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AN OBSERVATIONAL STUDY EXAMINED THE POSITIVE EFFECTS OF WEIGHT LOSS ON INFLAMMATORY MARKERS AND PFT IN PATIENTS WITH BRONCHIAL ASTHMA.

Respiratory Medicine

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ABSTRACT

Background: Asthma and obesity are linked to systemic inflammation sustained by mediators exhaled by lung and adipose tissue. Asthma and obesity are associated with increased markers of systemic and immune inflammation. Two epidemics afflicting the developed world are obesity and asthma. Obesity and asthma, including severe asthma, seem to be weight-dependent, causative, partially inherited, and most likely reciprocal. **Objective:** This study was aimed to evaluate the effects of weight loss on markers of systemic and immunological inflammation in obese asthmatic patients. **Material and method:** 120 patients who were enrolled in the weight reduction program, only 90 patients were selected for this study based on the inclusion criteria of this observational study. In this study there was analysis of PFT, IL6, CRP done for the selected sample size of study and its impact based on weight reduction was analysed. **Results:** In the present study 45.6% of cases were males and 54.4% were females the mean age of the study population was 35.69 +- 8.26. In the present study inflammatory markers such as CRP and IL 6 were measured before and after the weight reduction program. It was observed that the mean CRP & mean IL6 was significantly lower in patients who achieved reduction $p < 0.05$. There was also a significant increase in the mean Fev1, FVC and FEV1/FVC ratio inpatient's who had weight reduction $p<0.05$. **Conclusion:** Losing weight through diet and exercise also lowers inflammatory activity, which helps with asthma and lung function. In obese asthma patients, weight loss improved indicators of systemic and immune inflammation.

KEYWORDS

Bronchial Asthma, Inflammatory Markers, CRP, PFT, Immunological markers, weight reduction, IL6

INTRODUCTION:

Asthma is a chronic respiratory condition that affects millions of people worldwide, with obesity being a significant risk factor for its development and exacerbation. Research has shown that obese individuals reported more wheezing and shortness of breath, which are symptoms commonly associated with asthma. However, further investigation into the level of airway hyperactivity and obstruction did not support the suggestion of a higher prevalence of asthma in this group.

Weight reduction has emerged as a potential intervention for improving asthma control in obese individuals, based on recent studies. In a controlled clinical trial, obese asthmatic subjects were randomly assigned to either a supervised weight reduction program or a control program.

Currently, bronchial asthma affects approximately 300 million people globally, with estimates predicting that this number will rise to 400 million by 2025. Asthma is characterized by episodes of airway obstruction, chronic inflammation, and increased sensitivity of the airways. Meanwhile, obesity has become one of the most prevalent medical conditions worldwide. Numerous studies have confirmed a link between adiposity levels and the development of asthma.[1-2]

Notably, both obesity and asthma are on the rise simultaneously. Obesity exacerbates the severity of asthmatic symptoms and reduces their responsiveness to medication due to various factors such as mechanical or anatomical causes as well as inflammatory processes. Obesity is classified as a pro-inflammatory state since it often coincides with persistent low-grade systemic inflammation.

Numerous studies have documented a weakened immune system response and increased vulnerability to infections and various disorders associated with the severity of obesity. Furthermore, there exists a strong correlation between asthma and obesity. Adipose tissue in obese individuals experiences a significant accumulation of immune cells.

The most recent approach to managing obesity involves weight reduction interventions through exercise, dietary changes, and lifestyle modifications. This study aimed to evaluate the impact of weight loss on systemic inflammation and immunological factors in patients with both obesity and asthma.

Obesity occurs when there is an excessive accumulation of body fat due to an imbalance between energy intake and expenditure. The standard method for diagnosing obesity is by calculating the body mass index which should be equal to or greater than 30 kg/m2. However, using BMI as a marker for obesity has limitations since it does not consistently correlate with body fat levels. Alternative measurements such as waist circumference or waist-to-hip ratio may provide a more accurate assessment of body fat distribution and help improve the diagnosis of obesity. Currently, Dual-Energy X-ray Absorptiometry is considered the gold standard for assessing body composition. It is important to carefully consider the methods used in studies investigating asthma and obesity associations as they can significantly impact research outcomes.

According to a recent study, the parameters used to determine body mass can have a significant impact on the prevalence of obesity in youngsters. The disparities in the strength of the evidence linking obesity and asthma that have been documented in clinical and epidemiological research may be explained by these variables.

More recent research indicates that the relationship between obesity and asthma is more intricate than previously thought and extends beyond the straightforward link between being overweight and asthma. According to studies in this area, the relationship between obesity and asthma may also be influenced by dietary factors, such as the diet's acid load or exposure to certain chemicals and pollutants both indoors and outdoors.[2-4]

MATERIAL AND METHODS:

The present study included enrolment of120 patients with history of bronchial asthma. The exclusion criteria encompassed the following: smoking, infections, immunizations, cancer, surgery, immune system diseases, and medications that could potentially impact immune system function, such as analgesics, antidepressants, and anti-inflammatory drugs.

