UDC: 611.34:616.24-001

COMPARATIVE ASSESSMENT OF THE MORPHOLOGY OF THE SMALL INTESTINE IN EXPERIMENTAL PULMONARY FIBROSIS

Khasanova Dilnoza Akhrorovna – D.M.Sc, associate professor
Barnoev Ahtam Istamovich - independent researcher
Bukhara State Medical Istitute (Bukhara, Uzbekistan)

Abstract*. Study was conducted on 70 male rats. The dynamics of changes in morphometric parameters of the thickness of the mucous membrane of the small intestine is shown. Changes in morphometric parameters were observed in experimental pulmonary fibrosis of animals. Indicators of the mucous membrane of the duodenum and jejunum 12 increased on day 5 to the value of the control group after 30 days of the experiment. In the ileum, the indicators did not increase until the 5th day of the experiment.*
Keywords: *duodenum, jejunum, ileum, mucosa, pulmonary fibrosis.*

EKSPERIMENTAL O'PKA FIBROZIDA INGICHKA ICHAK MORFOLOGIYASINI QIYOSIY BAHOLASH

Xasanova Dilnoza Axrorovna - t.f.n., dotsent
Barnoyev Ahtam Istamovich - mustaqil tadqiqotchi
Buxoro Davlat Tibbiyot Instituti (Buxoro, O‘zbekiston)

Annotasiya. *70 ta yetilgan erkak kalamushlarda tadqiqot o'tkazildi. Ingichka ichak shilliq qavati qalinligining morfometrik ko'rsatkichlarining o'zgarish dinamikasi ko'rsatilgan. Tajribaviy o'pka fibrozida xayvonlar morfometrik ko'rsatkichlarida o'zgarishlarni chaqiradi. 12 barmoq va och ichak shilliq qavat ko'rsatkichlari 5 sutkada oshib tajribaning 30 sutkalarda asosiy guruhning qiymatigacha tiklandi. Yonbosh ichakda ko'rsatkichlar tajribaning 5 sutkasida u qadar oshmadi.*
Kalit so'zlar: *o'n ikki barmoq ichak, och ichak, yonbosh ichak, shilliq qavat, o'pka fibrozi.*

Introduction. Fibrosis is a widespread pathological process that affects almost every organ and has poor therapeutic efficacy. It leads to the terminal stage of organ failure and exacerbates dysfunction and is the main cause of mortality worldwide [2, 5, 11,13,17].

Currently, there are about 200 lung diseases with signs of interstitial, which is about 20% of all lung diseases, and half of them are of unclear etiology. Therefore, it is no longer possible to classify them as rare. The frequency of diagnostic errors in such patients is 75-80%, and adequate specialized care for them, as a rule, is provided much later than the appearance of the first signs of the disease, which significantly worsens the effectiveness of their treatment and prognosis. In this regard, an urgent task is the diagnosis of interstitial lung diseases (IBD) at early, still reversible stages. Considering the problem as a whole, it should be recognized that the diagnosis of IBD is among the most difficult tasks facing practical healthcare. To verify IBD, it is necessary to hold a consultation with the participation of clinicians, morphologists and radiologists [19].

Pulmonary fibrosis is a pathological process characterized by the replacement of normal lung tissue with fibrous (scar). As a result of such changes, serious disorders of the respiratory system occur. The development of fibrosis leads to a decrease in the volume of functioning lung tissue, resulting in reduced ventilation and respiratory efficiency. Manifestations of fibrosis in the gastrointestinal tract are associated with mucosal densification and impaired motility and include intestinal obstruction with meconium, constipation, distal intestinal obstruction syndrome, gastroesophageal reflux disease and excessive bacterial growth in the small intestine [16]. Pulmonary fibrosis (LF) is a chronic and life-threatening pulmonary interstitial disease that can be idiopathic or secondary to various lung diseases [3, 4, 6, 7, 8, 9, 10, 12, 14].

Violation of the intestinal barrier function is accompanied by numerous changes, including microcirculatory changes associated with damage to the endothelial lining of blood vessels, an imbalance between vasodilators and vasoconstrictors produced, activation of coagulation processes. As a result, hypoxic changes worsen, which is accompanied by the development of the so-called "vicious circle" [1, 18].

Pulmonary fibrosis is the final stage of a number of heterogeneous conditions and, to a greater or lesser extent, is a distinctive feature of interstitial lung diseases. It is characterized by excessive deposition of extracellular matrix proteins in the pulmonary interstitium, which leads to obliteration of functional alveolar units and in many cases to respiratory failure. Currently, the prevailing hypotheses are focused on the violation of the regulation of epithelial-mesenchymal interactions that contribute to the cycle of ongoing damage to epithelial cells and activa-

tion of fibroblasts, which leads to progressive fibrosis. Nevertheless, it is likely that multiple disorders in a variety of biological pathways affecting inflammation and wound healing, including matrix regulation, epithelial repair, coagulation cascade, neovascularization and antioxidant pathways, modulate these defective crosstalk and promote fibrogenesis [15].

