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Impact of life style modification on inflammatory cytokines and immune system parameters among obese type 2 diabetic patients

Abstract

Background: Systemic inflammation and activated immune system response are common features in obese patients with non-insulin dependent diabetes mellitus (NIDDM) as obesity-induced NIDDM represents a burden for healthcare systems worldwide. However, there is a strong association between BMI and the human immune system and systemic inflammation among obese patients with NIDDM.

Objective: This study aimed to examine effects of weight reducing program on selected immune and systemic inflammation parameters among obese patients with NIDDM.

Material and methods: Eighty obese patients with NIDDM participated in this study, their age ranged from 41-52 years and their BMI ranged from 31-36kg/m2. All Subjects were included in two groups: The first group received life style modification in the form of treadmill aerobic exercises in addition to diet control where, the second group received no therapeutic intervention. Parameters of CD4 and CD8 cells count were quantified, IL-6, TNF-α, leptin and body mass index (BMI) were measured before and after 3 months at the end of the study.

Results: The mean values of CD4 and CD8 cells count were significantly increased, where mean values of TNF-α, IL-6, IL-8 and body mass index (BMI) were significantly decreased in group (A). While group (B) showed non-significant changes in these parameters. Also; there were significant differences between mean levels of the investigated parameters in group (A) and group (B) at the end of the study.

Conclusion: Within the limit of this study, life style modification modulates systemic inflammation and immunological parameters among obese patients with NIDDM.

Keywords: obesity, type 2 diabetes mellitus, immune system, cytokines, weight reduction, dysregulation, abdominal obesity, inflammation

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Introduction

Non-insulin dependent diabetes mellitus (NIDDM) is now a worldwide epidemic[1] as the number of peoples with NIDDM will be greater than 345 million by 2030 and this number is progressively increased in parallel with increasing the incidence of obesity.[2] Abdominal Obesity induces a state of low-grade systemic inflammation in addition to immune system activation that plays a role in the pathogenesis of metabolic disorders that are related to obesity and induces insulin resistance and hyperglycemia that results in NIDDM.[3–5]

Immune system performance was found to be altered among obese subjects and the degree of its deterioration is parallel to the degree of obesity which is noticed by increase the incidence of infections and cancer among obese subjects.[6,7] Many authors reported dysregulation and alteration in number of immune cells in obese subjects as elevated numbers of circulating immune cells as neutrophil, monocyte, leukocyte and total white blood cells.[8–11]

As there is limitation in studies reporting the benefits of lifestyle modification on immune system response among obese type 2 diabetic patients. This study aimed to examine effects of weight reducing program on selected immune and systemic inflammation parameters among obese patients with NIDDM.

Patients and methods

Subjects

Eighty obese patients with NIDDM; their age ranged from 41 to 52 years, treated with oral hypoglycemic agents e.g. metformin and/or pioglitazone were selected studied on referral to Internal Medicine Department, King Abdulaziz University Teaching Hospital, Saudi Arabia. Exclusion criteria included patients with renal, cardiac and liver diseases. All participants will be free to withdraw from the study at any time. Following pre-training testing, all participants were enrolled into two equal groups: group (A): received weight reduction program in the form of treadmill aerobic exercises in addition to diet control, where group (B): received no therapeutic intervention.

Measurements

The following measurements were taken before the study and after 12 weeks at the end of the study.

Inflammatory cytokines: Serum interleukin-6 (IL-6), interleukin-8

(IL-8) and tumor necrosis-alpha (TNF-α) levels were measured using ELISA microplate strip washer (ELX 50), and ELISA microplate reader (ELX 808; BioTek Instruments, USA).

Flow cytometry analysis: The leukocyte differentiation antigens CD4 and CD8 (Beckman Coulter, Marseille, France) the samples were analyzed by flow cytometry with Cytomics FC 500 and CXP software (Beckman Coulter).

Body mass index (BMI): The participants height was measured with a digital stadiometer and their body weight was measured on a calibrated balance scale (HC4211, Cas Korea, South Korea), and BMI was calculated as BMI=Body weight/(Height)^2.

