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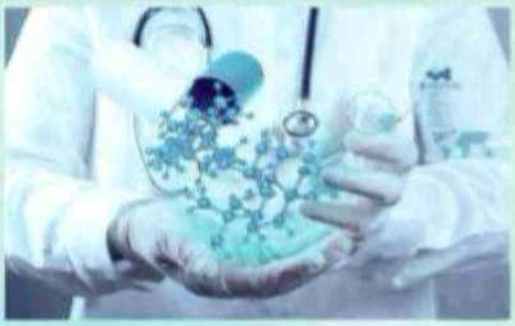

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ТИББИЁТДА ЯНГИ КУН

НОВЫЙ ДЕНЬ В МЕДИЦИНЕ

NEW DAY IN MEDICINE

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ОПТИМИЗАЦИЯ ПЕРСОНАЛИЗИРОВАННОГО ПОДХОДА К ДИАГНОСТИКЕ И ЛЕЧЕНИЮ БРОНХИАЛЬНОЙ АСТМЫ С УЧЁТОМ АДИПОКИНОВ И ИММУННЫХ БИОМАРКЕРОВ

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✓ ***Резюме***

В данной статье рассматриваются современные аспекты патогенеза, диагностики и терапии бронхиальной астмы (БА), с акцентом на оценку адипокинов (лептин, адипонектин) и иммунологических биомаркеров (IgE, ИЛ-4, ИЛ-5, ИЛ-13). Использованы данные научной литературы, клинических исследований, а также рекомендации GINA и национальные протоколы. Представлен анализ фенотипов БА, обсуждаются принципы пошаговой терапии, новые классы препаратов (анти-IgE, анти-ИЛ-5), подчёркивается значение метаболических и иммунных нарушений в формировании тяжёлых форм БА

Ключевые слова: бронхиальная астма, адипокины, лептин, адипонектин, иммунологические биомаркеры, цитокины, IgE, ИЛ-5, персонализированная медицина, терапия

IMPROVEMENT OF PERSONALIZED DIAGNOSIS AND THERAPY OF BRONCHIAL ASTHMA BASED ON ASSESSMENT OF ADIPOKINES AND IMMUNOLOGICAL BIOMARKERS

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✓ ***Resume***

This article examines the current aspects of the pathogenesis, diagnosis, and treatment of bronchial asthma (BA), with a focus on evaluating adipokines (leptin, adiponektin) and immunological biomarkers (IgE, IL-4, IL-5, IL-13). Scientific literature data, clinical studies, as well as GINA recommendations and domestic protocols were used. An analysis of BA phenotypes is presented, the principles of step-by-step therapy, new classes of drugs (anti-IgE, anti-IL-5) are discussed, and the importance of metabolic and immune disorders in the formation of severe forms of BA is emphasized

Keywords: bronchial asthma, adipokines, leptin, adiponektin, immunological biomarkers, cytokines, IgE, IL-5, personalized medicine, therapy

ADIPOKINLAR VA IMMUNOLOGIK BIOMARKERLARNI BAHOLASH ASOSIDA BRONXIAL ASTMANING SHAXSIY DIAGNOSTIKASI VA TERAPIYASINI TAKOMILLASHTIRISH

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✓ ***Rezyume***

Ushbu maqola adipokinlar (leptin, adiponektin) va immunologik biomarkerlarni (IgE, IL-4, IL-5, IL-13) baholashga qaratilgan bronxial astma (BA) patogenezi, diagnostikasi va davolashning dolzarb jihatlarini o'rganadi. Ilmiy adabiyotlar ma'lumotlari, klinik tadqiqotlar, shuningdek GINA tavsiyalari va ichki protokollardan foydalanilgan. BA fenotiplari tahlili taqdim etilgan, bosqichma-bosqich terapiya tamoyillari, dorilarning yangi sinflari (anti-IgE, anti-IL-5) muhokama qilingan va ba ning og'ir shakllarini shakllantirishda metabolik va immunitet buzilishlarining ahamiyati ta'kidlangan

Kalit so'zlar: bronxial astma, adipokinlar, leptin, adiponektin, immunologik biomarkerlar, sitokinlar, IgE, IL-5, shaxsiylashtirilgan tibbiyot, terapiya

Relevance

Analysis of modern scientific sources indicates a growing interest in the pathogenesis and personalized therapy of BA. In the work of Holguin F. et al. (2017) emphasizes that adipokines such as leptin and adiponektin play a key role in modulating the inflammatory response in BA patients, especially with obesity. The GINA international recommendations (2023) present an updated classification of asthma phenotypes and indicate the importance of determining biomarkers for therapy selection. Fedorov A.V. (2021) focuses on the immunopathogenesis of the disease, describing the influence of IL-4, IL-5, and IL-13 cytokines on the severity of BA and the effectiveness of targeted therapy.