Materials and methods of research. The study used 120 white randomized male rats, which were divided into three age groups, 7-, 8- and 9-month-old and control groups, respectively. In order to achieve modeling of lung fibrosis, white mongrel inbreeding rats were selected and an experimental model of "lung fibrosis with nitrogen dioxide, with animals inhaling poisonous gases in a closed box" was used. Before the start of the experiment, the animals underwent a two-week quarantine and got used to staying in the experimental chamber (requirements of the ethics committee and the commission for the control and use of laboratory animals in the BGMI).

The animals were divided into 2 groups (n=120): group I – control (n=60); group II – rats subjected to experimental pulmonary fibrosis for 90 days (n=60) from 7, 8 and 9 months of age.

Morphometric studies of the small intestine on experimental animals were carried out in the testing laboratories of the Bukhara State Medical Institute of the Ministry of Health of the Republic of Uzbekistan. on the basis of regulatory and methodological documents of the Republic of Uzbekistan, taking into account the requirements of the European Convention for the Protection of Vertebrate Animals Used for Experimental Research or for Other Scientific Purposes (ETS No. 123, Strasbourg, 1986), as well as the requirements of the National Guidelines for the Maintenance and Use of Laboratory Animals.

The slaughter of animals was carried out at the appropriate time in the morning, on an empty stomach by means of instant decapitation under ether anesthesia.

After opening the abdominal cavity, the small intestine was extracted. To conduct a morphological study, the mesentery of the small intestine was mobilized (along the planned line of intersection of the intestine), followed by its resection and dissection along the mesenteric edge along the entire length with micro-scissors. After that, the length of the mesenteric small intestine and the width of the small intestine in the initial, middle and final parts of the mesenteric small intestine were measured using a millimeter ruler. After washing the obtained total preparations of the small intestine in running water, they were stained with hematoxylin – H (Harris) and clarified with 3% acetic acid, followed by repeated washing of the preparations in distilled water.

Measurements were carried out: the thickness of the mucous membrane of the wall of the small intestine in rats. The pieces of tissue were fixed in a 10% solution of neutral formalin. After appropriate treatment, the material was poured into paraffin and sections 4-6 microns thick were prepared, which were stained with hematoxylin and eosin.

Mathematical processing of the material was carried out using standard methods of variational statistics: calculation of average values (M), errors of average values (m), Student's criterion (t). Differences were considered reliable at $p>0.05$. Comparison of these indicators with similar ones in the group of intact rats also showed that the reliability of the difference is not significant ($p>0.05$).

The results of the study. The thickness of the mucous membrane on day 1 was greater than the same indicator in the control group, but the reliability of the difference was not significant at $p>0.05$. On the 2nd day there is a significant increase in this indicator with a maximum value on the 5th day. Starting from day 7, the thickness of the mucous membrane decreases, this decrease was significant compared to the control group at $p>0.05$. Starting from the 10th to the 30th day, there is not a significant decrease in this indicator between the terms of the study at ($p> 0.05$). Comparison of mucosal thickness indicators between the control and experimental groups changed already from the 2nd to the 7th day of the study: the indicator increased with a maximum value on the 5th day of a similar indicator in the intact group, the reliability of the difference was significant at ($p>0.05$). On day 30, this indicator was still decreasing and was within the boundaries of the control group. Studying the morphometric parameters of the thickness of the ileum mucosa between the terms of the study, we identified the following changes: starting from the 1st to the 3rd day, the indicator increases slightly, and from 3 to 30 days it begins to decrease, while no significant difference between the terms was detected at $p > 0.05$. Comparing this indicator between groups of animals that were subjected to experimental pulmonary fibrosis and a group of control rats, we also revealed a significant difference throughout the study period at $p>0.05$. Thus, experimental pulmonary fibrosis causes changes in the metric parameters of the small intestine in rats.

Conclusions. Experimental pulmonary fibrosis causes changes in the morphometric parameters of the thickness of the mucous membrane of the wall of the small intestine (12-digit, skinny and iliac). Thus, the thickness of the mucous membrane in the duodenum and jejunum increased statistically significantly on day 5 with the restoration on day 30 of the experiment to the values of the control group. In the ileum, this indicator also increased on day 5, however, this increase is not statistically significant.

REFERENCES

1. Basil MC, Levy BD. Specialized pro-resolving mediators: endogenous regulators of infec-

tion and inflammation. Nat Rev Immunol. 2016;16(1):51–67.

