-4117.2015.26.94-101.
41. Roux, C., Bischoff-Ferrari, H. A., Papapoulos, S. E., de Papp, A. E., West, J. A., & Bouillon, R. (2008). New insights into the role of vitamin D and calcium in osteoporosis management: an expert roundtable discussion. *Curr. Med. Res. Opin.*, 24 (5), 1363-1370. https://doi.org/10.1185/030079908X301857.
42. Taylor, C. L., Sempos, C. T., Davis, C. D., & Brannon, P. M. (2017). Vitamin D: Moving Forward to Address Emerging Science. *Nutrients*, 9 (12), 130-138. https://doi.org/10.3390/nu9121308.
43. Tu, K. N., Lie, J. D., Wan, C. K. V., Cameron, M., Austel, A. G., Nguyen, J. K., … Hyun, D. (2018). Osteoporosis: A Review of Treatment Options. *PMC,* 43 (2), 92-104.
44. Zhao, J. G., Zeng, X. T., Wang, J., & Liu, L. (2017). Association Between Calcium or Vitamin D Supplementation and Fracture Incidence in Community-Dwelling Older Adults: A Systematic Review and Meta-analysis. *JAMA,* 318 (24), 2466-2482. DOI:10.1001/jama.2017.19344.
45. Zhou, H. H., Liu, Q., Cheng, G., & Li, Z. B. (2013). Aetiology, pattern and treatment of mandibular condylar fractures in 549 patients: a 22-year retrospective study. *J. Craniomaxillofac. Surg.,* 41 (1), 34-41. https://doi.org/10.1016/j.jcms.2012.05.007.

References

1. Afanas'ev, V. V. (2010). *Travmatologija cheljustno-licevoj oblasti [Maxillofacial traumatology].* M.: Izd. "GJeOTAR -

