Ivasivka Khrystyna. Dynamics of changes in the structural components of the mucosa and cartilage of the larynx of rats at the end of 42 days of experimental opioid exposure and after 56 days with opioid withdrawal. Journal of Education, Health and Sport. 2021;11(07): 201-218. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2021.11.07.019 https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2021.11.07.019 https://zenodo.org/record/5156375

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019. (a) The Authors 2021; This article is published with open access at License Open Journal Systems of Nicolaus Copernicus University in Torun, Poland Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article iscensed under the terms of the Creative Commons Attribution Non commercial use, distribution and reproduction in any medium, (http://creativecommons.org/license/by-necs/A/O/ which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited. The authors declare that there is no conflict of interests regarding the publication of this paper. Received: 25.06.2021. Revised: 12.07.2021. Accepted: 29.07.2021.

UDC: 611. 321 - 018.3/. 73: 615.214.24.035.8].08

Dynamics of changes in the structural components of the mucosa and cartilage of the larynx of rats at the end of 42 days of experimental opioid exposure and after 56 days with opioid withdrawal

Khrystyna Ivasivka

Danylo Halytsky Lviv National Medical University

Applicant of the Department of Normal Anatomy

https://orcid.org/0000-0003-4372-225x

Abstract

In our work we aimed to study the pathomorphological manifestations among the structural components of the laryngeal mucosa and cartilage in the later stages of the experimental opioid effect. This goal was achieved through the use of histological techniques to visualize the structural components of the laryngeal mucosa and cartilage. Histological sections with a thickness of 5 -7 mm were made. Histological specimens were prepared according to conventional methods using the dye hematoxylin, eosin, azan according to the method of Heidenhain, PAS-reaction according to Mc-Manus and Alcian blue according to Steedman. Microscopic examinations and photographing of the preparations were performed using an MBI-1 microscope and a Nicon D 3100 digital camera.

At the end of 42 days of experimental exposure, the epithelial layer of the epiglottis was inhomogeneously thickened, with excessive accumulation on its pharyngeal and apical part of the stratum corneum. Individual epitheliocytes of the pharyngeal part of the epiglottis underwent necrotic changes, the horny substance loosened in places. On the pharyngeal surface of the mucous membrane found a small amount of mucus with impurities of erythrocytes. Dyscirculatory processes were also registered in the animals of the experimental group. In particular, dilatation and overflow of erythrocytes of vessels of own plate of a mucous membrane of an epiglottis, and also polymorphonuclear infiltration of own plate of a mucous membrane were observed.

Key words: opioid; laryngeal mucosa; laryngeal cartilage; rat; early terms

Danylo Halytskyi Lviv National Medical University, Department of Normal Anatomy, Lviv, vul. Pekarska 69, tel. 8 (0322) 2368443. The results of the article correspond to the research plan of Lviv National Medical University named after Danylo Halytsky and are part of the research topic of the Department of Normal Anatomy "Morphofunctional features of organs in pre - and postnatal periods of ontogenesis, under the influence of opioids, supplements, reconstructive surgery and obesity "(state registration number 0120U002129) during 2020 - 2024.

Introduction. Opioid dependence has become a significant problem in the progression of pathopsychological changes in drug addicts, as well as the development of multiple multiorgan pathology, which together with great economic and moral damage make the problem of drug addiction one of the most important problems in many countries [1, 2]. In this regard, the study of pathomorphological, pathophysiological and pathochemical changes in the effects of drugs on the body is relevant [3, 4, 5, 6, 7, 8, 9].

The aim of the study. The aim of our study was to investigate the effect of opioid on changes in the structural components of the laryngeal mucosa and cartilage at the end of 42 days of experimental opioid exposure and 56 days after opioid withdrawal.

Object and methods of research. The material of the study were sexually mature, outbred male rats in the amount of 32 animals, weighing 92 g, aged 4.5 months. Animals were injected with nalbuphine intramuscularly once daily for 42 days (10-11 am) for 42 days. The dose of nalbuphine was 35 mg / kg during the week of the experimental study. Thus created the conditions for chronic opioid exposure [10, 11].

