MINI REVIEW

RECORDS OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES

Therapeutic Strategies for Asthma Concurrently Occurred with Obesity

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Abstract

One of major global problems is obesity, which can lead to inflammation in the form of hyperlipidemia, lung abnormalities, and asthma. An abnormal buildup of fat that poses a risk to health is obesity. The incidences of obesity in adults and children are still rising. Obesity is a disease that has a significant impact on asthma in both adults and children. Excessive obesity-induced systemic inflammation has been linked to the physiopathology of a number of diseases and has been suggested as a potential mechanism for the onset of asthma in obese people. Obesity-related inflammation is thought to be caused by M1 macrophage infiltration of adipose tissue and elevated expression of several mediators that intensify and spread inflammation. Adipose tissue serves as a significant reservoir for adipokines, including the pro-inflammatory leptin that is overpro8duced in obesity and the anti-inflammatory adiponectin that is synthesized at a reduced rate. Pro-inflammatory cytokines like IL-1β, TNFα, and NF-KB are synthesized during the inflammatory process and play a role in the pathogenesis of asthma. The objective of this review is to evaluate the role of medication in treatment obesity and its influence in improve asthma.

Keywords: Obesity, asthma, inflammatory markers, medication.

1. Introduction

The harmful effect of excessive body fat accumulation brought on by an imbalance between energy intake and energy expenditure is obesity. Many conditions, such as heart disease, type 2 diabetes, hypertension, chronic kidney disease, and some forms of cancer, are thought to be made more likely by obesity **(Goossens, 2017; Saltiel & Olefsky, 2017).** One of the numerous lung conditions associated with metabolic syndrome, a comorbidity of obesity, is asthma **(Dinger et al., 2016).** Worldwide, obesity affects about 13% of adults and 17% of individuals between the ages of 2 and 19 were obese between 2011 and 2014. Asthma causes inflammation of the lung airways. Numerous symptoms, such as wheezing, constricted airways, tightness in the chest, coughing, and dyspnea, are associated with it. Asthma can be brought on by a number of factors, such as physical activity, exposure to allergens, changes in the weather, and viral respiratory infections **(Chen et al., 2018).** Obesity alters lipid metabolism and encourages the production of pro-inflammatory markers in the lungs **(Dinger et al., 2016)**. For obese patients, asthma is particularly challenging to treat with corticosteroids because the immune system and underlying metabolism mechanism may not respond to these drugs. As a result, obesity-related asthma needs to be treated **(Chen et al., 2018).** Obesity increases the amount of adipose tissue, an endocrine organ. It is producing a class of inflammatory cytokines called adipocytokinases. Adipocytokinases include interleukin-1beta (IL-1β) and leptin.

These adipocytokinases may cause low-grade inflammation and have been connected to the pathophysiology of pulmonary abnormalities. For example, by regulating lung damage and repair, elevated leptin levels can contribute to weight gain associated with asthma. Furthermore, lung diseases were influenced by the development of IL-6 and tumor necrosis factor alpha (TNF alpha**) (Ji et al., 2017).**

Additional elements impacted by Dipeptidyl peptidase-4 (DPP-4) and sterol regulatory element binding proteins (SREBPs) are associated with obesity. Lipid production is regulated by the transcription factor SREBPS. It was divided into the categories of (SREPs1) and (SREPs2). Global lipid synthesis and growth are regulated by (SREBPs1a), a subunit of (SREBPs1). Conversely, (SREBPs1c) regulates the amount of fat and energy that is stored. However, a wide range of cell types, especially immune cells, express (DPP-4). It separated into a range of peptide hormones and chemokines that are involved in the pathophysiology of inflammation and the immune response **(Chen et al., 2018)**.

The objective of enhancing their quality of life, patients with obesity-related asthma should receive treatment. Medications controls how fat and carbohydrates are metabolized. They play a critical role in altering lipid metabolism, lowering total cholesterol, and decreasing the accumulation of body fat **(Murad et al., 2017)**. It can stop obesity before it starts **(Pala et al., 2020).** For the treatment of asthma, the medications function as an anti-asthmatic medication, and soon after administration, bronchodilation happens **(Showalter et al., 2018).**

2. Obesity

One of the biggest issues facing public health is obesity **(Showalter et al., 2018).** Numerous risk factors, including an imbalance between energy intake and expenditure, direct and indirect effects, gene-environment interactions, and social determinants of health, have been linked to it **(Abenavoli et al., 2019; Longo et al., 2019).** Social determinants of health include the settings in which people are born, raise, work, play, learn, and age. These factors can have an impact on risks to one's health, functioning, and quality of life **(Arroyo-Johnson & Mincey, 2016)**. Obesity has a significant impact on morbidity and mortality rates in the community **(Soliman et al., 2020)**. It raises the risk of a number of illnesses, including type 2 diabetes, hypertension, chronic kidney disease, cardiovascular disease, and a major risk factor for asthma in **(Ji et al., 2017; Longo et al., 2019; Yuan et al., 2018).** Body mass index (BMI) is typically used to categorize obesity **(Engin & Engin, 2017).** Body mass index (BMI) is computed as the kilogram of body weight divided by the square of one's height (kg/m2). Researchers and other healthcare professionals use it as a widely accepted standard procedure.