Media".
2. Barsukova, K. V., & Gorshkova, O. M. (2013). Gistohimicheskaja ocenka processa regeneracii kostnoj tkani pri ispol'zovanii preparata "Tizol'" [Histochemical evaluation of bone tissue regeneration using the "Tizol" drug]. *Zhurnal anatomii i gistopatologii - Journal of Anatomy and Histopathology*, 2 (3), 58-60.
3. Berezka, N. I., Litovchenko, V. A., Ivanov, A. N., & Garjachij, E. V. (2011). Optimizacija reparativnogo osteogeneza pri disregeneracii kostnoj tkani [Optimization of reparative osteogenesis in bone dysregulation]. Nauchnye vedomosti Belgorodskogo gosudarstvennogo universiteta. Serija: Medicina. Farmacija - *Scientific reports of Belgorod State University. Series: Medicine. Pharmacy,* 20 (141), 46-50.
4. Bragina, V. G., & Gorbatova, L. N. (2014). Travma cheljustno-licevoj oblasti u detej [Maxillofacial injury in children]. J*ekologija cheloveka - Human ecology,* 2, 20-24.
5. Vares, Ya. E., Filipskyi, A. V., & Filipska, T. A. (2011). Travmatohenez i struktura perelomiv nyzhnoi shchelepy [Traumatogenesis and structure of mandibular fractures]. *Praktychna medytsyna - Practical medicine,* 17 (5), 9-14.
6. Guljuk, A. G., & Zhelnin, E. V. (2013). Vzaimosvjaz' markerov osteogeneza i processov posttravmaticheskoj regeneracii al'veoljarnoj kosti u krys [The relationship between osteogenesis markers and posttraumatic regeneration processes in rat alveolar bone]. *Fundamental'nye issledovanija - Basic research,* 7, 534-539.
7. Guljuk, A. G., Tashhjan, A. Je., & Guljuk, L. N. (2012). Profilaktika oslozhnenij konsolidacii pri perelomah nizhnej cheljusti u bol'nyh so strukturno-metabolicheskimi izmenenijami kostnoj tkani [Prevention of complications of consolidation in fractures of the lower jaw in patients with structural and metabolic changes in bone tissue]. *Visnyk stomatolohii - Bulletin of dentistry,* 2, 65-71.
8. Deev, R. V., Bozo, I. Ja., Drobyshev, A. Ju., & Isaev, A. A. (2013). Jeffektivnost' gen-aktivirovannogo osteoplasticheskogo materiala s plazmidnymi DNK, soderzhashhimi gen VEGF, v zameshhenii kostnyh defektov [The effectiveness of gene-activated osteoplastic material with plasmid DNA containing the VEGF gene, in the replacement of bone defects]. *Probl. kriobiologii i kriomediciny - Problems of cryobiology and cryomedicine*, 23 (3), 355-358.
9. Zhelnin, E. V. (2012). Morfologicheskie osobennosti posttravmaticheskoj regeneracii al'veoljarnoj kosti v jeksperimente [Morphological features of post-traumatic regeneration of the alveolar bone in the experiment]. *Ukrainskyi morfolohichnyi almanakh - Ukrainian morphological almanac,* 10 (3), 35-38.
10. Zhelnin, E. V. (2013). Biohimicheskie kriterii prognozirovanija posttravmaticheskoj regeneracii al'veoljarnoj kosti v jeksperimente [Biochemical criteria for predicting post-traumatic regeneration of alveolar bone in an experiment]. *Fundamental'nye issledovanija - Basic research,* 9-6, 1006-1010.
11. Korzh, N. A., Deduh, N. V., & Nikol'chenko, O. A. (2006). Reparativnaja regeneracija kosti: sovremennyj vzgljad na problemu. Sistemnye faktory, vlijajushhie na zazhivlenie pereloma (soobshhenie 3) [Reparative bone regeneration: a modern view of the problem. Systemic factors affecting fracture healing (message 3)]. *Ortopedija, travmatologija i protezirovanie - Orthopedics, traumatology and prosthetics,* 2, 93-99.
12. Korotkih, N. G., Lesnikova, I. N., & Barsukova, K. V. (2013). Morfologicheskie kriterii regeneracii kosti nizhnej cheljusti u krolikov pri ispol'zovanii v terapii preparata "Tizol'" [Morphological criteria for lower jaw bone regeneration in rabbits when using the "Tizol" drug in therapy]. *Vestnik novyh medicinskih tehnologij.* Jelektronnoe izdanie - Bulletin of new medical technologies. Electronic edition, 1, 60.