The animals were divided into 3 groups. 1st group of animals received nalbuphine for 42 days in one period of time (10 - 11 hours in the morning) followed by collection of study material (end of 42 days of experimental opioid exposure) 2nd group control, which for 42

days received injections of saline domyazevo in one period of time (10 - 11 o'clock in the morning); 3- a group of animals that were during the two-week withdrawal of opioids. The experiment was conducted in accordance with the principles of bioethics in accordance with the provisions of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes (Strasbourg, 1986), Council Directive 86/609 / EEC (1986), Law of Ukraine № 3447-IV " On the protection of animals from cruel treatment ", general ethical principles of animal experiments, approved by the First National Congress of Ukraine on Bioethics (2001), as confirmed by the conclusion of the commission on bioethics of Lviv National Medical University named after Danylo Halytsky (Minutes № 10 of December 15, 2019). Before sampling, the animals were removed from the experiment using diethyl ether. As a material for microstructural study used structural components of the mucosa and cartilage of the larynx of rats, taking into account the preservation of the topographic ratio of structures. Histological sections 5 - 7 µm thick were made. Histological specimens were prepared according to the conventional method using the dye hematoxylin, eosin, azan according to the method of Heidenhain, PAS reaction according to McManus and Alcian blue according to Steedman [12, 13, 14]. Microscopic examinations and photographing of the preparations were performed using an MBI-1 microscope and a Nicon D 3100 digital camera.

Research results and their discussion. As a result of the collection of experimental material after 42 days in rats exposed to an opioid analgesic at a dose of 35 mg / kg at the microstructural level, it was found that the structural changes were slightly less pronounced compared to animals of the previous experimental group. In particular, no significant hypersecretion of mucus by glands located at the base of the epiglottis was observed in experimental rats. The epithelial layer of the epiglottis was inhomogeneously thickened, with excessive accumulation on its pharyngeal and apical part of the stratum corneum. Individual epitheliocytes of the pharyngeal part of the epiglottis underwent necrotic changes, the horny substance loosened in places. On the pharyngeal surface of the mucous membrane was found a small amount of mucus with impurities of erythrocytes (fig. 1). Dyscirculatory processes were also registered in the animals of the experimental group. In particular, dilation and overflow of erythrocytes of vessels of the own plate of the mucous membrane of the epiglottis, as well as polymorphonuclear infiltration of the own plate of the mucous membrane were observed (fig. 1).



Fig. 1 Mucosa of the epiglottis at the end of the 42nd day of experimental opioid exposure. Ehrlich hematoxylin staining and eosin. Photomicrograph. Coll. x 200.

1– dilation and overflow of erythrocytes of vessels of own plate of a mucous membrane of an epiglottis; 2– polymorphonuclear infiltration of own plate of mucous membrane; 3– erythrocytes and a small amount of mucus on the surface of the mucous membrane of the pharyngeal part of the epiglottis.

Collagen fibers of the epiglottis own plate were inhomogeneously thickened (fig. 2). In some areas, the destruction and stratification of collagen fibers was noted (fig. 2).



Fig. 2 Own plate of the epiglottis at the end of the 42nd day of the experimental opioid effect. Coloring Azan by Heidenhain. Photomicrograph. Coll. x 200.

1- inhomogeneous thickening and focal destruction and stratification of collagen fibers of the epiglottis plate.

PAS-positive substances were localized in the own plate of the mucous membrane and on the apical surface of the epithelium of the epiglottis (fig. 3). A significant amount of PAS- positive substances accumulated in the main substance of the elastic cartilage of the epiglottis (fig. 3), in the cytoplasm of the epithelium of the terminal secretory glands located at the base of the epiglottis (fig. 4). Preserved chondrocytes were visualized in most lacunae of the epiglottis cartilage.



Fig. 3. The epiglottis at the end of the 42nd day of the experimental opioid effect. PAS staining is a MacManus reaction. Photomicrograph. Coll. x 200.

1- a significant amount of PAS-positive substances in the main substance of the elastic cartilage of the epiglottis; 2- PAS-positive substances in the own plate of the mucous membrane and on the apical surface of the epithelium of the epiglottis



Fig. 4 Secretory glands of the epiglottis at the end of the 42nd day of experimental opioid exposure. PAS staining is a MacManus reaction. Photomicrograph. Coll. x 200.

1- a significant amount of PAS-positive substances in the cytoplasm of the epithelium of the terminal secretory divisions of the glands located at the base of the epiglottis and in the main substance of the cartilaginous tissue of the epiglottis.

