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PATHOPHYSIOLOGICAL AND CLINICAL CORRELATIONS BETWEEN BRONCHIAL ASTHMA AND METABOLIC SYNDROME: A REVIEW

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Abstract

Introduction: Bronchial asthma (BA) and obesity represent significant challenges in contemporary medicine, with escalating prevalence in developed nations. This review aims to systematically analyze the pathophysiological and clinical interplay between bronchial asthma and metabolic syndrome, emphasizing their role in severe asthma development.

Search strategy: A thorough literature search was conducted up to May 10, 2024, using PubMed, Web of Science, and the Cochrane Central Register of Controlled Trials. The search spanned the past decade and employed predefined keywords based on Medical Subject Headings (MeSH). *Inclusion criteria* encompassed studies meeting evidence-based medicine standards and fundamental experimental research, published in English or Russian. *Exclusion criteria* included clinical case descriptions, non-evidence-based publications, and abstracts.

Results: This review synthesizes current insights into the mechanisms underlying the association between bronchial asthma and metabolic syndrome. A conventional perspective links asthma and the syndrome through mechanical effects of abdominal adipose tissue, impacting respiratory tract resistance and volumes. Furthermore, emphasis is placed on metabolic dysregulation's role in altering proinflammatory cytokine levels and adipose tissue hormone profiles. The review also introduces the concept of a metabolic phenotype in asthma, characterizing it as an independent variant within the spectrum of "bronchial asthma – metabolic syndrome - obesity." Pathogenetic relationships involving insulin resistance, hyperinsulinemia's epithelial effects on the respiratory tract, chronic inflammation, and respiratory hyperreactivity are highlighted.

Conclusions: The findings support a clinical and pathophysiological framework distinguishing a distinct "metabolic phenotype" in asthma patients. This phenotype underscores the interconnected pathogenesis involving insulin resistance, chronic inflammation, and heightened respiratory tract reactivity. Such insights contribute to advancing targeted therapeutic approaches for this subset of patients.

Keywords: *metabolic syndrome, asthma, bronchospasm, obesity, insulin resistance.*

Резюме

ПАТОГЕНЕТИЧЕСКИЕ И КЛИНИЧЕСКИЕ АСПЕКТЫ ВЗАИМОСВЯЗИ БРОНХИАЛЬНОЙ АСТМЫ И МЕТАБОЛИЧЕСКОГО СИНДРОМА: ОБЗОР ЛИТЕРАТУРЫ

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Введение. Согласно имеющимся в настоящее время данным, бронхиальная астма (БА) и ожирение представляют собой одну из актуальнейших проблем современной медицины, значение которой приобретает

мировой характер. Эпидемиологические данные позволяют констатировать значительный рост этих заболеваний в развитых странах, что диктует необходимость тщательного анализа и всестороннего изучения.

Целью данного обзора являлась систематизация данных о патофизиологической и клинической взаимосвязи бронхиальной астмы и метаболического синдрома, а также роли его компонентов в формировании тяжелого течения бронхиальной астмы.

Стратегия поиска: Поиск актуальной литературы проводился в базах данных PubMed, Web of Science и Кокрановском центральном регистре контролируемых испытаний до 10 мая 2024 г. Глубина поиска составила 10 лет. В ходе анализа использовались предварительно сформулированные ключевые слова на основе терминов медицинских предметных рубрик (MeSH). *Критерии включения:* результаты исследований, выполненных с учетом всех требований доказательной медицины; данные фундаментальных экспериментальных исследований. Поиск ограничивался работами, опубликованными на английском и русском языках. *Критерии исключения*: описание клинических случаев, публикации, не соответствующие требованиям доказательной медицины, а также тезисы.

