Weight reduction improves immune system and inflammatory cytokines in obese asthmatic patients

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Abstract

Background: Activation of immunological and systemic inflammation markers are common in obesity and asthma.
Objective: The target of this study was to assess impact of weight reduction on immunological and systemic inflammation markers in obese asthma patients.
Material and methods: Eighty asthmatic patients of both sex; their age and body mass index (BMI) mean were 38.72 ± 7.14 year and 32.65 ± 3.18 Kg/m2 respectively. Exclusion criteria included smokers, infections, vaccinations, cancer, surgery, immune system disorders and medications that may influence immune system function as anti-inflammatory medications, analgesics and anti-depressant. All subjects were randomly enrolled in weight reduction group (group A) or control group (group B).
Results: The main findings in the present study indicated that weight reducing program in group (A) was associated with significant reduction in the mean values of IL6, TNF-α, and IL8 in addition to significant increase in the mean values of CD4 and CD8 cell count . However, findings of group (B) showed no significant changes. Moreover, Comparison between both groups at the end of the study revealed significant differences.
Conclusion: Weight reduction improved immunological and systemic inflammation markers in obese asthma patients.
Keywords: Bronchial asthma; cytokines; obesity; immune system; weight reduction.
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Introduction

Recently, bronchial asthma affects about 300 million subjects and this number will reach 400 million of worldwide subjects by 2025[1]. Asthma characterized with attacks of obstruction, chronic inflammation and airway hyper-responsiveness of airways[2]. However, obesity is a the most common medical problem worldwide[3,4]. Several studies confirm association between the degree of adiposity and asthma[5-7].

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Both obesity and asthma prevalence is increasing concomitantly[8]. Obesity elevates the severity of asthmatic symptoms[9] and reduce their response to medications[10,11], due to many mechanisms include mechanical, anatomical[12-14] or inflammatory causes[15,16]. Obesity is considered as a pro-inflammatory state as it is usually associated with persistent low-grade systemic inflammation[17].

Several studies reported impaired immune system response and high susceptibility for infections and many disorders related to the degree of obesity[18-21]. In addition, there is close relation between asthma and obesity[22]. Obese adipose tissue is the site of marked accumulation of immune cells[23-25].

Weight reduction intervention is the most recent management policy for control of obesity via exercise, diet regimen and life style modification[26]. The purpose of this research was to measure response of systemic inflammation and immunological parameters to weight loss in obese asthmatic patients.

Subjects and methods

Subjects

Eighty asthmatic patients of both sex; their age and body mass index (BMI) mean were 38.72 ± 7.14 year and 32.65 ± 3.18 Kg/m^2 respectively. Exclusion criteria included smokers, infections, vaccinations, cancer, surgery, immune system disorders and medications that may influence immune system function as anti-inflammatory medications, analgesics and anti-depressant. All subjects were randomly enrolled in weight reduction group (group A) or control group (group B) according to the CONSORT diagram that outline the details of the screening and randomization (figure 1). All participants signed the consent before joining the study. In addition, ethical clearance was obtained from the concerned committee of King Abdulaziz University.