In comparison with the animals of the previous term of the experiment at the end of the 42-nd day, we did not observe the accumulation of acidic glycosaminoglycans in the main substance and collagen fibers of the epiglottis mucosa. In the matrix of elastic cartilage, the content of acidic glycosaminoglycans decreased (fig. 5, 6).



Fig. 5 Epiglottis at the end of the 42nd day of experimental opioid exposure. Coloring Alcian blue by Steedman. Photomicrograph. Coll. x 100.

1– decrease in the content of acidic glycosaminoglycans in the matrix of elastic cartilage of the epiglottis; 2– small filamentous inclusions of acidic glycosaminoglycans on the surface of the mucous membrane of the pharyngeal part of the epiglottis.



Fig. 6 Elastic cartilage of the epiglottis at the end of the 42nd day of the experimental opioid effect. Coloring Alcian blue by Steedman. Photomicrograph. Coll. x 200.

1– decrease in the content of acidic glycosaminoglycans in the matrix of elastic cartilage of the epiglottis; 2– fine-grained inclusions of acidic glycosaminoglycans on the surface of the laryngeal mucosa of the epiglottis.

Small filamentous inclusions of acidic glycosaminoglycans were found on the surface of the pharyngeal mucosa (Pic. 5), and fine-grained inclusions of acidic glycosaminoglycans were localized on the laryngeal part (fig. 6).

In the ventricles of the larynx noted dilation and overflow of blood vessels of the own plate of the mucous membrane, moderate polymorphonuclear infiltration (fig. 7, 8). Filamentous masses containing single lymphocytes accumulated on the surface of the mucous membrane (fig. 7). Primary lymphoid nodules were formed in the laryngeal ventricle plate itself (fig. 8).



Fig. 7 Own plate of the epiglottis mucosa at the end of the 42nd day of the experimental opioid effect. Ehrlich hematoxylin staining and eosin. Photomicrograph. Coll. x 100.

1– dilation and overflow of blood vessels of the laryngeal mucosa of the larynx; 2– polymorphonuclear infiltration of the own plate of the mucous membrane.

The stratification of collagen fibers of the laryngeal mucosa of the larynx was noted (Fig. 9). Individual collagen fibers were thickened, they accumulated PAS-positive substances. Excessive amounts of PAS-positive substances were also detected in the walls of hyperemic vessels of the laryngeal mucosa of the larynx (fig. 10).

In the matrix of thyroid cartilage there was a decrease in the content of acidic glycosaminoglycans. On the surface of the ventricular mucosa of the larynx localized single fine-grained inclusions of acidic glycosaminoglycans (fig. 11).



Fig. 8 Own plate of the laryngeal ventricular mucosa at the end of the 42nd day of the experimental opioid effect. Ehrlich hematoxylin staining and eosin. Photomicrograph. Coll. x 200.

1– polymorphonuclear infiltration of the laryngeal mucosa of the larynx; 2– lymphoid nodule in the own plate of the mucous membrane; 3– filamentous masses of mucus with single lymphocytes on the surface of the mucous membrane.



Fig. 9 Own plate of the laryngeal mucosa at the end of the 42nd day of the experimental opioid effect. Coloring Azan by Heidenhain. Photomicrograph. Coll. x 100.

1 – stratification of collagen fibers of own plate of a mucous membrane of a ventricle of a larynx; 2– thickening of individual collagen fibers; 3– polymorphonuclear infiltration of the laryngeal mucosa of the larynx; 4– lymphoid nodule in the own plate of the mucous membrane.



Fig. 10 Own plate of the laryngeal ventricular mucosa at the end of the 42nd day of the experimental opioid effect. Coloring Azan by Heidenhain. Photomicrograph. Coll. x 100.

1– a significant amount of PAS-positive substances in inhomogeneously thickened collagen fibers; 2– a significant amount of PAS-positive substances in the walls of hyperemic vessels of the laryngeal mucosa of the larynx.



Fig. 11 Elastic cartilage of the epiglottis and ventricle of the larynx at the end of the 42nd day of the experimental opioid effect. Coloring Alcian blue by Steedman. Photomicrograph. Coll. x 200.

1– decrease in the content of acidic glycosaminoglycans in the matrix of thyroid cartilage; 2– fine-grained single inclusions of acidic glycosaminoglycans on the surface of the laryngeal mucosa.

