THE ROLE OF CONNECTIVE TISSUE BIOPOLYMERS IN THE PATHOGENESIS OF DOG BRONCHOPNEUMONIA AND CAT BROCHNIAL ASTHMA

Dmytro Morozenko, Roman Dotsenko, Yevheniia Vashchyk, Andriy Zakhariev, Seliukova Nataliia, Andrii Zemlianskyi, Kateryna Gliebova, Lidia-Mariia Kostyshyn

The aim: to analyze the pathogenetic role of connective tissue biopolymers in canine pneumonia and feline asthma.

Materials and methods. The study was conducted by analyzing the sources of scientific literature: PubMed, Elsevier, electronic resources of the National Library, named after V.I. Vernadsky and the results of our own scientific and clinical experience.

Results. Studies on the pathogenetic justification of the role of biochemical indicators of the connective tissue in the diagnosis and treatment of diseases of the respiratory system of dogs and cats were conducted. This is due to the need to expand knowledge about the peculiarities of the course, to determine the leading pathogenetic links of the most common pathologies – bronchopneumonia and bronchial asthma, which are found in clinical veterinary practice.

Conclusions. In bronchopneumonia of dogs on the background of severe clinical symptoms (cough, fever, wheezing in the lungs), radiological signs (inhomogeneous compaction of the lung tissue, lack of clear contours of the bronchi), anemic syndrome, general and neutrophilic leukocytosis, lymphocytopenia, hypoalbuminemia, dysproteinemia (increased concentration of α2- and β-globulins in the blood serum), hypercholesterolemia, hyper-β-lipoproteinemia, hyperfermentemia (increased activity of AST and alkaline phosphatase,) there is an increase in serum glycoproteins and chondroitin sulfates, sialic acids, total glycosaminoglycans (GAG) due to the chondroitin-4-sulfate fraction; urinary excretion of oxyproline and uronic acids increases. Disorders of connective tissue metabolism in dogs with bronchopneumonia are caused by an acute inflammatory process in the lungs with the development of pulmonary fibrosis. Bronchial asthma in cats is manifested by intermittent cough, shortness of breath, hypochromic normocytic anemia, leukocytosis, eosinophilia and lymphocytopenia, increased serum activity of AST and alkaline phosphatase, haptoglobin content, glial acid concentration sulfate; urinary excretion of oxyproline and uronic acids increases. Connective tissue disorders in cats with bronchial asthma are caused by increased mucus excretion with a high content of GAG, as well as chronic inflammation of the bronchial mucosa and their fibrosis.

Keywords: dogs, bronchopneumonia, cats, bronchial asthma, pathogenesis, connective tissue, glycoproteins, chondroitin sulfates, glycosaminoglycans, oxyproline, uronic acids


© The Author(s) 2022
This is an open access article under the Creative Commons CC BY license

1. Introduction
A wide range of pathological conditions, caused by connective tissue disorders, is determined by the complexity of its structure and variety of functions. Modern science considers connective tissue as a set of different types of tissues, united by a common origin and structure [1]. Studies of morphological, physiological and biochemical characteristics of the connective tissue in normal and pathology were conducted by such prominent scientists [2]. Over the past 20 years found out the general path of most human diseases, the basis of which is a violation of the integral role of the connective tissue. Combining the most severe diseases with a single connective tissue mechanism is the basis of a new connective tissue theory of biology and medicine. The treatment and prevention of diseases of the liver, kidneys, intestines, heart and other organs and systems should be carried out with a targeted effect on the connective tissue [3]. Most human diseases have been combined by medical scientists into an integrative disease – connective tissue insufficiency, the consequences of which accompany a person throughout life. According to the authors of this theory, the low efficiency of modern medicine is the lack of a single concept of many existing diseases, the main thing in the treatment of diseases – to take into account the variety of symptoms and syndromes and find common mechanisms of clinical manifestations of pathology in a particular patient. It is a well-known fact, that in any metabolic or inflammatory reaction, lysosomal hyaluronidase plays an important role, the activators of which are histamine and serotonin, and the inhibitor is heparin. Lysosomal hyaluronidase destroys the extracellular connc-
tive tissue matrix, and its integrative functions are lost. This matrix is represented by a system of protein-carbohydrate (glycoproteins) and carbohydrate-protein (proteoglycans) complexes [4].