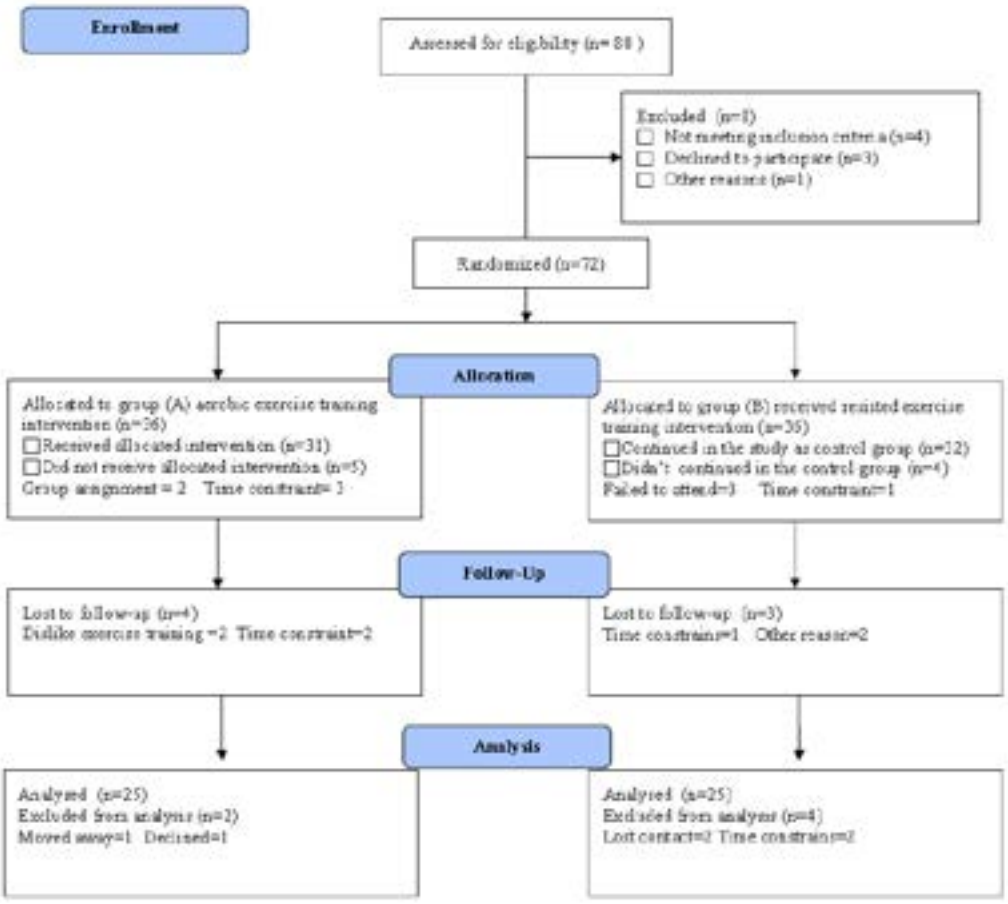

Figure (1) : Subjects screening and recruitment CONSORT diagram.

Measurements

A. Inflammatory cytokines: Overnight fasting venous blood sample will be drain and will be centrifuged at + 4 °C to measure interleukin -6 (IL-6) by "Immulite 2000" immunassay analyzer (Siemens Healthcare Diagnostics, Deerfield, USA). While, tumor necrosis factor-alpha (TNF-α) and interleukin- 8 (IL-8) were measured using ELISA.

B. Flow cytometry analysis: Immunological parameters CD4 and CD8 were measured by flow cytometry using Cytomics FC 500 and CXP software (Beckman Coulter).

Procedures

1. The training group (Group A) received aerobic treadmill exercise training for 12 weeks according to the standard recommendation of exercise training. Training session included warm up for 5 minutes, thirty minutes of 60-70% of maximum heart rate aerobic exercise training that followed by 10 minutes cooling down. Participants had 3 training sessions weekly for 3 months. Also, a dietician supervised diet regimen which provided 1200 Kilocalories/day for 3 months.
2. The control group (Group B) received no training intervention or diet control.

Statistical analysis

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

Results

The descriptive statistics proved that weight reduction group (group A) or control group (group B) were homogenous as there were no significant differences between both groups regarding the baseline criteria (table 1).

Table 1: Characteristics of participants in both groups.

Characteristic	Group (A)	Group (B)	Significance
Age (year)	39.57 ± 7.34	38.26 ± 6.81	0.021
BMI (kg/m^2)	31.72 ± 2.78	31.51 ± 3.23	0.018
SBP (mm Hg)	147.36 ± 10.14	145.17 ± 9.92	0.025
DBP (mm Hg)	86.64 ± 8.72	85.13 ± 7.25	0.009
Hemoglobin (gm/dl)	12.26 ± 2.83	12.48 ± 2.74	0.027
FVC (L)	2.82 ± 0.97	2.97± 0.83	0.013
FEV$_1$(L)	1.65 ± 0.86	1.83 ± 0.79	0.028
FEV$_1$/FVC (%)	57.91 ± 8.11	59.87 ± 7.32	0.011

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FVC= forced vital capacity; FEV_1= forced expiratory volume in the first second; FEV_1/FVC= Ratio between forced expiratory volume in the first second and forced vital capacity.

The main findings in the present study indicated that weight reducing program in group (A) was associated with significant reduction in the mean values of IL6, TNF-α, and IL8 in addition to significant increase in the mean values of CD4 and CD8 cell count (Tables 2). However, findings of group (B) showed no significant changes(table 3). Moreover, Comparison between both groups at the end of the study revealed significant differences (table 4).

Table 2: Mean value and significance of immune and systemic inflammation markers in group (A) before and after the study.

	Mean + SD		t-value	Significance
	Pre	Post		
BMI (kg/m^2)	31.72 ± 2.78	27.86 ± 2.42*	6.83	0.004
TNF- α (pg/mL)	11.97 ± 2.42	10.11 ± 1.93*	5.21	0.016
IL-6 (pg/mL)	4.78 ± 1.31	2.96 ± 1.12*	5.24	0.008
IL-8 (pg/mL)	16.52 ± 2.64	13.14 ± 2.15*	6.53	0.002
CD4 count (10^9/L)	1.32 ± 0.53	1.73 ± 0.64*	4.12	0.017
CD8 count (10^9/L)	0.61 ± 0.28	0.85 ± 0.39*	4.84	0.013

BMI: Body Mass Index; TNF-α: tumor necrosis factor – alpha; IL-6: Interleukin-6; IL-8: Interleukin-8; (*) indicates a significant difference, $P < 0.05$.