Significant polymorphonuclear infiltration of the lamina propria of the vocal folds, which was detected in animals of the previous experimental group, in animals at this time of the experiment was not detected. The vessels of the lamina propria of the vocal folds were

dilated, full of erythrocytes. Small accumulations of lymphocytes and macrophages were found in the main substance of the connective tissue.

Hyperemia of the vessels of the mucous membrane's own plate was also registered in the subchondral area. There were perivascular infiltrates, which were formed mainly by lymphocytes.

As a result of sampling of experimental material after 56 days in shurs who were during the two-week opioid withdrawal at the microstructural level, it was found that pronounced histological changes were recorded in the epithelium of the basal laryngeal surface of the epiglottis, as well as in vessels and the main substance of the gastric mucosa. In other areas of the larynx there was a decrease in the intensity of pathological changes that were found in animals of the experimental groups, which were administered daily, without withdrawal, nalbuphine.

On the surface of the epithelial layer of the mucous membrane of the pharyngeal part of the epiglottis observed a slight stratification of the horny substance (fig. 12).



Fig. 12 Pharyngeal surface of the epiglottis after 56 days of opioid exposure. Ehrlich hematoxylin staining and eosin. Photomicrograph. Coll. x 200.

1 - slight stratification of the horny substance on the surface of the epithelium of the mucous membrane of the pharyngeal part of the epiglottis.

In the basal part of the laryngeal surface of the epiglottis epithelial layer was of heterogeneous thickness. There were necrotized epitheliocytes. Flat and irregular cubic epitheliocytes were quite common. Polymorphonuclear infiltration of the lamina propria and the epithelial layer of the mucous membrane of the basal part of the laryngeal surface of the epiglottis was noted (fig. 13). In addition to lymphocytes and macrophages, the infiltrate also contained single neutrophils and tissue basophils.



Fig. 13 The laryngeal surface of the epiglottis after 56 days of opioid exposure. Ehrlich hematoxylin staining and eosin. Photomicrograph. Coll. x 200.

1 - polymorphonuclear infiltration of its own plate; 2 - polymorphonuclear infiltration of the epithelial layer of the mucous membrane of the epiglottis in the basal part of the laryngeal surface.

Individual collagen fibers of the epiglottis's own plate were slightly thickened (fig. 14, 15). A significant amount of PAS-positive substances was localized in the matrix of elastic cartilage of the epiglottis (fig. 16). An inhomogeneous accumulation of PAS-positive substances in the form of fine-grained inclusions, single scales, and in some places elongated layers on the surface of the epithelium of the laryngeal part of the epiglottis was noted (fig. 17).



Fig. 14 Own plate of the epiglottis mucosa after 56 days of opioid exposure. Painting Azan by Heidenhain. Photomicrograph. Coll. x 100.

1 - a slight thickening of the collagen fibers of the lamina propria of the epiglottis.



Fig. 15 Own plate of the epiglottis mucosa after 56 days of opioid exposure. Painting Azan by Heidenhain. Photomicrograph. Coll. x 200.

1 - thickening of collagen fibers of the lamina propria of the epiglottis.



Fig. 16 Elastic cartilage of the epiglottis after 56 days of opioid exposure. PAS - reaction according to McManus. Photomicrograph. Coll. x 100.

1– a significant amount of PAS-positive substances in the main substance of the elastic cartilage of the epiglottis; 2– inhomogeneous accumulation of PAS-positive substances on the surface of the epithelium of the laryngeal part of the epiglottis.

The content of PAS-positive substances in the main substance of the epiglottis mucosa, in the thickened collagen fibers and under the basement membrane of the epithelium also increased slightly. The content of acidic glycosaminoglycans in the matrix of elastic cartilage of the epiglottis was moderate (fig. 18, 19).



Fig. 17 Elastic cartilage of the epiglottis after 56 days of opioid exposure. PAS - reaction according to McManus. Photomicrograph. Coll. x 100.

1– a significant amount of PAS-positive substances in the matrix of elastic cartilage of the epiglottis; 2– excessive amount of PAS-positive substances on the apical surface of the epithelium and in the own plate of the mucous membrane of the basal part of the epiglottis.



100 µm

Fig. 18 Elastic cartilage of the epiglottis after 56 days of opioid exposure. Painting Alcian blue by Steedman. Photomicrograph. Coll. x 200.

