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Chronic Obstructive Pulmonary Disease: pathophysiology and the role of inflammation

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ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory condition characterized by persistent airflow limitation and a heightened lung inflammatory response. Systemic inflammation plays a crucial role in COPD pathogenesis, influencing disease progression and the development of comorbidities. This review explores the sequential stages of inflammation-driven pathological changes in COPD, from early airway alterations to advanced systemic effects. The disease process begins with chronic exposure to risk factors such as smoking, air pollution, and occupational hazards. This leads to increased mucus secretion and dysfunction of ciliated epithelial cells, which results in impaired mucociliary clearance and heightened susceptibility to infections. As inflammation persists, bronchial obstruction and airway remodeling occur, limiting airflow. Pulmonary hyperinflation and emphysema further exacerbate respiratory insufficiency by reducing elastic recoil and increasing the work of breathing. Future research should emphasize precision medicine approaches, biomarker identification, and novel anti-inflammatory therapies to mitigate disease progression and enhance patient outcomes.

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Surunkali obstruktiv o‘pka kasalligi: patofiziologiya va yallig‘lanishning roli

Kalit so‘zlar:
SOO‘K,
tizimli yallig‘lanish,
oksidlanish stressi,
nafas yo‘llarining obstruktsiyasi,
o‘pka gipertenziyasi,
yallig‘lanish mediatori.

ANNOTATSIYA

Surunkali obstruktiv o‘pka kasalligi (SOO‘K) — bu nafas olish tizimining yomonlashuvchi kasalligi bo‘lib, doimiy havo oqimining cheklanishi va o‘pka yallig‘lanishining kuchayishi bilan ajralib turadi. Tizimli yallig‘lanish SOO‘K patogenezida muhim rol o‘ynaydi, kasallikning rivojlanishi va hamroh kasalliklarning paydo bo‘lishiga ta’sir ko‘rsatadi. Ushbu sharhda SOO‘Kda yallig‘lanish tufayli yuzaga keladigan patologik o‘zgarishlarning ketma-ket bosqichlari, dastlabki nafas yo‘llari o‘zgarishlaridan tortib, rivojlangan tizimli ta’sirlargacha o‘rganiladi. Kasallik jarayoni uzoq muddatli xavf faktorlariga, masalan, chekish, havoning ifloslanishi va kasbiy xavflarga duchor bo‘lishdan boshlanadi. Bu shilliq qavatning sekretsiyasining oshishiga va manzarali epiteliya hujayralarining disfunktsiyasiga olib keladi, natijada mukotsilyar tozalashning buzilishi va infeksiyalarga nisbatan sezgirlikning oshishi kuzatiladi. Yallig‘lanish davom etgan sari, bronxial obstruktsiya va nafas yo‘llarining remodellashtirilishi yuzaga keladi, bu esa havo oqimini cheklaydi. O‘pkaning giperinflyatsiyasi va emfizema nafas olish yetishmovchiligini yanada kuchaytiradi, elastik tiklanishni kamaytiradi va nafas olish ishini oshiradi. Kelajakdagi tadqiqotlar aniq tibbiyot yondoshuvlari, biomarkerni aniqlash va yangi yallig‘lanishga qarshi davolash usullarini ishlab chiqishga e’tibor qaratishi kerak, bu kasallikning rivojlanishini sekinlashtirish va bemorlarning natijalarini yaxshilashga yordam beradi.

Хроническая обструктивная болезнь легких: патофизиология и роль воспаления

Ключевые слова:
ХОБЛ,
системное воспаление,
оксидативный стресс,
обструкция дыхательных путей,
легочная гипертензия,
воспалительные медиаторы.

АННОТАЦИЯ

Хроническая обструктивная болезнь легких (ХОБЛ) — прогрессирующее респираторное заболевание, характеризующееся стойким ограничением воздушного потока и усиленной воспалительной реакцией легких. Системное воспаление играет ключевую роль в патогенезе ХОБЛ, влияя на прогрессирование заболевания и развитие сопутствующих заболеваний. Этот обзор исследует последовательные этапы воспаления, приводящего к патологическим изменениям в ХОБЛ, от ранних изменений в дыхательных путях до поздних системных эффектов. Процесс заболевания начинается с хронического воздействия факторов риска, таких как курение, загрязнение воздуха и профессиональные опасности. Это приводит к увеличению секреции слизи и дисфункции реснитчатых эпителиальных клеток, что нарушает

мукоцилиарный клиренс и повышает восприимчивость к инфекциям. По мере продолжения воспаления возникает бронхиальная обструкция и ремоделирование дыхательных путей, что ограничивает воздушный поток. Пульмональная гиперинфляция и эмфизема усугубляют дыхательную недостаточность, снижая эластичность легких и увеличивая работу дыхания. Будущие исследования должны сосредоточиться на подходах точной медицины, идентификации биомаркеров и новых противовоспалительных терапиях для замедления прогрессирования заболевания и улучшения результатов лечения пациентов.