Table 3: Mean value and significance of immune and systemic inflammation markers in group (B) before and after the study.

	Mean + SD		t-value	Significance
	Pre	Post		
BMI (kg/m^2)	31.51 ± 2.85	32.75 ± 2.83	1.28	0.131
TNF- α (pg/mL)	11.64 ± 2.16	11.73 ± 2.24	0.93	0.084
IL-6 (pg/mL)	4.62 ± 1.23	4.85 ± 1.31	1.12	0.161
IL-8 (pg/mL)	16.48 ± 2.75	16.71 ± 2.88	1.25	0.214
CD4 count (10^9/L)	1.47 ± 0.56	1.32 ± 0.51	0.92	0.161
CD8 count (10^9/L)	0.66 ± 0.25	0.61 ± 0.23	0.85	0.245

BMI: Body Mass Index; TNF-α: tumor necrosis factor – alpha; IL-6: Interleukin-6; IL-8: Interleukin-8.

Table 4: Mean value and significance of immune and systemic inflammation markers in group (A) and group (B) after the study.

	Mean + SD		t-value	Significance
	Group (A)	Group (B)		
BMI (kg/m^2)	27.86 ± 2.42*	32.75 ± 2.83	6.71	0.013
TNF- α (pg/mL)	10.11 ± 1.93*	11.73 ± 2.24	5.93	0.018
IL-6 (pg/mL)	2.96 ± 1.12*	4.85 ± 1.31	4.55	0.009
IL-8 (pg/mL)	13.14 ± 2.15*	16.71 ± 2.88	5.76	0.006
CD4 count (10^9/L)	1.73 ± 0.64*	1.32 ± 0.51	4.74	0.015
CD8 count (10^9/L)	0.85 ± 0.39*	0.61 ± 0.23	4.65	0.024

BMI: Body Mass Index; TNF-α: tumor necrosis factor – alpha; IL-6: Interleukin-6; IL-8: Interleukin-8; (*) indicates a significant difference between the two groups, $P < 0.05$.

Discussion

Recently, millions of subjects are affected with asthma and obesity, therefore life style intervention is essential for clinical management of these population[28,29]. The present study aimed to detect to response of systemic inflammation and immunological parameters to weight loss in obese asthmatic patients. The main findings of this study indicated that weight reducing program resulted in modulation of immune system and inflammatory cytokines in asthma patients, our results agrred with manprevious researches[30-44].

A study conducted by Dandona et al. approved that TNF-α significantly reduced in obese subjects as result of weight reduction[30]. In addition, Sandoval and Davis found that approved that IL-6 reduced and insulin sensitivity improved following bariatric surgery[31]. While, Loria-Kohen et al. stated that weight reducing program resulted in reduced TNF-α and C-reactive protein (CRP)[32]. However, Balagopal et al. confirmed that three month life style intervention resulted in reduced level of IL-6, insulin resistance[33]. Moreover, an exercise program for 3 years resulted in reduction of body weight and TNF-α[34]. Similarly, You and Nicklas & Nicklas et al. weight loss by liposuction and life style intervention led to low level of CRP, TNF-α and IL-6[35,36]. Reduced mass of visceral fat and pro-inflammatory monocytes and increased number of regulatory T cells are the possible anti-inflammatory mecha¬nisms of weight reduction as result of exercise training[37-39].

Another main finding of our study, weight reduction was associated improved immunological parameters, these results agreed with Wasinski et al. reported that weight loss associated with low macrophage and greater number of CD8+ T and CD4+ T cells after exercise and diet control in mice[40]. In addition, Lamas et al. confirmed that one month of diet control significantly reduced body weight improved immunological parameters in overweight rats[41]. Reduction of serum level of pro-inflammatory cytokines as TNF-α , IL-6 and CRP[42-44], in addition to increased anti-inflammatory cytokines as IL-10 may be the mechanism for improved immunological parameters with weight reduction[43].

The main points of strength in current study were that all exercise sessions were supervised and the randomization of this study . In the other hand, the small sample size in both groups which limit the ability to generalize the findings of this study. Finally, it is recommended to have further studies to detect the impact of life style intervention in another biochemical parameters and quality of life in asthma patients.

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Conclusion
Weight reduction improved immunological and systemic inflammation markers in obese asthma patients.

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