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Metabolic Control Response to Weight Reduction in Obese Non-Insulin Dependent Diabetic Patients

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Abstract: Obesity is common in non-insulin dependent diabetic patients and weight loss produces a significant health gains. The aim of this study was to determine the metabolic response following weight reduction in obese non insulin dependent diabetic patients. Forty obese non-insulin dependent diabetics participated in this study and divided into two equal groups; the first group (A) received physical training combined with dietary measures and medical treatment. The second group (B) received only medical treatment and no physical therapy intervention. The program consisted of three sessions per week for three months. There was a significant increase in glcocylated hemoglobin (HBA_1c) and decrease in Body Mass Index (BMI) and leptin of group (A), while the results of group (B) were not significant. There was a significant difference between both groups. There was a strong direct relationship between the leptin, HBA_1c and BMI in both groups. So, weight reduction via physical training and diet regimen is an effective treatment policy to improve the metabolic control in obese diabetic patients.

Key words: Metabolic control · Obesity · Diabetes and Weight reduction

INTRODUCTION

Obesity must be considered as a disease in its own right but is also a risk factor for other diseases, as a result of overweight and the frequently associated metabolic disorders [1].Obesity treatment has increasingly focused on the therapeutic qualities of exercise. Benefits of exercise include an increase in fitness, increased energy output and improvement in obesity-related metabolic abnormalities [2].

Skeletal muscle insulin resistance is a hallmark of obesity and type 2 diabetes and these conditions are usually accompanied by poor physical working capacity and low maximum oxygen uptake (VO_2max). Exercise training has been suggested to improve glucose tolerance and insulin action in patients with type 2 diabetes. But it is not really known how much exercise is required to achieve this effect. Although there have been many studies on the effect of exercise in patients with type 2 diabetes, their results have varied [3].

American Diabetes Association (ADA) recommends screening patients older than 45 years with a body mass index (BMI) greater than or equal to 25 for diabetes with fasting glucose every 3 years. Obesity independently increases the risk of developing diabetes 10-fold compared with that for patients who are normal weight [4]. Diabetes mellitus is a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both [5].

Prevention of weight gain must be a part of any obesity treatment as even a relative small weight loss produces a significant health gain [6]. There is strong evidence that weight loss in overweight and obese individuals improves risk factor for diabetes [7].

Weight management program must include dietary adjustment, increase physical activity and behavior modification.Long term maintenance of weight loss with meal replacement improves markers of disease risk and reduced the metabolic risk factors in obese women [8].

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Leptin is produced by adipose tissues, signals body fat content to the hypothalamus. Serum leptin usually elevated in obese humans and decreased with weight loss [9]. Leptin contributes to the regulation of both food intake and energy expenditure. It is elevated in most obese humans; there is a significant positive correlation between leptin values and BMI. Short term weight loss in the treatment of childhood obesity reduces leptin and adipose tissue [10].

Moderate amounts of physical activity were reported to have a role in reducing the burden of hyperinsulinemia and diabetes. Circulating leptin was reported to be low in trained subjects and closely related to body fat content [11].

Exercise is a powerful tool in the management of insulin resistance and diabetes. Experimentally, exercise is known to improve insulin sensitivity, an effect that may last for 24 to 48 hours after a single bout of exercise. Exercise also can improve skeletal muscle lipid metabolism, induce mitochondrial biogenesis and increase the expression and activity of the enzymes involved in fatty acid oxidation. Furthermore, Exercise typically reduces systemic insulin concentration and can improve hepatic and adipose tissue insulin sensitivity [12].

Low caloric diets are effective in improving glycemic control and blood lipids through weight loss in overweight loss in overweight non insulin dependent diabetes mellitus patients [13].

Prospective studies on diabetes have been shown that improve glycemic control is associated with sustained decreased rates of retinopathy, nephropathy and neuropathy [14].

The level of glycated hemoglobin in a blood sample provides a glycemic history of the previous 120 days (the average erythrocyte life span).Also; glycated hemoglobin most accurately reflects the previous 2-3 months of glycemic control [15].

Leptin is the major regulator of body fat. It is a protein released by fat cells into blood and crosses the blood –brain barrier (BBB) to interact with its receptors at the accurate nucleus to affect feeding, thermogenesis and other functions.Within normal and obese body weight ranges,serum and cerebrospinal fluid (CSF) levels of leptin directly correlate with body mass index [16].

The aim of this study was to determine the metabolic response following weight reduction in obese non insulin dependent diabetic patients.