13. Kotel'nikov, G. P., Kolsanov, A. V., Shherbovskih, A. E., Nikolaenko, A. N., Prihod'ko, S. A., Popov, N. V., & Hassan, M. A. (2017). Rekonstrukcija posttravmaticheskih i postoperacionnyh defektov nizhnej cheljusti [Reconstruction of post-traumatic and postoperative defects of the lower jaw]. *Hirurgija - Surgery,* 7, 69-72. DOI: 10.17116/hirurgia2017769-72.
14. Majborodin, I. V., Kolesnikov, I. S., Shevela, A. I., Sheplev, B. V., Drovosekov, M. N., & Toder, M. S. (2011). Vlijanie fibrinovogo sgustka pri povrezhdenii kosti nizhnej cheljusti v jeksperimente [The effect of a fibrin clot in case of damage to the lower jaw bone in the experiment]. *Stomatologija - Stomatology,* 4, 9-12.
15. Majborodin, I. V., Matveeva, V. A., Kolesnikov, I. S., Drovosekov, M. N., Toder, M. S., & Shevela, A. I. (2012). Vlijanie autologichnyh mezenhimal'nyh stvolovyh kletok kostnomozgovogo proishozhdenija na regeneraciju povrezhdennoj kosti nizhnej cheljusti krys [The effect of autologous mesenchymal stem cells of bone marrow origin on the regeneration of damaged bone of the lower jaw of rats]. *Stomatologija - Stomatology*, 1, 5-8.
16. Majborodin, I. V., Matveeva, V. A., Shevela, A. I., Sheplev, B. V., Kolesnikov, I. S., Vybornov, M. S., … & Shevela, A. A. (2010). Primenenie biodegradiruemyh poligidroksialkanoatov posle povrezhdenija kosti nizhnej cheljusti v jeksperimente [The use of biodegradable polyhydroxyalkanoates after damage to the lower jaw bone in the experiment]. *Klinicheskaja stomatologija - Clinical Stomatology,* 4, 54-57.
17. Oskol'skij, G. I., & Jurkevich, A. V. (2013). *Cheljustno-licevaja ortopedija. Uchebnoe pocobie [Maxillofacial orthopedics. Tutorial].* Habarovsk: GBOU VPO DVGMU.
18. Saharov, A. V. (2011). Sravnitel'noe issledovanie reparativnoj regeneracii kostnoj tkani pri ispol'zovanii tkaneinzhenernoj matricy na osnove materiala "TIOPROST" i materiala "KOLLAPAN-M" [Comparative study of reparative regeneration of bone tissue using a tissue-engineering matrix based on the material "TIOPROST" and the material "KOLLAPAN-M"]. *Geny i kletki - Genes and cells*, 6 (4), 89-94.
19. Trifonov, B. V. (2013). Regeneracija kostnoj tkani pri zapolnenii ee defekta kompozitom "titanovoe volokno - kostnoplasticheskij material" [Bone tissue regeneration when filling its defect with a composite "titanium fiber - osteoplastic material"]. *Kompozity i nanostruktury - Composites and Nanostructures*, 2 (18), 59-64.
20. Fareniuk, O. O. (2014). Rozrobka metodyky indyvidualnoho pidboru varianta likuvannia patsiientiv iz perelomamy nyzhnoi shchelepy [Development of a method for individual selection of treatment options for patients with mandibular fractures]. *Ukrainskyi stomatolohichnyi almanakh - Ukrainian dental almanac,* 1, 51-62.
21. Chernichenko, A. A. (2008). Reparativnaja regeneracija kostnoj tkani nizhnej cheljusti pri ispol'zovanii titanovogo implantata v jeksperimente [Reparative regeneration of bone tissue of the lower jaw using a titanium implant in an experiment]. *Sibirskoe medicinskoe obozrenie - Siberian Medical Review,* 49 (1), 29-33.
22. Chernjaev, S. E., & Kiseleva, E. V. (2009). *Vozmozhnosti ispol'zovanija stvolovyh kletok u detej s patologiej cheljustno-licevoj oblasti [Possibilities of using stem cells in children with maxillofacial pathology].* Tezisy predstavleny v materialah III Vserossijskoj nauchno-prakticheskoj konferencii "Vrozhdennaja i nasledstvennaja patologija golovy, lica i shei u detej: aktual'nye voprosy kompleksnogo lechenija", Moskva (str. 190-192). M.: [b. i.].
23. Arosarena, O., Ducic, Y., & Tollefson, T. T. (2012). Mandible