1-acid glycosaminoglycans in the matrix of elastic cartilage of the epiglottis.

Acidic glycosaminoglycans were also visualized in the cytoplasm of the secretory epithelium of the terminal glands located at the base of the epiglottis. Excessive content of acidic glycosaminoglycans was found in some thickened collagen fibers of the lamina propria of the epiglottis base. In the ventricles of the larynx recorded moderate hyperemia of the vessels of the lamina propria of the mucous membrane and polymorphonuclear infiltration of the main substance of the connective tissue (fig. 20).



Fig. 19 Elastic cartilage of the epiglottis and terminal parts of the secretory glands after 56 days of opioid exposure. Painting Alcian blue by Steedman. Photomicrograph. Coll. x 200.

1– acidic glycosaminoglycans in the matrix of elastic cartilage; 2– acidic glycosaminoglycans in the cytoplasm of the secretory epithelium of the terminal glands located at the base of the epiglottis; 3– excessive content of acidic glycosaminoglycans in the thickened collagen fibers of the lamina propria of the epiglottis base.



Fig. 20 Ventricular mucosa of the larynx after 56 days of opioid exposure. Ehrlich hematoxylin staining and eosin. Photomicrograph. Coll. x 200.

1– moderate hyperemia of vessels of own plate of a mucous membrane of a ventricle of a larynx; 2– polymorphonuclear infiltration of the own plate of the mucous membrane.

The epithelial layer of the laryngeal ventricles and vocal folds was mostly preserved. No layers of mucus and cellular infiltrates were found in the lumen of the ventricles and in the subchondral region on the surface of the mucous membrane. There was a slight thickening of the collagen fibers of the lamina propria of the laryngeal mucosa (fig. 21). The content of PAS-positive substances in the walls of hyperemic vessels slightly increased (fig. 22). Acidic glycosaminoglycans were found in the matrix of thyroid cartilage adjacent to the laryngeal ventricles.



Fig. 21 The mucous membrane of the ventricle of the larynx after 56 days of opioid exposure. Painting Azan by Heidenhain. Photomicrograph. Coll. x 200.

1- slight thickening of collagen fibers of the laryngeal mucosa of the larynx.



Fig. 22 The mucous membrane of the laryngeal ventricle after 56 days of opioid exposure. PAS - reaction according to McManus. Photomicrograph. Coll. x 100.

1– slight increase in the content of PAS-positive substances in the walls of hyperemic vessels; 2– slight increase in the content of PAS-positive substances in the main substance of the laryngeal mucosa of the larynx.

Single grains of acidic glycosaminoglycans were found in the thickened collagen fibers of the laryngeal ventricles' own plate (fig. 23)



Fig. 23 The laryngeal mucosa of the larynx after 56 days of opioid exposure. Painting Alcian blue by Steedman. Photomicrograph. Coll. x 200.

1– acidic glycosaminoglycans in the cartilage matrix of the laryngeal ventricle; 2– single grains of acidic glycosaminoglycans in thickened collagen fibers.

In the subchondral region, only moderate vascular hyperemia of the mucosal lamina propria and slight polymorphonuclear infiltration of the main connective tissue substance, mainly lymphocytes, macrophages and single tissue basophils, were registered.

Conclusions:

1. At the end of 42 days of experimental exposure, the epithelial layer of the epiglottis was inhomogeneously thickened, with excessive accumulation on its pharyngeal and apical part of the stratum corneum. Individual epitheliocytes of the pharyngeal part of the epiglottis underwent necrotic changes, the horny substance loosened in places. On the pharyngeal surface of the mucous membrane found a small amount of mucus with impurities of erythrocytes. Dyscirculatory processes were also registered in the animals of the experimental group. In particular, dilatation and overflow of erythrocytes of vessels of own plate of a mucous membrane of an epiglottis, and also polymorphonuclear infiltration of own plate of a mucous membrane were observed.

2. Animals that were at the microstructural level during the two-week opioid withdrawal found that pronounced histological changes were recorded in the epithelium of the basal part of the laryngeal surface of the epiglottis, as well as in the vessels and the main substance of the laryngeal mucosa. In other areas of the larynx there was a decrease in the

intensity of pathological changes that were found in animals of the experimental groups, which were administered daily, without withdrawal, nalbuphine.