2.1. Effect of obesity in organs

Obesity is a medical condition brought on by having an excessive amount of body fat **(Yuan et al., 2018).** Obesity contributes significantly to the global burden of chronic disease such as cardiovascular disease, nonalcoholic fatty acid, type2 diabetes mellitus, asthma and some types of cancer **(Goossens, 2017).**

Moreover, obesity- related inflammation affects a number of organs, including a dispose tissue, the pancreas, liver, type2 diabetes mellitus, asthma and some types of cancer**,** skeletal muscles, the heart and the brain **(Goossens, 2017; Saltiel & Olefsky, 2017).**

2.2. Effect of obesity on adipose tissue

The body's primary lipid storage location is adipose tissue **(Goossens, 2017).**It is crucial to the control of systemic energy hemostasis and serves as a safe haven for excess fat. Adipocytes sense energy demands, secrete paracrine substances that regulate the activity of other metabolic tissues, and act as a source of energy storage and utilization .For example, in a high-energy state, adipocytes release leptin, which centrally reduces food intake and increases energy expenditure **(Longo et al., 2019).**

As a result, the ability of adipose tissue to store potential calorie surplus is necessary for the body to adapt to changes in caloric intake (**figure1**) **(Goossens, 2017).** In sustained positive energy balance conditions, adipocytes proliferate and enlarge to compensate for the need for greater lipid storage. The subcutaneous adipose tissue may not grow appropriately to absorb the excess energy storage in obese individuals. This flaw caused an unnatural accumulation of fat in other tissues **(Longo et al., 2019).**

2.3. Effect of obesity on HDL

Obesity raises the risk of developing dyslipidemia, hypertension, and coronary artery disease. When dyslipidemia is commonly characterized by high levels of triglyceride-rich lipoprotein and low levels of high-density lipoprotein cholesterol (HDL-C). In addition to abnormal HDL metabolism and changes in HDL distribution pattern, obesity has been linked to altered HDL levels **(Stadler & Marsche, 2020)**. A higher BMI has been linked to an increased risk of hypertriglyceridemia, high LDL cholesterol (LDL-C), and low HDL-C. Non-HDL cholesterol (non-HDL-C) and triglyceride (TG) levels are positively correlated with BMI **(Nienov et al., 2020).** The dysfunction of the HDL particles is the result of all these changes. Obesity-related modifications to HDL functionality and composition **(figure2) (Stadler & Marsche, 2020).**

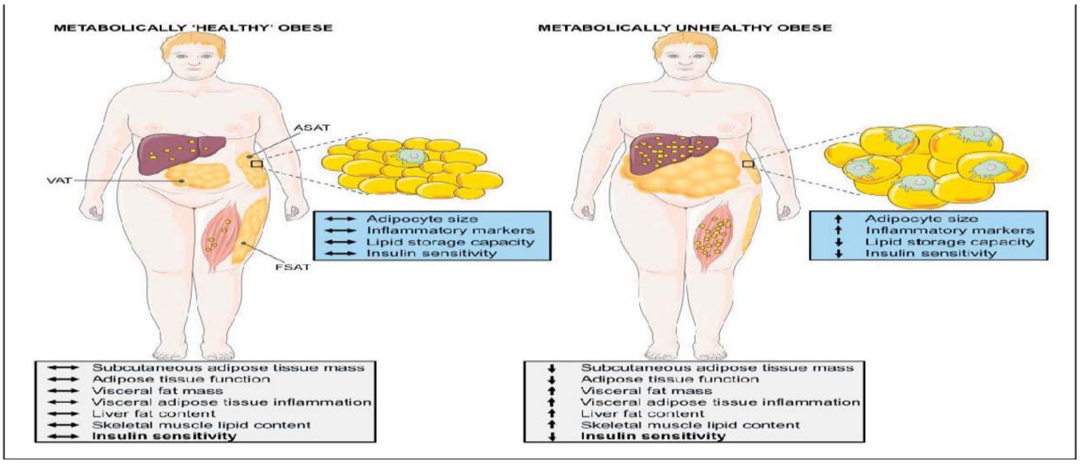

Figure 1. Lipids may be stored in subcutaneous adipose tissue before marked expansion of the visceral adipose tissue depot occurs **(Goossens, 2017).**