Результаты: В представленном обзоре систематизированы современные взгляды на механизмы формирования фенотипа бронхиальной астмы, ассоциированного с метаболическим синдромом. В классическом и наиболее упрощенном варианте связь астмы и синдрома основывается на механических эффектах жировой ткани брюшной полости на сопротивление дыхательных путей с изменением соответствующих дыхательных объемов. Представлена попытка актуализировать роль метаболического дисбаланса в уровнях провоспалительных факторов, в первую очередь цитокинов, а также гормонов жировой ткани. Кроме того, сформулирована концепция связи метаболического синдрома и бронхиальной астмы, отражающая влияние данного синдрома на варианты клинического течения заболевания.

Выводы: Представленные данные позволяют сформулировать клинико-патофизиологический подход к обоснованию выделения специфического «метаболического фенотипа» пациентов с БА, представляющего самостоятельный вариант синдемии - «бронхиальная астма – метаболический синдром - ожирение». Основой такого подхода является показанный факт патогенетических связей, а именно развитие инсулинорезистентности с прямым повреждающим эффектов гиперинсулинемии на эпителий респираторного тракта, формирование хронического малоинтенсивного воспаления, типичного для двух заболеваний, а также развитие на этом фоне гиперреактивности дыхательных путей.

Ключевые слова: *метаболический синдром, астма, бронхоспазм, ожирение, инсулинорезистентность.*

Түйіндеме

БРОНХ ДЕМІКПЕСІ МЕН МЕТАБОЛИКАЛЫҚ СИНДРОМНЫҢ ӨЗАРА ПАТОГЕНЕТИКАЛЫҚ БАЙЛАНЫСЫНА ЖӘНЕ КЛИНИКАЛЫҚ КӨРІНІСТЕРІНЕ: ӘДЕБИЕТТІК ШОЛУ

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Кіріспе. Заманауи мәліметтерге сәйкес, бронх демікпесі (БД) және семіздік қазіргі заманғы медицинаның өзекті мәселелерінің бірі болып табылады және оның маңыздылығы әлемдік сипатқа ие. Эпидемиологиялық деректер дамыған елдерде бұл аурулардың айтарлықтай өсуін анықтауға мүмкіндік береді, бұл өз кезегінде мұқият талдау мен жан-жақты зерттеу қажеттілігін тудырады.

Бұл шолудың мақсаты бронх демікпесі мен метаболикалық синдромның патофизиологиялық және клиникалық байланысын, сондай-ақ, оның құрлымдарының бронх демікпесінің ауыр ағымын қалыптастырудағы рөлі туралы деректерді жүйелеу болды.

Іздеу стратегиясы: маңызды әдебиеттерді ізденіс PubMed, Web of Science дерекқорларынан және Cochrane орталықтан бақыланатын сынақтар тізімінен 2024 жылдың 10 мамырына дейін жүргізілді. Талдау барысында медициналық пәндік мәліметтер (MeSH) терминдеріне негізделген алдын ала тұжырымдалған түйіндік сөздерді қолдану арқылы жүзеге асты. *Тізімге енгізу критерийлері*: дәлелді медицинаның барлық талаптарын ескере отырып орындалған зерттеулердің нәтижелері; іргелі эксперименттік зерттеулердің нәтижесі. Іздеу тек ағылшын және орыс тілдерінде жарияланған жұмыстармен шектелді. *Тізімге енгізілмеген критерийлері*: клиникалық жағдайлардың сипаттамасы, дәлелді медицина талаптарына сәйкес келмейтін мақалалар, сондай-ақ тезистер.

Нәтижесі: ұсынылған шолуда метаболикалық синдроммен байланысты БД фенотипін қалыптастыру механизімдері жайлы заманауи көзқарастар жүйеленген. Классикалық және жеңілдетілген нұсқада демікпе мен метаболикалық синдромның байланысы іштің майлы тінінің тыныс алу жолдарының кедергісіне механикалық

әсеріне негізделгенін, тиісті тыныс алу көлемінің өзгеруі айтылған. Қабынуға қарсы факторлардың, ең алдымен цитокиндердің, сондай-ақ май тінінің гормондарының деңгейіндегі метаболикалық теңгерімсіздіктің рөлін өзектендіру әрекеті ұсынылған. Сонымен қатар, метаболикалық синдром мен БД арасындағы байланыс жайлы тұжырымдалған, бұл синдромның аурудың клиникалық ағымына әсерін көрсетеді.