fractures: discussion and debate. *Facial. Plast. Surg.Clin. North. Am.,* 20 (3), 347-363. DOI: https://doi.org/10.1016/j.fsc.2012.05.001.
24. Avenell, A., Mak, J. C., & O'Connell, D. (2014). Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men. *Cochrane Database Syst. Rev.,* 14 (4), CD000227. https://doi.org/10.1002/14651858.CD000227.pub4.
25. Bauer, D. C. (2013). Clinical practice. Calcium supplements and fracture prevention. *N. Engl. J. Med.*, 369, 1537-1543. DOI: 10.1056/NEJMcp1210380.
26. Caplan, A. I., & Correa, D. (2011). PDGF in bone formation and regeneration: New insights into a novel mechanism involving MSCs. *J. Orthop. Res.*, 29, 1795-1803. https://doi.org/10.1002/jor.21462.
27. Claes, L., Recknagel, S., & Ignatius, A. (2012). Fracture healing under healthy and inflammatory conditions. *Nat. Rev. Rheumatol.,* 8, 133-143. https://doi.org/10.1038/nrrheum.2012.1.
28. Dillon, J. K., Christensen, B., McDonald, T., Huang, S., Gauger, P., & Gomez, P. (2012). The financial burden of mandibular trauma. *J. Oral. Maxillofac. Surg.*, 70 (9), 2124-2134. https://doi.org/10.1016/j.joms.2012.04.048.
29. Feng, J., Liu, S., Ma, S., Zhao, J., Zhang, W., Qi, W., … Lei, W. (2014). Protective effects of resveratrol on postmenopausal osteoporosis: regulation of SIRT1-NF-?B signaling pathway. *Acta Biochim Biophys Sin* (Shanghai), 46 (12), 1024-1033. https://doi.org/10.1093/abbs/gmu103.
30. Garcia, P., Histing, T., Holstein, J. H., Klein, M., Laschke, M. W., Matthys, R., … Menger, M. D. (2013). Rodent animal models of delayed bone healing and non-union formation: A comprehensive review. *European Cells and Materials*, 26, 1-14.
31. Goldhahn, I., Little, D., Mitchell, P., Fazzalari, N. L., Reid, I. R., Aspenberg, P., & Marsh, D. (2010). Evidence for anti-osteoporosis therapy in acute fracture situations - recommendations of a multidisciplinary workshop of the International Society for Fracture Repaire. *Bone,* 46 (2), 267-271. https://doi.org/10.1016/j.bone.2009.10.004.
32. Govindarajan, P., Bocker, W., El Khassawna, T., Kampschulte, M., Schlewitz, G., Huerter, B., … Heiss, C. (2014). Bone matrix, cellularity, and structural changes in a rat model with high turnover osteoporosis induced by combined ovariectomy and a multiple-deficient diet. *Am. J. Pathol.,* 184 (3), 765-777. https://doi.org/10.1016/j.ajpath.2013.11.011.
33. Han, N. R., Park, C. L., Kim, N. R., Kim, H. Y., Yoou, M. S., Nam, S. Y., … Kim, H. M. (2015). Protective effect of porcine placenta in a menopausal ovariectomized mouse. *Reproduction,* 150 (3), 173-181. DOI: 10.1530/REP-15-0157.
34. Hong, J. W., Lee, W. J., Hahn, S. B., Kim, B. J., & Lew, D. H. (2010). The effect of human placenta extract in a wound healing model. Ann. Plast. Surg., 65 (1), 96-100. DOI: 10.1097/SAP.0b013e3181b0bb67.
35. Ibrahim, N., Mohamad, S., Mohamed, N., & Shuid, A. N. (2013). Experimental fracture protocols in assessments of potential agents for osteoporotic fracture healing using rodent models. *Curr. Drug. Targets,* 14, 1642-1650.
36. Kanis, J. A., Cooper, C., Rizzoli, R., Abrahamsen, B., Al-Daghri, N. M., Brandi, M. L., … & Thomas, J.-Y. T. (2017). Identification and management of patients at increased risk of osteoporotic fracture: outcomes of an ESCEO expert consensus meeting. *Osteoporos Int.,* 28 (7), 2023-2034. https://doi.org/10.1007/s00198-017-4009-0.
37. Li, Y., Tan, Y., Zhang, G., Yang, B., & Zhang, J. (2009). Effects of calcitonin Gene-Related Peptide on the expression and activity of Nitric Oxide Synthase during mandibular bone healing in rabbits: An Experimental study. *J. Oral MaxIllofac Surg.*, 67, 273-279. https://doi.org/10.1016/j.joms.2008.06.077.
38. Marini, F., Cianferotti, L., & Brandi, M. L. (2016). Epigenetic Mechanisms in Bone Biology and Osteoporosis: Can They Drive Therapeutic Choices? *Int. J. Mol. Sci.,* 17 (8), 13-29. https://doi.org/10.3390/ijms17081329.
39. Naveen Shankar, A., Naveen Shankar, V., Hegde, N., & Sharma, P. R. (2012). The pattern of the maxillofacial fractures - A multicentre retrospective study. *J. Craniomaxillofac Surg.*, 40 (8), 675-679. https://doi.org/10.1016/j.jcms.2011.11.004.
40. Robbins, J. A., Aragaki, A., Crandall, C. J., Manson, J. E., Carbone, L., Jackson, R., … & Wactawski-Wende, J. (2014). Women's Health Initiative clinical trials: interaction of calcium and vitamin D with hormone therapy. *Menopause,* 21, 116-123. https://doi.org/10.18370/2309-4117.2015.26.94-101.
41. Roux, C., Bischoff-Ferrari, H. A., Papapoulos, S. E., de Papp, A. E., West, J. A., & Bouillon, R. (2008). New insights into the role of vitamin D and calcium in osteoporosis management: an expert roundtable discussion. *Curr. Med. Res. Opin.*, 24 (5), 1363-1370. https://doi.org/10.1185/030079908X301857.
42. Taylor, C. L., Sempos, C. T., Davis, C. D., & Brannon, P. M. (2017). Vitamin D: Moving Forward to Address Emerging Science. *Nutrients*, 9 (12), 130-138. https://doi.org/10.3390/nu9121308.
43. Tu, K. N., Lie, J. D., Wan, C. K. V., Cameron, M., Austel, A. G., Nguyen, J. K., … Hyun, D. (2018). Osteoporosis: A Review of Treatment Options. *PMC,* 43 (2), 92-104.
44. Zhao, J. G., Zeng, X. T., Wang, J., & Liu, L. (2017). Association Between Calcium or Vitamin D Supplementation and Fracture Incidence in Community-Dwelling Older Adults: A Systematic Review and Meta-analysis. *JAMA,* 318 (24), 2466-2482. DOI:10.1001/jama.2017.19344.
45. Zhou, H. H., Liu, Q., Cheng, G., & Li, Z. B. (2013). Aetiology, pattern and treatment of mandibular condylar fractures in 549 patients: a 22-year retrospective study. *J. Craniomaxillofac. Surg.,* 41 (1),