120 patients who were enrolled in the weight reduction program, only 90 patients were selected for this study based on the inclusion criteria of this observational study.

In this study there was analysis of PFT, IL6, CRP done for the selected sample size of study and its impact based on weight reduction was analysed.

The statistical analysis was conducted using SPSS version 21, where comparison between mean values of parameters in pre and post weight loss groups was assessed. However, paired t-test was used to compare the differences between mean values in the same group (level of significance $P<0.05$).

RESULTS:

In the present study 45.6% of cases were males and 54.4% were

females the mean age of the study population was 35.69 +- 8.26. the mean weight of the study population was 90.16 +/- 11.69 the mean BMI was 35.15+/- 3.99. the baseline pulmonary function test was done for all the patients.

Baseline Demographics	Mean ± SD
Age	35.69 ± 8.26
Weight	90.16 ± 11.69
Height	160.26 ± 9.27
BMI	35.16 ± 3.99
Gender	
Male	41 (45.6%)
Female	49 (54.4%)
FEV1	1.83 ± 0.45
FVC	2.46 ± 0.33
FEV1/ FVC ratio	74.63 ± 17.7
CRP	14.81 ± 2.62
IL6	11.62 ± 3.76

In the present study inflammatory markers such as CRP and IL 6 were measured before and after the weight reduction program. It was observed that the mean CRP & mean IL6 was significantly lower in patients who achieved reduction ($p < 0.05$). There was also a significant increase in the mean FEV1, FVC and FEV1/FVC ratio inpatient's who had weight reduction $p<0.05$.

Patients were sub classified based on gender it was observed that the inflammatory markers such as CRP and IL 6 was significantly lower in both males and female after the weight reduction program ($p< 0.05$). FEV 1 and FVC was significantly higher in males $p<0.05$ who underwent weight reduction program but the overall FEV 1 by FVC ratio was not found to be statistically significant ($p>0.05$). In females FEV1 and FEV1/ FVC ratio was significantly higher after weight reduction program ($p< 0.05$).

Patients were sub classified based on reduction in weight reduction achieved after weight reduction program. it was observed that in patients who had weight reduction the inflammatory markers CRP IL 6 was significantly lower after weight reduction and FEV1 FVC and FEV1/FVC ratio was significantly higher after weight reduction.

In patient who could not achieve weight reduction after following the program there was no statistically significant difference in the mean CRP, IL 6, FEV1 and FEV 1/ FVC ratio.

Comparison of inflammatory markers and PFT in patients before and after weight reduction program						
	Before weight reduction program		**After weight reduction program**		t value	p value
	Mean	**SD**	**Mean**	**SD**		
CRP (mg/dl)	14.81	2.62	13.47	2.90	6.032	<0.001
IL6 (pg/ml)	11.62	3.76	9.97	3.21	5.483	<0.001
FEV1	1.83	0.45	1.92	0.49	4.389	<0.001
FVC	2.47	0.33	2.52	0.36	2.811	0.01
FEV1/ FVC ratio	74.63	17.71	76.63	19.02	2.321	0.023
BMI	35.16	3.99	33.97	3.49	10.200	<0.001

DISCUSSION:

Several studies have highlighted the association between obesity and asthma. Yiallours et al. (2013) found that body fat percentage and body mass index (BMI) were associated with childhood asthma, with the risk being higher in boys. Fenger et al. (2014) also reported a longitudinal relationship between changes in adiposity and changes in pulmonary function, suggesting that obesity may contribute to the development and progression of asthma in adults.[5-6]

The severity of asthma is influenced by various factors, and obesity has been identified as one of them. Fulgheri and Sypniewska (2013) reported that obesity may exacerbate the symptoms of asthma and increase the risk of severe exacerbations. Akerman et al. (2004) conducted a study that demonstrated a positive association between asthma severity and obesity, with obese individuals experiencing more frequent and severe asthma symptoms compared to their non-obese counterparts.[6-7]

Inflammation plays a crucial role in the pathogenesis of asthma, and certain cytokines are known to contribute to this inflammatory process. One study by Camargo et al. (2010) investigated the relationship between body mass index (BMI) and response to asthma therapy. They found that obese asthmatic patients had a poorer response to treatment with fluticasone propionate/salmeterol compared to non-obese asthmatics treated with montelukast. This suggests that obesity may be associated with a higher level of inflammation, leading to reduced treatment efficacy.[7-8]