Қорытынды: ұсынылған деректер зерттеу келесі синдемияның тәуелсіз нұсқасы-"бронх демікпесі - метаболикалық синдром – семіздік" болып табылатын БД науқастарының ерекше "метаболикалық фенотипін"оқшаулауды негіздеуге клиникалық - патофизиологиялық тәсілді тұжырымдауға мүмкіндік береді. Бұл тәсілдің негізі патогенетикалық байланыст арының негізі болып табылады, атап айтқанда гиперинсулинемияның тыныс алу жолдарының эпителийіне тікелей зақымдайтыны, инсулинге төзімділіктің дамуы, екі ауруға тән созылмалы төмен қарқынды қабынудың пайда болуы, сондай-ақ осы жағдайда тыныс алу жолдарының гиперреактивтілігінің дамитыны анықталды.

Түйінді сөздер: *метаболикалық синдром, демікпе, бронхоспазм, семіздік, инсулинге төзімділік.*

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Introduction

Currently, metabolic syndrome (MS) is defined as a composite of clinical components such as hyperglycemia and hypertriglyceridemia with abdominal obesity, arterial hypertension and low cholesterol high density lipoprotein [3, 16]. These conditions are known to increase the risk of cardiovascular disease, type 2 diabetes and stroke [29]. However, unlike the already known syntropy asthma and obesity, the outcome of the metabolic syndrome on the reduced respiratory function is not well understood.

The association between metabolic syndrome and lung disease has been studied in several clinical studies. Leone and colleagues first verified the relationship between lung diseases and MS [18]. At present time, we have a numeral of different studies significant relationship bronchial asthma and metabolic syndrome. Epidemiological study in United States between 1990 and 2000 demonstrated that more than 250,000 new asthma cases were related to metabolic syndrome [8]. The prevalence of bronchial asthma in the group of 2559 patients with obesity and BMI> 60, the prevalence of asthma was 32.7% [4]. The cross-sectional HUNT study in a group of 10,038 Korean patients aged 40 to 69 years demonstrated that patients with metabolic syndrome were more likely to describe symptoms of bronchial asthma (wheezing and shortness of breath) than patients without components of the metabolic syndrome [9].

According to the results of another work, among patients suffering from metabolic syndrome more than 69, 3% have severe asthma [33].

In additional, the most aggressive component of the MS, in particular diabetes mellitus, also studied in the large Kaiser Permanente health care program and this analysis has helped to determine the risk of developing asthma among people with diabetes [11]. In adults participants (≥18 years of age) without diabetes, the incidence of asthma was 0.16 per 1000 people, and in patients with diabetes, the corresponding parameter was 0.41, which shows a higher risk of asthma [17].

Therefore, the epidemiological evidence suggests a potential association between metabolic syndrome and the development of reversible bronchial obstruction. However, it remains uncertain whether chronic low-intensity inflammation, a hallmark of metabolic syndrome, directly contributes to the susceptibility to severe bronchial asthma. Consequently, **the study aimed** to organize data concerning the pathophysiological and clinical connections between bronchial asthma and metabolic syndrome, alongside exploring the impact of its components on the development of severe bronchial asthma.

Search Strategy: During the preparation of this review, a systematic search was conducted in PubMed, Web of Science, and the Cochrane Central Register of Controlled Trials up to May 10, 2024, covering a period of 10 years. Publications exceeding this timeframe were separately included due to their significant relevance to the study's focus. The search utilized predefined keywords based on Medical Subject Headings (MeSH), including metabolic syndrome, asthma, bronchospasm, and obesity.

Inclusion criteria encompassed studies meeting the standards of evidence-based medicine and fundamental experimental research, published in English or Russian. *Exclusion criteria* comprised clinical case descriptions, publications not meeting evidence-based medicine criteria, and abstracts. A total of 37 relevant sources were identified through this search strategy (Figure 1).