Recently, in the diagnosis of internal diseases of animals, the concept of polymorbidity is increasingly used, in which several diseases have a simultaneous course, similar etiology, and the main – interdependent pathogenetic mechanisms [5, 6]. Indicators of the connective tissue – oxyproline, glycoproteins, glycosaminoglycans can increasingly be found in the literature among the diagnostic markers for internal human diseases [7, 8]. This trend, in our opinion, is associated with the growing interest of doctors of human medicine therapeutic profile to the pathogenetic and diagnostic role of glycoprotein, collagen and proteoglycan metabolism in diseases of the respiratory system – pneumonia [9], bronchial asthma [10, 11], chronic obstructive lung disease [12]. Thus, research on the pathogenetic justification of the role of biochemical indicators of the connective tissue in the diagnosis and treatment of respiratory diseases of dogs and cats is due to the need to expand knowledge about the course, to determine the leading pathogenetic links of the most common pathologies in clinical veterinary practice.

The aim of the research is to analyze the pathogenetic role of connective tissue biopolymers in canine pneumonia and feline asthma.

2. Materials and methods

The study was conducted by analyzing the sources of scientific literature: PubMed, Elsevier, electronic resources of the National Library of Ukraine named after V. I. Vernadsky and the results of our own scientific and clinical experience.

3. Research results

In bronchopneumonia in dogs, the clinical symptoms of the disease (depression, anorexia, fever, etc.) indicated the development of severe endogenous intoxication in animals due to the acute inflammatory process in the lungs. The results of radiography showed compaction of the lung tissue and the absence of clear contours of the bronchi, hematological examination revealed anemic syndrome, general and neutrophilic leukocytosis with a shift of the nucleus to the left and lymphocytopenia due to inflammation and immunodeficiency. It is obvious, that bronchopneumonia in dogs had a severe clinical course and was accompanied by a number of changes in hemocytopenia.

Biochemical changes in the serum of bronchopneumonia are manifested by hypoalbuminemia and an increase in the concentration of α1-globulins – acute phase proteins and β-globulins, which are chemically protein glycoproteins. The development of the inflammatory process in the lungs of dogs with bronchopneumonia can be determined by the content of glycoproteins in the serum, without conducting a full study of protein fractions. In dogs of some breeds (such as pugs and French bulldogs), bronchopneumonia often has a latent course with fever and depression in the absence of wheezing and coughing. For dogs of these breeds, determining the degree of inflammation by laboratory tests in combination with radiography is important in veterinary practice. Hypoxia and ischemia of organs and tissues with insufficient oxygenation cause impaired energy metabolism and endogenous intoxication, increased permeability of the capillaries of the pulmonary alveoli for histamine and serotonin. Hypercholesterolemia and hyper-β-lipoproteineemia may be associated with impaired alveolar surfactant properties in bronchopneumonia. At the same time, due to a severe inflammatory process in the lungs, the concentration of fibroblast proliferation increases, which causes a reorganization of the collagen structure and synthesizes an increased amount of proteoglycans, which leads to the development of pulmonary fibrosis. This was confirmed by an increase in the concentration of chondroitin sulfate in the blood due to chondroitin-4-sulfate, the content of which in the lungs of dogs may be higher compared to chondroitin-6-sulfate. Due to the re-arrangement of collagen fibers and inflammatory-destructive changes in the intercellular substance of the loose connective tissue of the lungs, there is an increase in the excretion of oxyproline and uronic acids (Fig. 1).

During treatment of dogs with bronchopneumonia, there was a decrease in anemic syndrome and inflammation in animals, which was reflected in a gradual increase in hemoglobin and erythrocytes, as well as a decrease in leukocytosis and neutrophilia. The decrease in biochemical parameters of the connective tissue in the blood and urine of patients with dog bronchopneumonia occurred only on the 21st day of treatment, which, in our opinion, is due to fibroplastic processes in the lungs with bronchopneumonia.

Features of the pathological process in the lungs of cats with bronchial asthma are determined by three main pathophysiological mechanisms: cellular infiltration of bronchioles (lymphocytic, eosinophilic), bronchial hyperplasia and mucus hypersecretion, bronchospasm and bronchial edema. These components of bronchitis in bronchial asthma develop after the initial contact with the allergen and sensitization of mast cells of the bronchial mucosa. A chronic inflammatory process develops in the lungs of sick animals, which is manifested by anemic syndrome, leukocytosis, lymphocytopenia, and eosinophilia due to eosinophilic infiltration of the walls of the bronchioles by the allergen.