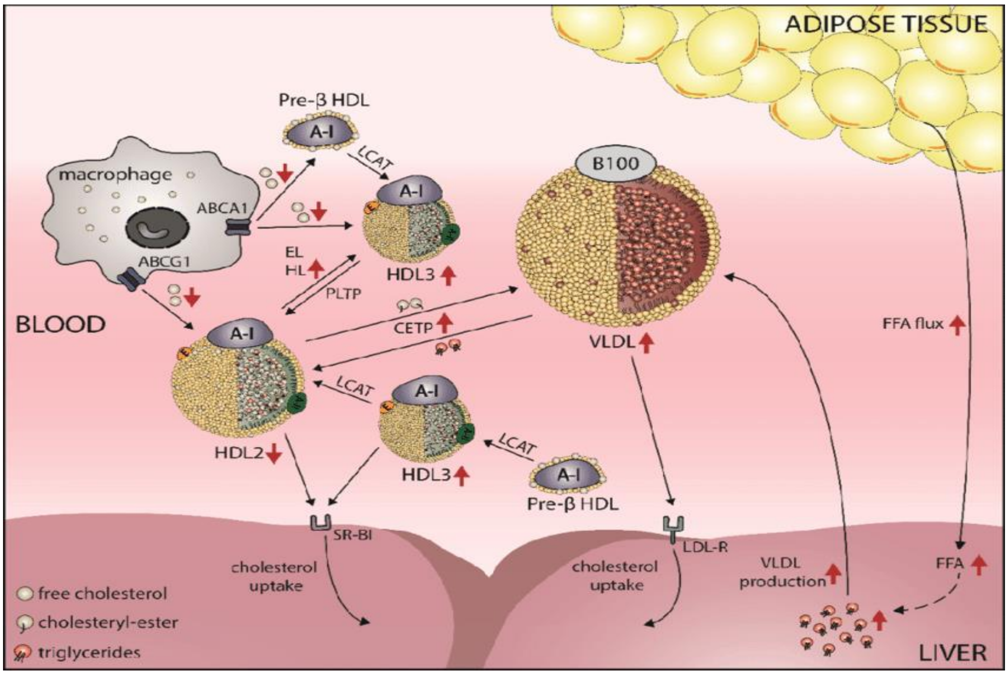

Figure2. Proposed mechanisms involved in the obesity-induced shift in HDL subclass distribution **(Stadler & Marsche, 2020).**

2.4. Effect of obesity on lungs

Medical conditions such as obesity and metabolic syndrome are frequently linked to a number of lung conditions, most notably asthma **(Showalter et al., 2018).** Asthma linked to obesity has become much more common and severe **(Yuan et al., 2018)**. The hallmark of bronchial asthma, a long-term inflammatory illness of the airways, is allergen-induced airway blockage. The late phase of obstruction, which appears 8–24 hours after allergen exposure, is linked to an influx of airway inflammatory cells. The early phase of obstruction is characterized by acute bronchospasm. Airway hyper responsiveness (AHR) and remodeling (structural alterations including subepithelial fibrosis and increases in goblet cell numbers and smooth muscle thickness) are markers of the severity of inflammation **(Murad et al., 2017)**.

Variations in wheezing, shortness of breath, chest tightness, and/or coughing, along with variations in expiratory airflow limitations, are characteristics of chronic inflammatory asthma. Numerous factors can trigger it, such as physical activity, contact with allergens or irritants, alterations in climate, or viral respiratory infections. Previous research demonstrating the strong association between these two illnesses shows that fat aggravates asthma. There has been a concerning increase in asthma cases linked to obesity in epidemiological studies conducted worldwide **(Yuan et al., 2018)**.

2.5. Obesity and lung abnormalities

The obesity epidemic is a serious public health concern, particularly in developed countries. Numerous problems, including adverse effects on the respiratory system, are associated with obesity, Obesity is a major disease modifier and risk factor for pulmonary hypertension, obesity hypoventilation syndrome (OHS), obstructive sleep apnea, and asthma. It also influences the course of acute respiratory distress syndrome (ARDS) and chronic obstructive pulmonary disease (COPD) **(Forno et al., 2018)**. Hospitalization rates are higher for obese patients with respiratory diseases compared to subjects of healthy weight. Obesity also increases susceptibility to respiratory infections **(Dixon & Peters, 2018)**.