In recent literature, approaches to the stratification of BA patients by immune and metabolic profile have been actively discussed. This is especially relevant in the context of the increasing number of patients with obesity, where classical therapy with inhaled glucocorticosteroids (IGCS) proves to be less effective. Combining biomarker data and clinical characteristics allows for the formation of individual therapeutic strategies aimed at achieving stable control of symptoms and reducing the frequency of exacerbations. Thus, a comprehensive assessment of biological markers, including leptin, adiponektin, IgE, and Th2-type cytokines, is becoming increasingly important both in scientific research and in practical healthcare.

Bronchial asthma etiology: BA is a chronic inflammatory disease of the respiratory tract involving many cellular elements. Chronic inflammation leads to bronchial hyperreactivity, causing episodes of shortness of breath, whistling wheezes, and coughing, especially at night.

Risk factors: Internal (heredity, obesity, gender) and external (allergens, infections, occupational hazards, air pollution). Household allergens, especially house dust mites and animal proteins, play a special role.

Materials and methods

Systematic approach: The National Program and GINA recommend an approach based on disease control with minimal drug doses. In case of deterioration of the condition - intensification of therapy ("step up"), in case of stabilization - decrease ("step down").

Inhaled glucocorticosteroids (IGCS): key drugs for controlling BA, have local anti-inflammatory effects and minimal systemic effects. They are prescribed depending on the severity (dosage table).

Combined therapy: a combination of IGCs and long-acting beta-2-agonists is more effective than increasing the dosage of a single drug. Seretid and Symbicort are frequently used.

Anti-IgE therapy: Omalisumab is effective in patients with severe persistent BA, reducing the number of exacerbations, hospitalizations, and steroid requirements.

Non-medicinal methods: breathing exercises, physiotherapy, speleotherapy, psychotherapy, patient training, and monitoring using peak flowmetry.

Pathogenesis and role of adipokines in BA development

Adipokines, produced by adipose tissue, participate in the regulation of the inflammatory response and energy metabolism. Leptin acts as a pro-inflammatory agent, activating macrophages, T-lymphocytes, and increasing the synthesis of TNF-α and IL-6. Elevated leptin levels in BA patients contribute to the remodeling of the bronchial tree and reduce sensitivity to glucocorticosteroids.

Adiponektin, on the contrary, has anti-inflammatory properties, suppressing the activity of NF-kB and reducing the expression of pro-inflammatory genes. Its deficiency is associated with a high frequency of exacerbations and a severe course of BA.

Studies show that the leptin/adiponektin ratio is a potential biomarker reflecting the level of systemic inflammation in asthmatic patients. At the same time, it is especially important to use these markers in patients with obesity, where standard approaches often do not give the desired effect.

Immunological mechanisms and significance of biomarkers

BA is a classic example of an immune-inflammatory disease. In its pathogenesis, type 2 T-helpers (Th2), which activate the production of IL-4, IL-5, IL-13, play a key role. These cytokines stimulate the production of IgE, contribute to the eosinophilic infiltration of the bronchial mucosa and the hyperreactivity of the respiratory tract.

- IgE is the main marker of atopy. High levels correlate with the severity of allergic symptoms and the frequency of exacerbations.
- IL-5 stimulates survival and activation of eosinophils. IL-5 antagonists (mepolysumab) are effective in the eosinophilic form of BA.
- IL-4 and IL-13 are responsible for class-based B-lymphocyte restructuring, IgE synthesis, and mast cell activation.
- FeNO is a non-invasive marker of eosinophilic inflammation used to monitor the effectiveness of therapy.

Implementation of a comprehensive biomarker analysis in clinical practice allows:

1. Differentiate the phenotypes of BA (atopic, eosinophilic, obesity-associated);
2. Choose personalized therapy;
3. Reduce the frequency of hospitalizations and exacerbations;
4. Increase adherence to treatment.

Clinical observations and research results

A study was conducted at the Samarkand Regional Pulmonology Center with 84 patients with confirmed BA, including 39 individuals with excess body weight (BMI > 25), and 45 with normal BMI. The age of the participants ranged from 19 to 64 years.