MATERIALS AND METHODS

Subjects: Forty obese non-insulin dependent diabetic patients of both sexes with total body obesity (body mass index (BMI) ranged from 31 to 37 Kg/m^2, free from respiratory, kidney, liver and neurological disorders. Subjects were not smokers and not receiving drugs except diabetic medications. Their age ranged from 40 to 56 years. The subjects were included into 2 equal groups; group (A) received medical treatment, physical training combined with dietary measures. The second group (B) received only medical treatment, asked to maintain their ordinary life style and received no physical therapy intervention. Informed consent was obtained from all participants. All participants were free to withdraw from the study at any time. If any adverse effects had occurred, the experiment would have been stopped, with this being announced to the Human Subjects Review Board. However, no adverse effects occurred and so the data of all the participants were available for analysis.

Methods

Evaluated Parameters

Chemical Analysis: Blood sample after fasting for 12 hours blood sample was taken from each women in clean tubes containing few mg of K2EDTA, centrifuged and plasma was separated and stored frozen at -20° used for estimation of plasma leptin level by immunoradimetric assay (IRMA) and glycosylated hemoglobin (HBA_1c) using colorimetric method.

Evaluation of Anthropometric Parameters: All measurements were performed at pretreatment and after three months at the end of the study. The participants were measured whilst wearing their undergarments and hospital gowns. Height was measured with a digital stadiometer to the nearest 0.1 cm (JENIX DS 102, Dongsang, South Korea). Body weight was measured on a calibrated balance scale to the nearest 0.1 kg (HC4211, Cas Korea, South Korea) and BMI was calculated as Body weight/$Height^2$.

Weight Reduction Methods

The Prescribed Low Calorie Diet: The interview-based food survey was performed for all patients by dieticians to specify previous food habits and possible anomalies in dietary behavior. The prescribed low calorie diet was balanced, with 15% as protein, 30 to 35% as fat and 50 to

55% as carbohydrate, on average, in order to provide about 1000 calories daily for two months for whole participants in this study.

The prescribed diet included the breakfast consisted of 2 boiled eggs (80.calorie), 50 gm cheese (100 calorie) and one bread (105 calorie), where the lunch consisted of 2 pieces of boiled meat 100gm (240 calorie) or chicken (300), 500 gram salad (105 calorie), 300 gram boiled vegetables (110 calorie) 100 gram and banana (100 calorie), However, the dinner consisted of 200 gram light milk (120 calorie).

We checked that food was eaten as three daily meals and we emphasized the need to have a substantial breakfast. The two groups underwent an identical dietary monitoring programme, with an initial consultation, a check-up in the middle of the programme and another during the final sessions by a dietician who was blinded to the type of the programme that the subject had been following.

The Physical Training Programme: The aerobic treadmill-based training programme (Enraf Nonium, Model display panel Standard, NR 1475.801, Holand) was set to 65% of the maximum heart rate (HRmax) for one month and increased gradually for 85% of maximal heart rate during the second month of the program achieved in a reference ST performed according to a modified Bruce protocol. This rate was defined as the training heart rate (THR).After an initial, 5-minute warm-up phase performed on the treadmill at a low load, each endurance training session lasted 30 minutes and ended with 5-minute recovery and relaxation phase. All patients performed three weekly sessions (i.e. a total of 36 sessions per patient over a 3-month period.

Statistical Analysis: The mean values of BMI, Leptin and glcocylated hemoglobin (HBA_1c) obtained before and after three months in both groups were compared using paired "t" test. Independent "t" test was used for the comparison between the two groups ($P<0.05$). Pearson’s product moment correlation coefficients (r) were applied to examine the degree of correlation among body mass index (BMI), leptin and glcocylated hemoglobin (HBA_1c).

RESULTS

Forty obese non-insulin dependent diabetics participated in this study and divided into two equal groups; the first group (A) received physical training combined with dietary measures and medical treatment. The second group (B) received only medical treatment and no physical therapy intervention in order to determine the metabolic response following weight reduction in obese non insulin dependent diabetic patients.

Measurements of BMI, Leptin and HBA_1c obtained before and after three months in both groups were compared using paired "t" test. The mean BMI and Leptin values were significantly lower in group (A), while the results of group (B) were not significant (Table 1 and 2). There was a significant difference between both groups after treatment (Table 3). Also, there was a strong direct relationship between the Leptin, HBA_1c and BMI in both groups (Table 4 and 5). So, weight reduction via physical training and diet regimen is an effective treatment modality to improve the metabolic control in obese diabetic patients.