Furthermore, The observed correlation between obesity and respiratory symptoms has been explained by a number of tenable mechanisms, including reduced lung volumes, increased airway resistance, decreased total respiratory system compliance, and altered ventilation and gas exchange.

Additionally linked to increased asthma incidence, asthma morbidity, and therapy resistance are overweight and obesity. Research indicates that obesity is associated with a later decline in lung function and that weight gain occurs before symptoms of asthma appear **(Forno et al., 2018)**.

3. Asthma

The common chronic airway disease known as asthma is characterized by varying airflow restriction caused by the concomitant thickening, constriction, hypersensitivity, and
increased mucus hypersecretion of the airways. Constriction of the airways is caused by both chronic manifestations (phenotypes) and complex pathophysiological pathways **(Bantulà et al., 2021).**

3.1. Dietary factor affecting asthma

The types of lifestyle modifications include dietary changes like cutting back on fresh fruit and vegetables while increasing access to processed fats and sweeteners made from carbohydrates. A number of theories have been proposed to explain how diet influences asthma, including low vitamin D levels, oxidative stress, epigenetic regulation, and an imbalance in the gut flora. Eating fruits and vegetables can reduce your chance of developing asthma.Several additional studies, irrespective of age or gender, corroborated the notion that obese patients had a higher chance of developing asthma than non-obesity subjects. The association is also stronger for those with central obesity as opposed to widespread obesity (**Bantulà et al., 2021).**

Diets high in fat may also worsen inflammation by changing gut flora. Therefore, by avoiding these inflammatory reactions to high-fat foods, a low-fat vegan diet that limits added oils and nuts may alleviate symptoms of asthma **(Alwarith et al., 2020).**

Moreover, a number of studies compared the relative risk population in the highest intake group for fruits and vegetables with participants in the lowest intake group.It was found that eating a lot of fruits and vegetables reduced the chance of developing asthma (**Alwarith et al., 2020).**

3.2. Pathophysiology and role of inflammation

A chronic inflammatory disease of the airways that is clinically heterogeneous, bronchial asthma is typified by restricted airflow and hyper-responsiveness to environmental stimuli. The intricate web of reciprocal influences formed by the regulatory mechanisms and consequences of inflammation in asthma includes a series of events that involve the irreversible remodeling of the bronchial wall by structural and infiltrating cells and their signaling molecule.

Moreover, Toll-like receptor-4 is activated by saturated fat, which triggers an inflammatory cascade and an immunological reaction. Reducing dietary saturated fat consumption was expected to lower neutrophilic airway inflammation in male asthma patients **(Pala et al., 2020).**

4. Asthma and Obesity: Two Linked Diseases

The epidemiological link between obesity and asthma was first proposed. A BMI of 30 kg/m2 or higher was found to significantly increase the risk of developing late-onset asthma in earlier studies. Several additional studies, irrespective of age or gender, corroborated the notion that obese patients had a higher chance of developing asthma than non-obesity subjects. The association is also stronger for those with central obesity as opposed to widespread obesity, per **(Bantulà et al., 2021).**

Similar to asthma, obesity is regarded as a pro-inflammatory condition. seems to be a complex relationship between obesity and asthma. However, it is noted that the underlying mechanisms and causality of this association remain unclear. Adults' BMI and lung volumes have an inverse relationship, suggesting that obesity causes a restrictive lung deficit. However, some research has also shown that adults with asthma have somewhat reduced FEV1/FVC **(Madeira et al., 2021)**.

5. Medications for treatment asthma and obesity

Obesity and asthma are complicated illnesses that frequently combine and affect each other's care and prognosis. These disorders have distinct pathophysiological pathways that overlap, and their pharmacological treatment needs to be customized to address these differences. The mechanisms of action, effectiveness, and possible adverse effects of the drugs used to treat obesity and asthma are covered in detail in this document**(Marko & Pawliczak, 2018)**.

5.1. Medications for asthma

5.1.1. Corticosteroids inhaled (ICS)

The inhaled corticosteroids act by preventing the release of inflammatory cytokines and other mediators, ICS lessen inflammation in the airways. Common medications in this class include beclomethasone, budesonide, and fluticasone. The effectiveness In terms of decreasing the frequency and intensity of exacerbations, inhaled corticosteroids (ICS) are the best long-term asthma control medicine. Oral thrush, hoarseness, and even systemic side effects such adrenal suppression during extended use are examples of adverse reactions **(Bel et al., 2014)**.