GOLD international research group members have extensively studied the prevalence of Chronic Obstructive Pulmonary Disease (COPD). The GOLD study covers 18 countries worldwide, aiming to identify risk factors and epidemiology of COPD. Currently, 12 out of 18 countries have completed data collection and analysis, and the results are published in The Lancet journal. According to this study, the prevalence of moderate-to-severe COPD (according to the international classification) is 10% (12% among men and 8.5% among women). Compared to previous studies, this figure has increased. The incidence of COPD rises with smoking and aging (doubling every 10 years). Notably, both smokers and non-smokers have an equal risk of developing COPD over 10 years [15]. Among patients over 45 years old, COPD ranks fourth among causes of death and continues to be a leading contributor to mortality, surpassing other diseases [21].

The primary risk factor for COPD development is smoking, accounting for 80-90% of cases. Mortality rates among smokers due to COPD remain high, with irreversible obstructive changes in respiratory function and increasing dyspnea. However, COPD also occurs and progresses among non-smokers [15]. Currently, a key diagnostic criterion for COPD and chronic non-obstructive bronchitis is long-term and persistent smoking [7, 13]. In recent years, passive smoking has received significant attention [19, 22]. Inflammatory response plays a central role in COPD pathogenesis. This reaction initially leads to reversible bronchial obstruction, later becoming irreversible, resulting in airflow limitation [12]. Inflammation develops throughout the respiratory tract and is influenced by pollutants in genetically susceptible individuals. Long-term and persistent smoking primarily affects the oral mucosa, transferring harmful substances through saliva to the bronchopulmonary system and lymphoid tissue [15]. Occupational exposure to cadmium and silicon dust has been identified as a significant risk factor for COPD development. High-risk professions include miners, railway workers, grain, cotton, paper processors, cement workers, and those in the metal industry. Mining occupations are particularly at risk. Notably, occupational exposure combined with smoking exacerbates COPD progression [15]. Genetic predisposition plays a significant role in COPD development, as evidenced by the fact that not all chronic smokers develop the disease. Currently, alpha-1 antitrypsin deficiency is the only well-studied genetic pathology leading to emphysema, chronic obstructive bronchitis, and bronchiectasis.

However, its role in COPD development is less significant compared to smoking. In the U.S., alpha-1 antitrypsin deficiency is found in less than 1% of COPD patients [15]. Smoking accelerates COPD onset. Dyspnea develops after 40 years of age in smokers,

whereas in non-smokers, it appears 13-15 years later [15]. The European Respiratory Society has classified COPD etiological risk factors based on their significance (Table 1) [15].

Table 1.

Classification of COPD risk factors

Risk Factor Probability	External Risk Factors	Internal Risk Factors
Established	Smoking; Occupational exposure (cadmium, silicon)	Alpha-1 antitrypsin deficiency
High	Air pollution (SO2, NO2, O3); Occupational exposure; Low socioeconomic status; Childhood passive smoking	Prematurity; Elevated IgE levels; Bronchial hyperreactivity; Family history of COPD
Probable	Adenoviral infection; Vitamin C deficiency	Genetic predisposition (Blood type I, IgA deficiency)

It is well known that bronchial hyperreactivity and elevated immunoglobulin E levels are observed in asthma patients. However, when these factors combine with smoking, they accelerate COPD progression [15]. Key processes in COPD pathogenesis include [15] Inflammation, Imbalance between proteases and antiproteases in the lungs, and Oxidative stress. Chronic inflammation affects the entire respiratory tract, lung parenchyma, and vasculature, leading to irreversible structural damage over time. Environmental and genetic factors disrupt enzyme balance and oxidative stress. COPD is characterized by increased macrophages, neutrophils, and CD8+ T-lymphocytes, particularly interleukin-8 (IL-8), tumor necrosis factor-alpha (TNF-α), and leukotriene B4 (LTB4), which contribute to lung tissue damage and neutrophilic inflammation [15].