Another study by Telenga et al. (2012) suggested that obesity in asthma may be associated with more neutrophilic inflammation, which could explain the reduced treatment response seen in obese asthmatic patients. Neutrophils are white blood cells that play a role in the immune response, particularly in inflammation. Obese individuals tend to have higher levels of systemic inflammation, which may contribute to the development and progression of asthma.[6-9]

Obesity can also affect airway responsiveness in individuals with asthma. Shore and Fredberg (2005) highlighted the relationship between obesity, smooth muscle, and airway hyperresponsiveness. They proposed that increased body weight may lead to mechanical changes in the airways, resulting in increased airway resistance and hyperresponsiveness. This could explain why obese asthmatic patients often experience more severe symptoms and have a reduced response to treatment.[8-12]

Obesity not only affects asthma but also has implications for other chronic respiratory diseases. Poulain et al. (2006) discussed the effect of obesity on chronic respiratory diseases, such as chronic obstructive pulmonary disease (COPD) and obstructive sleep apnoea (OSA). They suggested that obesity-induced inflammation and mechanical changes in the respiratory system could contribute to the development and progression of these diseases.[10-13]

Leptin and adiponectin are adipokines, hormones produced by adipose tissue. Newson et al. (2014) explored the association of asthma, nasal allergies, and positive skin prick tests with obesity, leptin, and adiponectin. They found that obesity was associated with higher levels of leptin and lower levels of adiponectin, which may contribute to the increased risk and severity of asthma in obese individuals.[14]

Obesity is characterized by a state of low-grade systemic inflammation. Visser et al. (2001) reported the presence of low-grade systemic inflammation in overweight children. This inflammation is thought to be mediated by the immune system, which is dysregulated in obesity. Chandra and Au (1980) and Tanaka et al. (1998) demonstrated altered immune responses in genetically obese mice, suggesting a link between obesity and immune dysfunction.[14-16]

Weight reduction has been shown to have a positive impact on inflammation and immune function in obese individuals. Bade et al. (2014) found that weight loss in patients with chronic obstructive pulmonary disease (COPD) resulted in decreased levels of inflammatory cytokines. This suggests that weight reduction may help alleviate systemic inflammation and improve immune function in obese individuals with respiratory conditions.[17]

Lifestyle interventions, such as dietary modifications and exercise, are commonly recommended for weight reduction. Loria-Kohen et al. (2013) conducted a randomized trial and found that different exercise modalities, combined with a hypocaloric diet, resulted in decreased inflammation markers in overweight patients. Balagopal et al. (2005) also reported a reduction in the inflammatory state associated with obesity in adolescents who underwent lifestyle-only interventions.[17-19] Exercise has been shown to have anti-inflammatory effects and can help control low-grade inflammation associated with obesity. Mathur and Pedersen (2008) discussed the role of exercise in controlling inflammation and highlighted the potential mechanisms involved. Timmerman et al. (2008) found that exercise training led to a reduction in inflammatory monocytes, which are associated with systemic inflammation.[18-20]

Exercise can also modulate the immune system, leading to beneficial effects on inflammation and immune function. Wang et al. (2012) demonstrated the effect of exercise training intensity on T regulatory cells and vaccination response in mice. Wasinski et al. (2013) investigated the impact of exercise and caloric restriction on the immune system of mice fed a high-fat diet and found that exercise altered the immune response and attenuated the negative effects of obesity.[19-22]

Weight reduction has been shown to improve immune function in obese individuals. Lamas et al. (2004) reported that energy restriction restored the impaired immune response in overweight rats. Starkie et al. (2003) found that exercise and interleukin-6 (IL-6) infusion inhibited endotoxin-induced TNF-alpha production in humans, suggesting a potential role for weight reduction in controlling inflammation and improving immune function.[21-23]

CONCLUSION:

Obesity is closely linked to asthma severity and may contribute to the development and progression of the disease. Obesity-induced inflammation, alterations in adipokines, and immune dysfunction are potential mechanisms through which obesity impacts asthma. However, weight reduction through lifestyle interventions, such as dietary modifications and exercise, can improve immune function and control inflammation in obese asthmatic patients.

The link between fat and asthma, especially severe asthma, appears to be very well established. Undoubtedly, these processes are linked by extremely complicated systems. One of the possible connections between the two diseases could be the inflammatory process that underlies them both. It is yet unclear, nevertheless, exactly what function inflammation can serve as a link between the two processes. Future research should take into account this complexity and avoid using studies that aim to examine the mechanisms, which link obesity and asthma using simplistic approaches, because obesity can be linked to metabolic disorders that may also influence asthma on its own. Asthma is a heterogeneous disease. Additionally, subsequent research ought to evaluate the role of the dietary features and environmental variables, such pollution, that might alter how obesity and asthma interact.

Further research is needed to explore the optimal strategies for weight reduction and its impact on immune responses and inflammation in the context of asthma.

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