Results and discussions

Contemporary literature increasingly discusses the concept of "syndemia," which denotes the synergistic impact of two or more diseases resulting in greater adverse effects than each disease individually [9].

Traditionally applied in cardiometabolic contexts such as "arterial hypertension - metabolic syndrome - obesity" [1]

this concept is relevant to understanding the interplay between asthma (AD) and obesity/metabolic syndrome. The interaction between these conditions exacerbates symptoms and disease severity, necessitating an integrated treatment approach that addresses their mutual influence and associated risk factors.

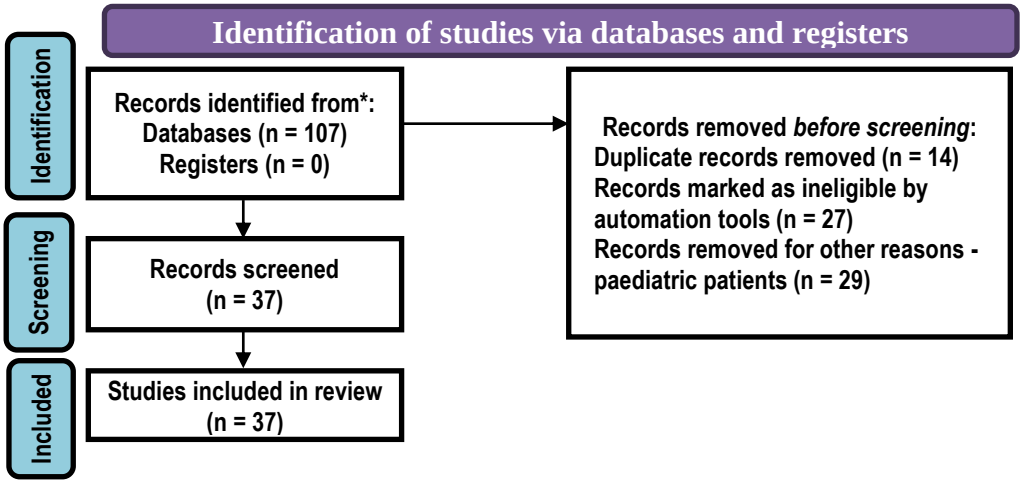

Figure 1 illustrates the overall search approach, adhering to the PRISMA algorithm.

The mechanical effects of adipose tissue on the lungs

The simplest theory of the association of asthma and MS is focused on the mechanical effects of abdominal fat on the resistance and compliance of the respiratory system. Obesity reduces the total lung capacity (TLC), in particular by reducing the residual volume (RV) and, consequently, the functional residual capacity (FRC) [32]. The consequence of this is shallow breathing. In addition, the increased volume of soft tissues compresses the chest, which leads to a decrease in the diameter of the peripheral airways, and this leads to a change in the structure and function of the smooth muscles of the bronchi and, as a result, to hyperreactivity [17, 27].

Among the clinical elements of the metabolic syndrome, abdominal obesity has the strongest association with impaired lung function. Estimated mechanisms for the increased risk of obesity-related asthma include changes in the extensibility of the smooth muscles of the airways, due to the presence of shallow breathing associated with obesity, sleep disturbance, genetic polymorphism, and the effects of systemic adipokines and oxidative stress on both pulmonary and extrapulmonary inflammation [33].

Brumpton et al determined that only two components of the metabolic syndrome have an association with the frequency of asthma: a large waist circumference and hyperglycemia/diabetes mellitus [33]. In the CARDIA study, abdominal obesity, high blood pressure, and hyperglycemia were associated with the incidence of asthma [17]. The mechanisms underlying the potential link between asthma and MS are yet to be understood.