Procedures

Following tacking the previous measurements , all participants were divided into two groups:

The training group received supervised treadmill aerobic exercise training for 3 sessions/week for 3 months on the treadmill which was conducted in line with the recommendation of exercise training approved by American College of Sports Medicine.[12] Each session included warming–up for 5 minutes in the form of stretching exercises and range motion, aerobic exercise training for 30 minutes with intensity equal 60-70% of the individual maximum heart rate followed by cooling down for 10 minutes. Also, a dietician performed an interview-based food survey for all participants of group (A) for detection of feeding habits, abnormal dietary behavior and to prescribe the balanced low caloric diet[13] that provided 1200 Kilocalories/day for 3 months. The same dietitian continuously monitored all participant caloric intakes through reviewing the detailed record of food intake every 2 weeks.[14,15] The control group (Group B) received no exercise intervention or diet regimen.

Statistical analysis

Statistical analysis Student paired "t" test was used to compare the mean values of the investigated parameters obtained before and at the end of the study in both groups, while the independent "t" test was used for the comparison between the two groups at the end of the study (P<0.05).

Results

Eighty obese patients with NIDDM completed the screening evaluation, none of the baseline characteristics differed significantly between the two groups as listed in (Table 1).

In the lifestyle intervention group (A) of NIDDM patients, the mean values of BMI, TNF-α, IL6 and IL8 were considerably reduced to significant levels, while the mean values of CD4 cell count and CD8 cell count were considerably increased to significant levels over the period of therapy (Tables 2). In the other hand, results of the control group (B) showed no significant changes (Table 3). Moreover, comparison between both groups found significant differences in the measured variables at the end of the study (Table 4).

Table 1 Baseline and demographic characteristics of all participants

Characteristic	Group (A)	Group (B)	Significance
Age (years)	46.71±5.26	47.35±6.13	P>0.05
BMI (kg/m^2)	32.43±3.82	31.56±4.11	P>0.05
SBP (mm Hg)	143.26± 8.91	144.16±7.35	P>0.05
DBP (mm Hg)	86.27±5.31	84.98±6.58	P>0.05
Fasting glucose (mg/dl)	125.12±7.36	123.73±6.52	P>0.05
HbA1c (%)	7.35±1.21	7.22±1.43	P>0.05
Total cholesterol (mg/dl)	190.74±10.33	193.97±9.66	P>0.05
HDL-cholesterol (mg/dl)	32.61±3.36	31.15±3.62	P>0.05
LDL-cholesterol (mg/dl)	134.14±7.22	136.13±7.16	P>0.05
Triglyceride (mg/dl)	155.88±11.34	158.17±10.32	P>0.05

Table 2 Mean value and significance of TNF-☐, IL-6, IL-8, BMI, CD4 cell count and CD8 cell count in group (A) before and at the end of the study

	Mean±SD		t-value	Significance
	Pre	Post		
BMI (kg/m^2)	32.43±3.82	28.24±2.76*	5.28	P<0.05
TNF- α (pg/mL)	13.16±2.87	9.13±2.45*	6.11	P<0.05
IL-6 (pg/mL)	5.49±1.25	3.61±1.28*	6.54	P<0.05
IL-8 (pg/mL)	17.12±3.24	14.22±3.19*	5.52	P<0.05
CD4 count (10^9/L)	1.21±0.66	1.56±0.78*	5.75	P<0.05
CD8 count (10^9/L)	0.57±0.27	0.88±0.36*	5.14	P<0.05

BMI, body mass index; TNF-☐, tumor necrosis factor -alpha; IL-6, interleukin-6; IL-8, interleukin-8; (*) Indicates a significant difference between the two groups, P<0.05

Table 3 Mean value and significance of TNF-☐, IL-6, IL-8, BMI, CD4 cell count and CD8 cell count in group (B) before and at the end of the study

	Mean+SD		t-value	Significance
	Pre	Post		
BMI (kg/m^2)	31.56±4.11	31.78±4.15	0.87	P>0.05
TNF- α (pg/mL)	12.52±3.18	12.77±3.14	0.96	P>0.05
IL-6 (pg/mL)	5.59±1.51	5.72±1.58	1.23	P>0.05
IL-8 (pg/mL)	17.66±3.34	18.01±3.41	1.47	P>0.05
CD4 count (10^9/L)	1.18±0.71	1.13±0.69	0.82	P>0.05
CD8 count (10^9/L)	0.55±0.26	0.54±0.27	0.73	P>0.05

BMI, body mass index; TNF-☐, tumor necrosis factor -alpha; IL-6, interleukin-6; IL-8, interleukin-8; (*) Indicates a significant difference between the two groups, P<0.05.