References

1. Byelovyts'kyy O. V. Submikroskopichna morfolohiya mozku u vyhlyadi krystalichnoho alkoholyu, intoksykatsiya morfinom na eksperymenti / ov // Bilovyts'kyy Tavriys'kyy med. Biol. vestn. - 2010. - № 1. - S. 13-16.[in Russian]

2. EU Drugs Strategy (2005–2012), 15074/04, Council of the European Union, Brussels. — 2004.[in Engish]

3. Clausen T, Anchersen K, Waal H.Mortality prior to, during and after opioid maintenance treatment (OMT): a national prospective cross-registry study. Drug Alc. Dep. 2010. Vol. 94, № 1. P.151–157 [in English].

4. Akshat S, Ramachandran R, Rewari V. Morphine versus Nalbuphine for open
gynaecological surgery: a randomized controlled double blinded trial [Електронний
pecypc]Pain Res. Treat. 2014. Режим доступу:
http://www.hindawi.com/journals/prt/2014/727952/.[in English].

5. Narver HL. Nalbuphine, a non-controlled opioid analgesic, and its potential use in research mice. Lab. An. 2015. Vol. 44, № 3. P. 106–110.

6. Copeland L, Robertson J, McKenzie J. [et al.]Premature mortality in Scottish injecting drug users: a life-history approach. Scott. Med. J. 2012. Vol. 57. P. 59-65. [in English].

7. Deering D, Sellman JD, Adamson S. Opioid substitution treatment in New Zealand: a 40 year perspective. N Z Med J Online.2014;127(1397):57–66. [in English].

8. Schnabel A, Reichl SU, Zahn PK. Nalbuphine for postoperative pain treatment in children [Електронний ресурс]. Cochr. Lib. 2014. Режим доступу:http://onlinelibrary.wiley.com/doi/10.1002/ 14651858.CD009583.pub2/full. [in English].

9. Tabachnikov SI, Viyevs'kyyAM, Zhdanova MP. Klinichni osoblyvosti ta providni chynnyky vzhyvannya psykhoaktyvnykh rechovyn u ditey ta pidlitkiv u svitli rozrobky kompleksnoyi bahatorivnevoyi systemy yoho medyko-sotsial'noyi korektsiyi ta profilaktyky Ukrayins'kyy zhurnal klinichnoyi ta laboratornoyi medytsyny. 2012. T. 7, № 1. S.4–10. [in Ukrainian].

217

10. Onys'ko RM., Onys'ko IO. Mikrostrukturna orhanizatsiya tkanyn yazyka na 28 dobu pislya vidminy opioyida. Novyny stomatolohiyi.-2013.-№3 (76).-S.101-106. [in Ukrainian].

11. Yakymiv N. YA. Ul'trastrukturna kharakterystyka struktur rayduzhnorohivkovoho kuta ochnoho yabluka shchuriv na 7-u, 14-u, 21-u, 28-u dobu opioyidnoho vplyvu / N. YA. Yakymiv // Ukrayins'kyy morfolohichny al'manakh. – 2014. – N_2 2. – S. 28– 31. [in Ukrainian].

12. Yakymiv N. YA. Morfolohycheskaya kharakterystyka struktur raduzhnorohovychnoho uhla krys na raznykh srokakh deystvyya y na rannykh srokakh posle otmeny éksperymental'noho opyoydnoho vlyyanyya / N. YA. Yakymyv // Oftal'molohyya. Vostochnaya Evropa. – 2014. – № 2. – S. 89–97. [in Russian].

13. Pal'tov E.V., Chelpanova I.V., Fik V.B., Vil'khova I.V., Kyryk KH.A., Kyryk KH.A., Kyryk KH.A., Kryvko YU.YA / Patomorfolohichni zminy u sharakh sitkivky cherez shist' tyzhniv opioyidnoho vplyvu v eksperymenti // Svit medytsyny ta biolohiyi. – \mathbb{N} 2 (60). – 2017. – S. 146 – 150. [in Ukrainian].

14. Pal'tov E.V., Kryvko YU.YA / Patomorfolohichni zminy u sharakh sitkivky cherez visim tyzhniv opioyidnoho vplyvu v eksperymenti // Visnyk problem biolohiyi i medytsyny. – 2017 - Vyp.4, tom 2 (140). – S. 118 – 122. [in Ukrainian].