Systemic inflammation

In MS, accumulation of visceral fat and insulin resistance are associated with an increased expression of mediators that activate inflammatory mechanisms both locally and systemically. This includes recruitment of inflammatory cells by chemokines, such as monocytic chemoattractant protein-1 (MCP-1), as well as direct synthesis of predominantly pro-inflammatory cytokines and chemokines, such as interleukin 6 (IL-6), interleukin 1β (IL-1β), tumor necrosis factor-α (TNF-α), C-reactive protein (CRP), transforming growth factor β1 (TGF-β1) and leptin. The developing variation between Th1 and Th2 inflammation is to be one of the mechanisms by which obesity can increase the risk of asthma and change phenotype [27].

Interleukins and TNF-α

Obesity maintain persistent low-intensity inflammation through overproduction of cytokines (IL-6 and IL-1β). IL-6 has been demonstrated to play an important role in the pathogenesis of asthma by activating neutrophils and stimulating the differentiation of Th2 helper cells into Th17 (in the presence of TGF-β) or by contributing to the production of IL-13 by T-helpers [13]. Th17 cells characterized by high level of resistant to steroids (unlike, for example, Th2 cells) and have a dominant role in severe asthma [17]. It has been shown that increased levels of Th17 and IL-17 are determined in the peripheral blood of patients with obese type 2 diabetes. In addition, the level of Th2/Th17 cells and IL-17 in patients with metabolic syndrome positively correlates with bronchial hyperresponsiveness and eosinophils and negatively correlates with FEV1 [14]. This data show that Th2/Th17 cell activity is associated with severe asthma [13-15].

Increased levels of IL-6, CRP, and soluble CD163 (a macrophage activation marker) have been connected with impaired lung function (especially in severe asthma) and non-specific airway inflammation. Experimental studies have shown that TNF-α increases the survival of eosinophils, which is important in the pathogenesis of bronchial asthma, which is accompanied by hypereosinophilia [15].

IL-1 and IL-17 have been shown to cause airway hyperreactivity in response to a high fat diet, the process mediated by Node-like receptor protein 3 (NLRP3). Activated NLDP3 contribute to the production of IL-1β which stimulates IL-17A-producing type 3 lymphoid cells (ILC3s) in the lungs [4]. Patients with severe asthma had a high number of IL-17-positive ILC3-like cells in the bronchoalveolar lavage fluid (BALf) as compared to healthy controls or patients with mild asthma [7]. NPLP3 can also be activated by a wide range of mediators, in particular,

high levels of extracellular glucose, amyloid-β, oxidized LDL and extracellular acidosis, all observed in MS [7, 12].

However, the role of systemic inflammation in airway damage asthma associated with obesity is currently controversial. Most studies have not confirmed this relationship. Prospective studies have shown increased levels of interleukins (Il-1β, Il-5, Il-6 and Il-8) in the sputum of asthmatics, however, no significant differences between obese and lean asthmatics were found [26]. However, it should be noted that changes in sputum reflect only local changes; the data obtained cannot characterise the degree of activity of systemic inflammation, especially low-intensity inflammation, which is a key characteristic of obesity.

Thus, conclusions regarding whether the activity of systemic inflammation in asthma are different from those of asthma in obesity should be left open until further evidence is obtained [12].

Leptin

Adipose tissue is now known to be metabolically active and is involved in the regulation of homeostasis and the pathogenesis of diseases associated with obesity. Obesity is associated with elevated levels of leptin and resistin (pro-inflammatory hormones), as they are directly secreted by adipose tissue [20].

Leptin and its receptors are present in the membrane of bronchial epithelial cells, and elevated leptin levels can modulate the immune response in the airways by inducing a persistent inflammatory response or biasing the cell response according to the Th1 phenotype [6]. In particular, leptin induces an increase in the expression of pro-inflammatory cytokines, such as TNF-α, IL-6, and IL-12, which leads to the development of systemic inflammation and activation of the inflammasoma-dependent pathway, as described above [34].

At the same time, clinical and experimental studies demonstrate that leptin acts by increasing bronchial hyperresponsiveness through its own receptors in the bronchial wall [38]. It has been determined that obese patients with asthma, airway reactivity significantly correlates with leptin's level (rho = 0.8, P <0.001) [4, 5].