5.1.2. Long-Acting Beta Agonists (LABA)

The mechanism of action of this class is relaxing the smooth muscle in the airways, which results in long-term bronchodilation. When administered in conjunction with ICS, LABAs are effective in controlling moderate to severe asthma and preventing nighttime symptoms. If ICS are not taken, the side effects include tremors, tachycardia, and an increased risk of asthma-related death. Major drugs like salmeterol and formoterol**(Dixon&Peters,2018).**

5.1.3. Leukotriene modifiers

The way that it works is by preventing the body from producing leukotrienes, which are substances that exacerbate asthma attacks. Commonly Used Substances: monteplazast, zafirlukast. The effectiveness of them as they are used as an adjunctive therapy for mild to severe asthma and help reduce symptoms, particularly in patients who are experiencing exercise-induced bronchoconstriction. Headaches, nausea, and, in rare cases, psychological reactions like antagonism and sadness are possible adverse effects. **(Choi & Azmat, 2024)**.

5.2. Biologic therapies

The action's mechanism is Biologics target specific cells or pathways involved in the inflammatory process of asthma. Common drugs include mepolizumab and reslizumab (anti-IL-5), dupilumab (anti-IL-4Rα), and omalizumab (anti-IgE). When used to treat severe asthma that is not responding to other therapies, it is effective in significantly reducing exacerbations and improving quality of life. Possible side effects include allergic reactions, reactions at the injection site, and high expenses **(Fildan et al., 2021).**

5.3. Medications for obesity

5.3.1. Appetite Suppressants (Anorectics)

Method of Action Certain drugs reduce appetite by improving feelings of fullness or satiety. Common Substances such as Phentermine, Diethylpropion. The effectiveness for short-term weight loss when combined with lifestyle modifications. Increased blood pressure, heart rate, insomnia, and dependence risk are among the side effects **(Abdi Beshir et al., 2023)**.

5.3.2. Selective Serotonin Reuptake Inhibitors (SSRIs)

Although SSRIs are primarily used to treat depression, their mechanism of action alters appetite, which has an effect on weight. fluoxetine and sertraline are examples of common drugs. The effectiveness of medications may aid in weight loss for obese individuals, particularly those with binge eating disorders. The potential for weight gain over time, nausea, insomnia, and sexual dysfunction are among the side effects**(Ghusn et al., 2022**).

5.3.3. GLP-1 Receptor Agonists

Method of Action of these drugs are decrease hunger, suppress glucagon release, and boost insulin production by imitating the GLP-1 hormone. common drugs like ligglutide and semaglutide. They have shown significant weight loss effects and are beneficial for obese individuals with type 2 diabetes. Pancreatitis, nausea, vomiting, and a higher risk of thyroid cancer are possible side effects**(Tchang et al., 2000)**.

5.3.4. Lipase Inhibitors

The Way It Works Certain drugs reduce the amount of fat absorbed by inhibiting the lipase enzyme, which breaks down fat in the intestine. Commonly used like Orlistat. Moderate weight loss is achieved with possible long-term maintenance advantages. The negative consequences include oily stools, gas, and perhaps liver damage after prolonged use **(Abdi Beshir et al., 2023)**.

6. Conclusion

Asthma and obesity are both regarded as pro-inflammatory conditions. Asthma may occur in obese people due to systemic inflammation, which is a result of excess adiposity and plays a role in the physiopathology of many diseases. The greatest option for treating both asthma and obesity is to address both conditions together.

7. Future prospective of the study

The future perspective of treating asthma in the context of obesity holds promising advancements in personalized medicine and integrated care approaches. As our understanding of the genetic, molecular, and environmental factors that contribute to both conditions deepens, treatments are likely to become more targeted and effective. Personalized medicine, driven by biomarker research and genetic profiling, will enable healthcare providers to tailor treatments to individual patients, optimizing therapeutic outcomes and minimizing side effects.
This approach could lead to the development of new pharmacological agents that specifically address the unique pathophysiological mechanisms of asthma in obese individuals, such as drugs that simultaneously target metabolic dysregulation and airway inflammation. Moreover, the integration of digital health technologies, such as telemedicine and mobile health apps, will play a significant role in managing asthma and obesity concurrently. These technologies can facilitate better patient monitoring, adherence to medication, and lifestyle modification, allowing for real-time adjustments in treatment plans. The emphasis on multidisciplinary teams comprising pulmonologists, endocrinologists, dietitians, and behavioral therapists will enhance the comprehensive care of patients. In conclusion, the future of treating asthma in the context of obesity is likely to be characterized by more precise, effective, and patient-centered approaches, leveraging advances in science and technology to improve quality of life and health outcomes.

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