СУЧАСНІ УЯВЛЕННЯ ПРО ЕТІОПАТОГЕНЕЗ ТРАВМАТИЧНИХ УШКОДЖЕНЬ НИЖНЬОЇ ЩЕЛЕПИ НА ТЛІ ОСТЕОПОРОЗУ І ЗАСТОСУВАННЯ ПРЕПАРАТІВ ДЛЯ КОРЕКЦІЇ ПРОЦЕСІВ РЕПАРАТИВНОГО ОСТЕОГЕНЕЗУ

Ліхіцький О. О.

Анотація. *Мета роботи - провести аналіз сучасних поглядів на етіопатогенез травматичних ушкоджень нижньої щелепи на тлі остеопорозу і застосування препаратів для корекції процесів репаративного остеогенезу. Аналіз зроблено на основі огляду вітчизняних і зарубіжних статей та досліджень за 2006-2018 роки, користуючись наукометричними базами PubMed, eLIBRARY.RU, Web of Science. Ушкодження нижньої щелепи, а саме її переломи, є досить розповсюдженою патологією як в Україні, так і в інших країнах світу, що пов'язана з порушенням багатьох ключових функцій, зокрема, харчуванням і спілкуванням, а у випадку ускладнень - навіть порушенням естетичної функції. Одним з факторів, що підвищує вірогідність формування переломів є остеопороз - системне захворювання кісткової тканини, що характеризується зменшенням маси кістки в одиниці об'єму та порушенням її мікроархітектури. І якщо проблематика переломів нижньої щелепи є досить розкритою, то особливості формування переломів даної кістки на фоні захворювань, зокрема і на фоні остеопорозу, є недостатньо висвітленою темою як в українських, так і в іноземних джерелах. У даній статті представлені сучасні роботи щодо етіології і патогенезу травматичних ушкоджень нижньої щелепи на тлі остеопорозу та сучасних методів корекції процесів репаративного остеогенезу.*

Ключові слова: *репаративний остеогенез, ушкодження нижньої щелепи, остеопороз, етіологія та патогенез.*

СОВРЕМЕННЫЕ ПРЕДСТАВЛЕНИЯ О ЭТИОПАТОГЕНЕЗЕ ТРАВМАТИЧЕСКИХ ПОВРЕЖДЕНИЙ НИЖНЕЙ ЧЕЛЮСТИ НА ФОНЕ ОСТЕОПОРОЗА И ИСПОЛЬЗОВАНИЯ ПРЕПАРАТОВ ДЛЯ КОРРЕКЦИИ ПРОЦЕССОВ РЕПАРАТИВНОГО ОСТЕОГЕНЕЗА

Лихицкий А. А.

Аннотация. *Цель работы - провести анализ современных взглядов на этиопатогенез травматических повреждений нижней челюсти на фоне остеопороза и применения препаратов для коррекции процессов репаративного остеогенеза. Анализ сделан на основе обзора отечественных и зарубежных статей и исследований за 2006-2018 годы, пользуясь наукометрическими базами PubMed, eLIBRARY.RU, Web of Science. Повреждения нижней челюсти, а именно ее переломы, достаточно распространенная патология как в Украине, так и в других странах мира, и связана с нарушением многих ключевых функций, в частности, с питанием и общением, а в случае осложнений - даже с нарушением эстетической функции. Одним из факторов, повышающих вероятность формирования переломов, является остеопороз - системное заболевание костной ткани, характеризующееся уменьшением массы кости в единице объема и нарушением ее микроархитектуры. И если проблематика переломов нижней челюсти достаточно раскрыта, то особенности формирования переломов данной кости на фоне заболеваний, в том числе и на фоне остеопороза, недостаточно освещена как в украинских, так и в иностранных источниках. В данной статье представлены современные работы по этиологии и патогенезу травматических повреждений нижней челюсти на фоне остеопороза и современным методах коррекции процессов репаративного остеогенеза.*

Ключевые слова: *репаративный остеогенез, повреждения нижней челюсти, остеопороз, этиология и патогенез.*