Adiponectin

Adiponectin is an adipokine with insulin-sensitizing and anti-inflammatory effects. A low level of adiponectin is determined both in asthma and in metabolic syndrome.

It has also been shown that epithelial cells of the respiratory tract express adiponectin. Clinical studies have demonstret conflicting results regarding the effect of adiponectin levels on respiratiry function, including CARDIA study in which it was found that after BMI control, adiponectin levels were positively associated with lung function. Pretreatment with adiponectin has been shown to reduce eotaxin-mediated chemotactic responses by binding to the adiponectin receptors AdipoR1 and AdipoR2, which are expressed in human eosinophils, thereby inhibiting the pathogenetic mechanism of AD [34].

Fatty Acid Inflammation

One of the important component of the metabolic syndrome is hyperlipidemia, which contributes potential communication mechanism for the metabolic syndrome and decreased lung function due to low-intensivity inflammation caused by fatty acid. The level of fatty acids is regulated by insulin uptake and release of triglycerides and free fatty acids (FFAs) by adipocytes. However, in patients with metabolic syndrome, adipose tissue cannot effectively regulate fat deposition, and excess amounts of triglycerides and FFA remain in the bloodstream. FFA can activate the mechanisms of innate immunity, which is the cause of the appearance of a lipotoxic state. Such mechanisms include activation of pattern recognition receptors (PPR), intracellular signaling pathways, and stress induction of the endoplasmic reticulum [37].

Various studies have shown a relationship between hyperlipidemia and a worsening prognosis of diseases of the respiratory system. In particular, a link has been demonstrated between elevated triglyceride levels and airway hyperreactivity, and symptoms of obstruction in adults. In addition, in patients with asthma, the level of sputum neutrophils positively correlated with levels of plasma fatty acids, which is compatible with the hypothesis that excess FFA stimulate innate immune responses of the respiratory tract. Only one study directly examined the effect of fatty acids on innate immune responses in the respiratory tract in asthma. As a result, it was shown that food consumption exclusively saturated with fats led to an increase in circulating FFA levels for 4 hours, which was associated with an increase in the level of neutrophils in the airways and the expression of Toll-like receptor 4 mRNA in sputum cells. These result demonstrate the probable role of hyperlipidemia in inducing airway inflammation through different mechanisms [5].

Mitochondrial Dysfunction

It was found that key inflammatory cytokines associated with asthma and MS, such as interleukin-4 (IL-4) and IL-13, induce mitochondrial dysfunction by regulating the oxidized metabolite of linoleic acid 13-S-HODE [21-22, 28].

Recent observations, in many respects, are focused on mitochondrial dysfunction, which is considered as the main pathophysiological mechanism of the relationship between metabolic syndrome and asthma. Defective mitochondrial biogenesis in adipose tissue has already been demonstrated by studies in metabolic syndrome [34]. Mitochondrial dysfunction, especially in the main tissues sensitive to insulin, such as the liver and muscles, potentiates hyperinsulinemia and fatty degeneration, which increases the risk of asthma in a number of ways described above [2].

At present time, there is limited data on the cause of the development of mitochondrial dysfunction in asthma, however, experimental studies indicate a persistent association between mitochondrial damage resulting from the development of MS and bronchial asthma.

Insulin resistance and hyperinsulinemia

Diabetes and insulin resistance have been shown to be linked to decreased lung function, and some studies have also found a relationship between insulin resistance and lung function among non-diabetics even after controlling for BMI.

However, hyperinsulinemia triggers pathological changes in metabolism which indirectly affect the lungs. Published data show that insulin mediates hypersensitivity of the respiratory tract by expressing laminin via phosphoinositide 3-kinase and Rho kinase dependent pathways [5, 36]. The connection between insulin and muscarinic receptors of bronchial tract might also be

important. Clinical studies demonsrate that hyperinsulinemia (as a result of obesity or MS) led to vagus-mediated bronchoconstriction and the loss of the inhibitory effect of type 2 muscarinic receptors on parasympathetic endings [32, 33].