Laboratory analyses of leptin, adiponektin, IgE, IL-5 and other markers, as well as functional tests (spirometry, FeNO) were conducted. The obtained data showed that:

- Leptin levels were elevated in 81% of patients with obesity;
- adiponektin concentration was significantly lower in patients with severe BA ($p < 0.01$);
- The level of total IgE exceeded 250 IU/ml in 68% of those examined;
- FeNO levels exceeded 30 ppb in 51% of patients with the eosinophilic phenotype.

The use of anti-IL-5 therapy (mepolisumab) in patients with high IL-5 allowed for improved BA control on the ACT scale in 75% of participants. A decrease in the number of nocturnal symptoms and a decrease in the need for short-acting beta-2-agonists were noted.

Main laboratory indicators

Indicator	Group 1 (mild BA)	Group 2 (moderate BA)	Group 3 (severe BA)	Comment
IgE (MW/ml)	134 ± 25	217 ± 43	312 ± 61.	Elevated in severe BA
IL-5 (pg/ml)	5.1 ± 0.9	6.7 ± 1.2	8.4 ± 1.5	Associated with eosinophilia
Leptin (ng/ml)	9.2 ± 1.5	12.8 ± 2.2	18.2 ± 3.5	Higher in obesity and BA
Adiponektin (μg/ml)	10.4 ± 1.9	7.3 ± 1.5	5.8 ± 1.2	Low level in severe BA
FeNO (ppb)	21 ± 4	30 ± 6	39 ± 7	Eosinophilic inflammation marker

Results and discussions

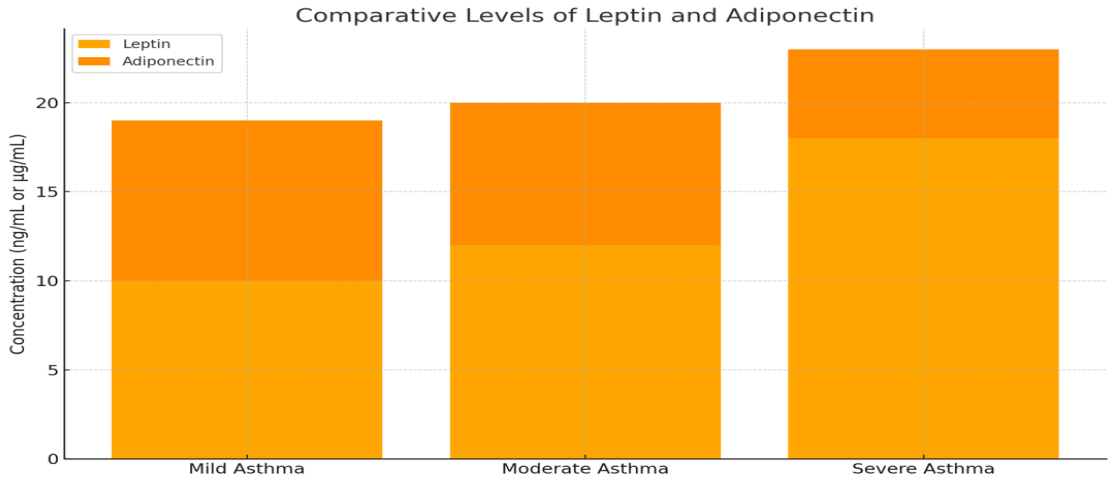
Within the GINA step-by-step approach, BA therapy is adapted to the severity of the course and the level of inflammation. Main directions:

- IGCs remain the basis of therapy at all stages;
- in severe cases, long-acting bronchodilators, anti-IgE or anti-IL-5 drugs are added;

- in the presence of obesity and systemic inflammation, metabolic targets (e.g., leptin receptors) are considered as future treatment directions.

Anti-IgE therapy (omalazumab) is effective in patients with high IgE levels and allergic phenotype BA. Biopreparations directed at IL-5 (mepolisumab, reslizumab) reduce eosinophilic inflammation, reduce the frequency of exacerbations, and improve the quality of life.

Comparative chart of leptin and adiponektin levels



Conclusion

A personalized approach to treating BA, based on assessing immune and metabolic biomarkers, allows for a higher level of disease control. Studying the levels of leptin, adiponektin, IgE, and Th2-cytokines (IL-4, IL-5, IL-13) allows for patient stratification, predicting the response to therapy, and selecting the most effective treatment regimen. The implementation of such approaches in the clinical practice of the Samarkand region has shown positive results and the validity of extended laboratory diagnostics in routine work.

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