In 1963, Laurell and Eriksson reported that individuals with alpha-1 antitrypsin deficiency risk developing emphysema due to uncontrolled neutrophil elastase activity. Today, the connection between alpha-1 antitrypsin deficiency and COPD is well established. Neutrophils, epithelial cells, and macrophages release various proteases, which suppress antiprotease activity in the presence of oxidative stress and tobacco smoke, worsening the protease-antiprotease imbalance in COPD pathogenesis [15]. Markers such as hydrogen peroxide (H2O2) and nitric oxide (NO) are elevated in COPD patients and smokers' urine, exhaled breath, and epithelial surface fluid. This confirms the role of oxidative stress in COPD. During disease exacerbations, hydrogen peroxide levels in exhaled air significantly increase, while nitric oxide levels also rise. F2α-III, an oxidative stress biomarker, is elevated in COPD patients' urine and exhaled air, reaching higher levels during exacerbations [15]. Oxidants degrade proteins, lipids, and nucleic acids, leading to cellular dysfunction and extracellular matrix destruction. Oxidative stress exacerbates protease-antiprotease imbalance, further accelerating lung damage. Additionally, it activates nuclear factor kappa-B (NF-kB), which increases inflammatory gene expression, including IL-8 and TNF-α. Oxidative stress can also induce bronchial obstruction: hydrogen peroxide contracts smooth muscle cells in vitro, while F2α-III causes pronounced bronchoconstriction [15]. It is well known that bronchial

hyperreactivity and elevated immunoglobulin E levels are observed in asthma patients. However, when these factors combine with smoking, they accelerate COPD progression [15]. Chronic inflammation affects the entire respiratory tract, lung parenchyma, and vasculature, leading to irreversible structural damage. Environmental and genetic factors disrupt enzyme balance and oxidative stress. COPD is characterized by increased macrophages, neutrophils, and CD8+ T-lymphocytes, particularly interleukin-8 (IL-8), tumor necrosis factor-alpha (TNF-α), and leukotriene B4 (LTB4), which contribute to lung tissue damage and neutrophilic inflammation [15]. In 1963, Laurell and Eriksson reported that individuals with alpha-1 antitrypsin deficiency risk developing emphysema due to uncontrolled neutrophil elastase activity. Today, the connection between alpha-1 antitrypsin deficiency and COPD is well established. Neutrophils, epithelial cells, and macrophages release various proteases, which suppress antiprotease activity in the presence of oxidative stress and tobacco smoke, worsening the protease-antiprotease imbalance in COPD pathogenesis [15]. Markers such as hydrogen peroxide (H2O2) and nitric oxide (NO) are elevated in COPD patients and smokers' urine, exhaled breath, and epithelial surface fluid. This confirms the role of oxidative stress in COPD. During disease exacerbations, hydrogen peroxide levels in exhaled air significantly increase, while nitric oxide levels also rise. F2α-III, an oxidative stress biomarker, is elevated in COPD patients' urine and exhaled air, reaching higher levels during exacerbations [15]. Oxidants degrade proteins, lipids, and nucleic acids, leading to cellular dysfunction and extracellular matrix destruction. Oxidative stress exacerbates protease-antiprotease imbalance, further accelerating lung damage. Additionally, it activates nuclear factor kappa-B (NF-kB), which increases inflammatory gene expression, including IL-8 and TNF-α. Oxidative stress can also induce bronchial obstruction: hydrogen peroxide contracts smooth muscle cells in vitro, while F2α-III causes pronounced bronchoconstriction [15].

Pathological changes in COPD include

Category	Key Features
Early Airway Alterations	Increased mucus secretion, Dysfunction of ciliated epithelial cells
Obstruction and Structural Changes	Bronchial obstruction, Airway narrowing
Lung Overinflation and Tissue Damage	Pulmonary hyperinflation, Emphysema development
Gas Exchange Impairment and Vascular Effects	Reduced oxygen diffusion, Hypercapnia (CO2 retention)
Pulmonary Hypertension and Systemic Inflammation	Increased vascular resistance, Cardiovascular complications

Immune dysregulation in COPD is significant, primarily characterized by increased neutrophils, macrophages, and CD8+ T-lymphocytes [18]. Key inflammatory mediators include IL-6, TNF-α, and IL-8, which are involved in immune responses and inflammation [8, 16]. Research shows elevated IL-6, IL-8, and IL-4 levels in COPD patients, while IL-10

levels decrease. This imbalance indicates that pro-inflammatory cytokines are crucial in COPD progression [2].

CONCLUSION

A literature review confirms that inflammation is a key driver of COPD pathogenesis. This chronic inflammatory response initially leads to reversible bronchial obstruction; however, persistent inflammation causes structural airway remodeling over time, resulting in irreversible airflow limitation. Various interleukins, including IL-6, IL-8, and IL-1β, contribute to these pathological changes by promoting mucus hypersecretion, epithelial dysfunction, and immune cell infiltration. These processes collectively exacerbate disease progression, leading to declining lung function and increased susceptibility to exacerbations.

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