2. Bettenworth, D., and Rieder, F. (2017). Pathogenesis of intestinal fibrosis in inflammatory bowel disease and perspectives for therapeutic implication. *Dig. Dis.* 35, 25–31.

3. Dalli J, Vlasakov I, Riley IR, et al. Maresin conjugates in tissue regeneration biosynthesis enzymes in human macrophages. Proc Natl Acad Sci U S A. 2016;113(43):12232–12237.

4. Datta A., Scotton C.J., Chambers R.C. Novel therapeutic approaches for pulmonary fibrosis // British Journal of Pharmacology. - 2011. - Vol. 163. -P. 141 - 172.

5. Di Ciaula, A., Baj, J., Garruti, G., Celano, G., De Angelis, M., Wang, H. H., et al. (2020). Liver steatosis, gut-liver axis, microbiome and environmental factors. A never-ending bidirectional cross-talk. *J. Clin. Med.* 9:2648.

6. Han J, Li H, Bhandari S, et al. Maresin conjugates in tissue regeneration 1 improves alveolar fluid clearance by up-regulating alveolar ENaC, Na, K-ATPase in lipopolysaccharide-induced acute lung injury. J Cell Mol Med. 2020;24(8):4736–4747.

7. Li H, Hao Y, Yang LL, et al. MCTR1 alleviates lipopolysaccharide-induced acute lung injury by protecting lung endothelial glycocalyx. J Cell Physiol. 2020;235(10):7283–7294.

8. Maher TM, Wuyts W. Management of fibrosing interstitial lung diseases. Adv Ther. 2019;36(7):1518–1531.

9. Meyer KC. Pulmonary fibrosis, part I: epidemiology, pathogenesis, and diagnosis. Expert Rev Respir Med. 2017;11(5):343–359.

10. Pan J, Li X, Wang X, Yang L, Chen H, Su N, Wu C, Hao Y , Jin S , Li H //MCTR1 Intervention Reverses Experimental Lung Fibrosis in Mice/Volume 2021:14 Pages 1873—1881

11. Richeldi L, Collard HR, Jones MG. Idiopathic pulmonary fibrosis. Lancet. 2017;389(10082):1941–1952.

12. Richeldi L, Collard HR, Jones MG. Idiopathic pulmonary fibrosis. Lancet. 2017;389(10082):1941–1952.

13. Rosenbloom, J., Macarak, E., Piera-Velazquez, S., and Jimenez, S. A. (2017). Human fibrotic diseases: current challenges in fibrosis research. *Methods Mol. Biol.* 1627, 1–23.

14. Sabharwal S. «Gastrointestinal Manifestations of Cystic Fibrosis» Gastroenterol Hepatol (N Y). 2016 Jan; 12(1): 43–47.

15. Serhan CN, Chiang N, Dalli J. The resolution code of acute inflammation: novel pro-resolving lipid mediators in resolution. Semin Immunol. 2015;27(3):200–215.

16. Wijsenbeek M, Cottin V. Spectrum of fibrotic lung diseases. N Engl J Med. 2020;383(10):958–968.

17. Winter DH, Manzini M, Salge JM, Busse A, Jaluul O, Jacob Filho W, Mathias W, Terra-Filho M. Aging of the lungs in asymptomatic lifelong nonsmokers: findings on HRCT. (2015) Lung. 193 (2): 283-290.

18. Yang Y, Zhu Y, Xiao J, et al. Maresin conjugates in tissue regeneration 1 prevents lipopolysaccharide-induced cardiac dysfunction through improvement of mitochondrial biogenesis and function. Biochem Pharmacol. 2020;177:11-40.

19. Казымова Д. В. «Интерстициальные болезни легких у детей: Клинико-лучевая характеристика» Самара 2015 г., С.79-83.

СРАВНИТЕЛЬНАЯ ОЦЕНКА МОРФОЛОГИИ ТОНКОЙ КИШКИ ПРИ ЭКСПЕРИМЕНТАЛЬНОМ ФИБРОЗЕ ЛЕГКИХ

Хасанова Дильноза Ахроровна - д.м.н., доцент
Барноев Ахтам Истамович - соискатель
Бухарский Государственный Медицинский Институт (Бухара, Узбекистан)

Аннотация*. Исследование было проведено на 70 крысах-самцах. Показана динамика изменения морфометрических показателей толщины слизистой оболочки тонкой кишки. При экспериментальном лёгочном фиброзе животных наблюдались изменения в морфометрических показателях. Показатели слизистой оболочки 12 перстной и тощей кишки увеличились на 5 сутки до значения контрольной группы через 30 дней эксперимента. В подвздошном кишечнике показатели не увеличивались до 5-го дня эксперимента.*

Ключевые слова: *12-перстная, тощая и подвздошная кишка, слизистая оболочка, фиброз лёгких.*