Result of the study using inhaled human insulin demonstrate that those receiving this drug are more likely to show respiratory symptoms, like coughing and shortness of breath, as well as a decrease in FEV1 and diffuse capacity for carbon monoxide [17]. This intermediate result confirms the hypothesis that insulin can have a direct effect on the human respiratory tract through ciliated epithelial cells or inhibition of muscarinic receptors [25, 30].

US National Health and Nutrition Survey data provide additional evidence on the link between insulin sensitivity and lung function [10]. Regardless of asthma diagnosis, insulin sensitivity was directly proportional to the FEV1 and VC values. In contrast, the presence of insulin resistance negatively correlated with parameters of lung function. Metabolic syndrome was associated with a more significant decrease in FEV1 / VC in patients with asthma (12.6%) and without asthma (2.3%). Thus, even in healthy controls, abnormalities in glucose metabolism can lead to impaired lung function [31].

In another national review, individuals with elevated levels of glycated hemoglobin (HbA1c> 5.7) showed a decrease in FEV1 twice as likely as individuals with normal HbA1 levels [26].

Insulin also stimulates the proliferation and differentiation of fibroblasts, resulting in the accumulation of collagen and remodeling of the airways. In experimental studies, hyperglycemia increases the sensitivity of smooth muscle cells in the bronchial tract to contractile agents and intracellular calcium excretion [36]. On the other hand, mechanisms explaining in lung dysfunction in patients with diabetes are microangiopathy of the alveolar capillaries and pulmonary arterioles and autonomic neuropathy [17, 35].

Therefore, the data presented enable the construction of a conceptual framework for clinically and pathophysiologically justifying the "metabolic phenotype" of bronchial asthma (Figure 2).