The concentration of haptoglobin and other proteins of the acute phase (glycoproteins), as well as sialic acids in the blood serum increases. One of the important pathogenetic links in bronchial asthma in cats is a violation of glycosaminoglycan metabolism (GAG) – and the destruction of collagen structures in the own plate of the bronchial mucosa, which is manifested by increased excretion of oxyproline. At the same time, other biochemical indicators of blood serum practically do not change. There is only an increase in the activity of asparagine aminotransferase (AST) as a marker of myocardial dysfunction and alkaline phosphatase due to the destruction of a significant number of neutrophils in the lungs during prolonged inflammation.
Clinical symptoms in cats with bronchial asthma were manifested mainly during the onset of asthma attacks, so it can be argued, that the clinical symptoms cannot effectively control the condition of patients. Therefore, the content of glycoproteins and sialic acids in the serum and the level of excretion of oxyproline and uronic acids can be recommended as effective biochemical markers for diagnosing the activity of the inflammatory process in the lungs of cats with bronchial asthma (Fig. 2).

**Fig. 1.** Pathogenetic role of connective tissue metabolism disorders in bronchopneumonia in dogs:

↑ – growth of the indicator; ↓ – reduction of the indicator; ↔ – normal rate
In bronchial asthma, this can be explained by the chronic course of the disease, the clinical manifestation of which is only an exacerbation of the pathological process in the lungs. Therefore, in cats complete recovery from bronchial asthma after treatment does not occur, chronic inflammatory and destructive processes, which are reflected in increased biochemical parameters of the connective tissue, remain in the bronchial tree and alveoli. Thus, the goal of treatment for asthma in cats is to prevent exacerbation of the disease by constantly monitoring the health of patients.

**Research limitations.** The studies were analytical in nature and based on data from literature sources that characterize the pathogenetic mechanisms of development of canine bronchopneumonia and bronchial asthma in cats, as well as on the results of our own clinical experience.

**Prospects for further research.** A promising area of further research is to determine changes in biochemical markers in the treatment of canine bronchopneumonia and feline asthma.

**6. Conclusions**

In bronchopneumonia of dogs on the background of severe clinical symptoms (cough, fever, wheezing in the lungs), radiological signs (inhomogeneous compaction of the lung tissue, lack of clear contours of the bronchi), anemic syndrome, general and neutrophilic leukocytosis, lymphocytopenia, hypalbuminemia, dysproteinemias (increased concentration of α2- and β-globulins in the blood serum), hypercholesterolemia, hyper-β-lipoproteinemia, hyperfermentemia (increased activity of AST and alkaline phosphatase, ) there is an increase in se-
rum glycoproteins and chondroitin sulfates, sialic acids, total glycosaminoglycans (GAG) due to the chondroitin-4-sulfate fraction; urinary excretion of oxyproline and uronic acids increases. Disorders of connective tissue metabolism in dogs with bronchopneumonia are caused by an acute inflammatory process in the lungs with the development of pulmonary fibrosis.

Bronchial asthma in cats is manifested by intermittent cough, shortness of breath, hypochromic normocytic anemia, leukocytosis, eosinophilia and lymphocytopenia, increased serum activity of AST and alkaline phosphatase, haptoglobin content, glial acid concentration sulfate; urinary excretion of oxyproline and uronic acids increases. Connective tissue disorders in cats with bronchial asthma are caused by increased mucus excretion with a high content of GAG, as well as chronic inflammation of the bronchial mucosa and their fibrosis.

**Conflict of interests**
The authors declare that they have no conflicts of interest.

**Financing**
The study was performed without financial support.

**References**

Morozenko Dmytro*, Doctor of Veterinary Sciences, Senior Researcher, Head of Department, Department of Veterinary Medicine and Pharmacy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Roman Dotsenko, PhD, Senior Researcher, Associate Professor, Department of Veterinary Medicine and Pharmacy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Yevheniia Vashchyk, Doctor of Veterinary Sciences, Associate Professor, Department of Veterinary Medicine and Pharmacy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Andriy Zakhariev, PhD, Associate Professor, Department of Veterinary Medicine and Pharmacy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Andrii Zemlianskyi, PhD, Assistant, Department of Veterinary Medicine and Pharmacy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Nataliia Selukova, Doctor of Biological Sciences, Associate Professor, Department of Veterinary Medicine and Pharmacy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Kateryna Gliebova, PhD, Senior Researcher, Veterinary clinic “Terra-vet”, 23 Serpnia str., 59, Kharkiv, Ukraine, 61000

Lidia-Mariia Kostysyn, Assistant, Department of Surgery, S. Z. Gzyhetsy National University of Veterinary Medicine and Biootechnologies Lviv, Pekarska str., 50, Lviv, Ukraine, 79010

*Corresponding author: Morozenko Dmytro, e-mail: d.moroz.vet@gmail.com

Veterinary research