Table 4 Mean value and significance of TNF-☐, IL-6, IL-8, BMI, CD4 cell count and CD8 cell count in group (A) and group (B) at the end of the study

	Mean + SD		t-value	Significance
	Group (A)	Group (B)		
BMI (kg/m^2)	28.24 ± 2.76*	31.78 ± 4.15	5.71	P <0.05
TNF- α (pg/mL)	9.13 ± 2.45*	12.77 ± 3.14	6.26	P <0.05
IL-6 (pg/mL)	3.61 ± 1.28*	5.72 ± 1.58	6.82	P <0.05
IL-8 (pg/mL)	14.22 ± 3.19*	18.01 ± 3.41	5.63	P <0.05
CD4 count (10^9/L)	1.56 ± 0.78*	1.13 ± 0.69	5.85	P <0.05
CD8 count (10^9/L)	0.88 ± 0.36*	0.54 ± 0.27	5.7	P <0.05

BMI, body mass index; TNF-☐, 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, there is a growing concern for NIDDM as the next big therapeutic challenge because of the possible evolution of NIDDM toward different medical complications. The novel of this study is that although exercise and diet improvement may reduce the overall magnanimity of insulin resistance, hyper lipidemia and abnormal cytokine metabolism, there has been only limited research on the effects of weight reduction as the sole intervention on these abnormal biochemical parameters in individuals with NIDDM. However, the limitation of this study is no recoding of the histological changes to the treatment intervention. This trial was designed to detect response of the immune and systemic inflammation parameters to weight loss in obese patients with NIDDM. Mean values of TNF-α, IL-6, IL-8 and BMI reduced significantly in group (A), where the mean value of CD-4 cell count and CD-8 cell count were significantly increased, while there were no significant changes in group (B). Also; at the end of the study there was a significant difference between both groups, the findings of the present study are in line with many previous studies.[16–23]

Results of our study was confirmed with Dandona et al.[24] Who reported that weight loss reduces TNF-α in obese.[24] Also, Sandoval and Davis approved that patients who had bariatric surgery gained reduction in IL-6 concentration and improved insulin sensitivity in parallel to weight loss.[25] However, Loria-Kohen and colleagues conducted a study of weight reducing program of combined diet regimen and exercise training that resulted in significant reduction in the values of inflammatory cytokines.[16] Also, Balagopal et al.[17] reported that obese adolescents who underwent a 3-month lifestyle intervention of enhanced physical activity and nutrition habits had decreased body fat percentage, insulin resistance and IL-6.[17] Likewise, an exercise intervention of 3 years, which gave detailed advice in regard to physical activity, in 60 obese women, resulted in weight loss along with decreased levels of TNF-α.[18] Moreover, You and Nicklas et al.[19,20] and colleagues stated that loss of weight led to remarkable reduction in systemic inflammation parameters.[19,20] The three possible mechanisms of exercise anti-inflammatory effects include reduction in visceral fat mass,[21] reduction in pro-inflammatory monocytes[22] and an increase in the regulatory T cells numbers.[23] Restoration of immune function as a result of weight reducing program is major finding in the present study which agreed with several previous studies suggesting improvements in body composition promote the modulation of immune system markers.[26–30]

Finally, the present study was randomized; so that, we can extrapolate adherence to the NIDDM general population. In the other hand, the major limitation is the small sample size in both groups may limit the possibility of generalization of the findings in this study. So that within the limit of this study, life style modification modulates systemic inflammation and immunological parameters among obese patients with NIDDM.

Conclusion

Within the limit of this study, life style modification modulates systemic inflammation and immunological parameters among obese patients with NIDDM.

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Conflict of interest

The author declares no conflict of interest.

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