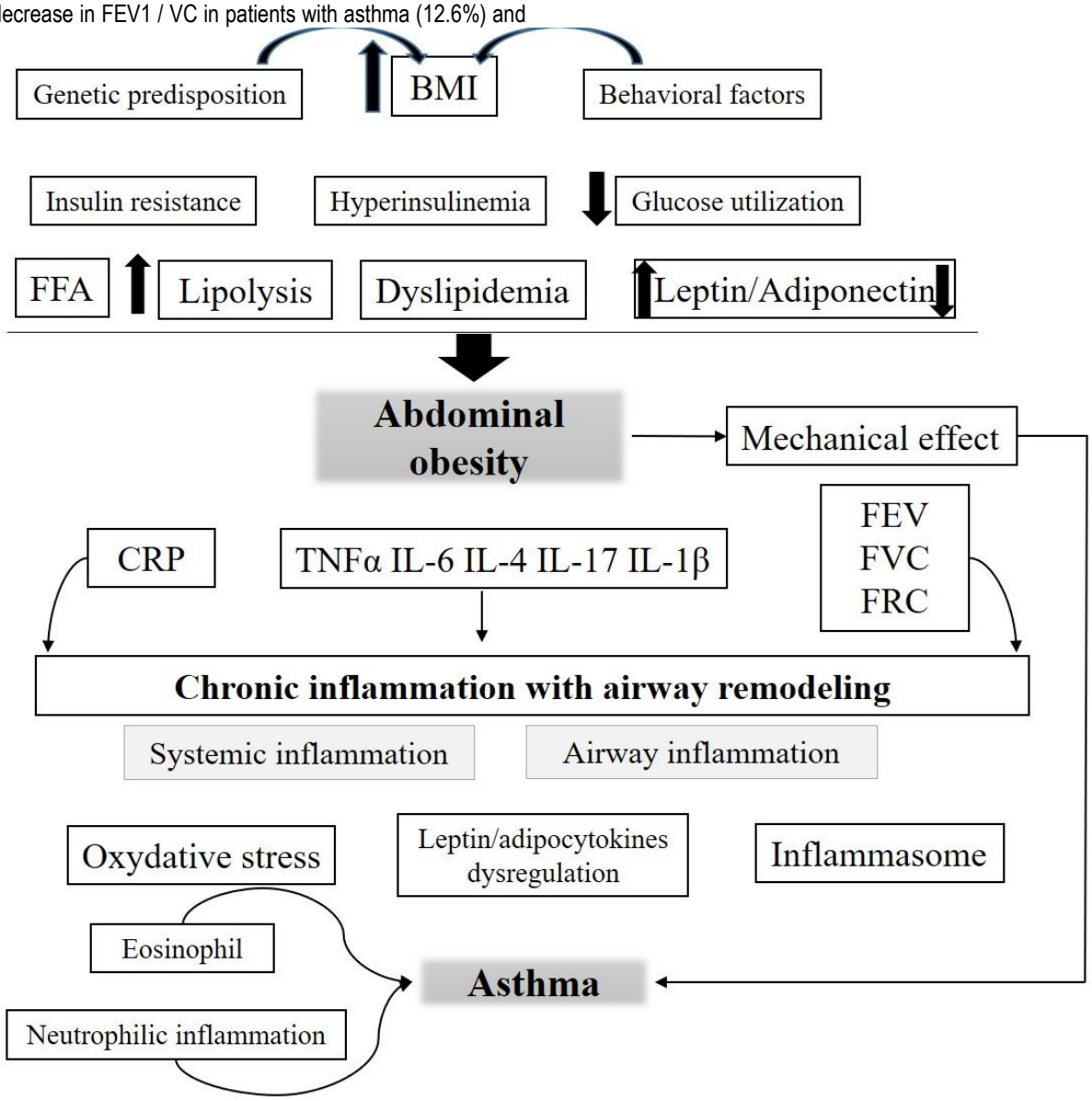

Figure 2. The "Metabolic phenotype" of bronchial asthma, emphasizing the interrelationship between asthma and metabolic syndrome (revised, Listyoko A. 2024). [19].

Clinical features observed in patients with asthma and obesity include frequent and severe exacerbations, respiratory tract inflammation, reduced lung function, heightened respiratory tract hyperreactivity, with more pronounced manifestations observed in females.

Conclusion

The problem of MS-associated AD remains relevant today due to the high prevalence of these comorbid conditions. The primary clinical and pathogenetic connections between the two conditions can be summarized as follows:

1. Insulin resistance leads to the loss of the inhibitory effect of parasympathetic fibers on smooth muscle cells of the respiratory tract and hypersensitivity, while hyperinsulinemia directly induces laminin expression through phosphoinositide-3-kinase and Rho-kinase dependent pathways, which together lead to a decrease in FEV1 and triggering the development mechanism BA.

2. The consequence of obesity is a change in the hormonal profile due to the independent production of adipokines by adipose tissue. Leptin is a pro-inflammatory cytokine and induces an immune response, induces an increase in the expression of pro-inflammatory cytokines, such as TNF-α, IL-6 and IL-12. In addition, it acts on its own receptors in the wall of the respiratory tract, which leads to bronchoconstriction and hyperreactivity with the further development of AD.

3. The most important mechanism for the association of MS and AD is a systemic inflammatory response that is carried out by cytokines (TNFα, IL-6, IL-4, IL-17, IL-1β, etc.) that induce the differentiation of Th2 cells into Th2 / Th17 cells. Obesity and insulin resistance stimulate systemic inflammation, and cytokines of systemic inflammation lead to airway hyperresponsiveness, neutrophilic infiltration, and bronchospasm.

Further studies are required to elucidate the link between metabolic syndrome and asthma development and severity. Further studies are required to elucidate the link between metabolic syndrome and asthma development and severity.

Contribution of the authors:

Maimysheva S.Yu. - literature review, data collection, data analysis.

Orekhov A.Yu. - development of research design and methodology, data analysis.

Karazhanova L.K. – scientific editing.

Chinybaeva A.A. - data collection, editing of the article.

Ashirov B.A. - data collection, article editing.

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