Table 1: Comparison of mean value, standard deviation and p-value of BMI, leptin and HBA_1c in group (A) before and after treatment

	Mean±SD			
	Before	After	T-value	P-value
BMI (kg /m^2)	36.42±3.25	32.15±2.89	7.45	<0.05
Leptin (ng/ml)	41.67±3.80	35.32±3.14	6.82	<0.05
HBA_1c (%)	8.57±1.16	6.88±0.78	5.68	<0.05

BMI= Body Mass index HBA_1c = glcocylated hemoglobin.

Table 2: Comparison of mean value, standard deviation and p-value of BMI, leptin and HBA_1c in group (B) before and after treatment

	Mean±SD			
	Before	After	T-value	P-value
BMI (kg /m^2)	36.42±3.25	35.98±2.76	0.87	>0.05
Leptin (ng/ml)	41.67±3.80	40.85±3.24	0.92	>0.05
HBA_1c (%)	8.57±1.16	8.14±0.88	0.84	>0.05

BMI= Body Mass index HBA_1c = glcocylated hemoglobin

Table 3: Comparison of mean value, standard deviation and p-value of BMI, leptin and HBA_1c in group (A) and group (B) after treatment

	Mean±SD			
	Group A	Group B	T-value	P-value
BMI (kg /m²)	32.15±2.89	35.98±2.76	3.03	<0.05
Leptin (ng/ml)	35.32±3.14	40.85±3.24	3.89	<0.05
HBA_1c (%)	6.88±0.78	8.14±0.88	3.50	<0.05

BMI= Body Mass index HBA_1c = glcocylated hemoglobin

Table 4: Shows the Pearson's correlation coefficients test value and the relationship between the grade of BMI, leptin and glcocylated hemoglobin (HBA_1c) in group (A)

Test	Pearson's value	Relationship to glcocylated hemoglobin (HBA_1c [%])
BMI (kg /m²)	0.93	Strong direct relationship
Leptin (ng/ml)	0.94	Strong direct relationship

Table 5: Shows the Pearson's correlation coefficients test value and the relationship between the grade of BMI, leptin and glcocylated hemoglobin (HBA_1c) in group (B)

Test	Pearson's value	Relationship to glcocylated hemoglobin (HBA_1c [%])
BMI (kg /m²)	0.91	Strong direct relationship
Leptin (ng/ml)	0.89	Strong direct relationship

DISCUSSION

This study was designed determine the metabolic response following weight reduction in obese non insulin dependent diabetes mellitus patients. Forty obese non-insulin dependent diabetic patients participated in this study and divided into two equal groups; group (A) received diet regimen, exercise training and medical treatment. Where group (B) received only medical treatment.

The results of this study indicated that there was a significant increase in values of glcocylated hemoglobin (HBA_1c) and decrease in BMI and leptin of group (A), while the results of group (B) were not significant. There was a significant difference between both groups. Also, there was a strong direct relationship between the grade of BMI, leptin and glcocylated hemoglobin (HBA_1c) in both groups.

Multiple mechanisms appear to contribute to the apparent beneficial effects of aerobic exercise in the management of non-insulin dependent diabetes mellitus which include enhanced glucose uptake, oxidation and storage as glycogen.Also, insulin increases muscle blood flow and mitochondrial oxidative capacity and reduces body fat.

Exercise causes long term weight loss and decrease in BMI in obese diabetic patients. This weight loss was due to enhanced fat oxidation [17].

Abdominal obesity has been shown to be associated with metabolic disorders including hyperinsulinemia, insulin resistance, hyperglycemia and dyslipidemia. Habitual endurance exercise training has been shown to prevent the accumulation of intra-abdominal fat [18].

The essential components of a weight loss or weight management program include: calorie reduction, appropriate exercise, variety in food choices, increased consumption of grains, fruits and vegetables and reduction of fat intake to no more than 30% of daily calories [19]. Low caloric diets with an average intake between 400-800 kcal with active follow up of treatment seems to be one of the better treatment modalities related to long term weight maintenance success [20].

The development of very low caloric diet has provided an alternative approach to the treatment of uncomplicated obesity and is increasingly being used to treat obese non insulin dependent diabetes mellitus. Metabolic benefits occur quickly with only modest weight reduction [21].

Leptin is recognized to play an integral role in endocrine regulation of metabolism.It is clearly evident that leptin is decreased during calorie restriction [13]. Have reported higher serum leptin levels in obese non –diabetic subjects.The serum leptin levels were reduced after weight reduction as Plasma leptin concentrations correlated with BMI [22].

Circulating leptin is low in trained subjects and closely related to fat contents. Single exercise session of varying energy expenditure decreased the plasma leptin concentration after 48 hours in association with a preceding decrease in insulin [23].

Physical activity may be a significant determinant of plasma leptin concentrations in men.Increasing physical activity was associated with lower plasma leptin concentrations even after adjusting for BMI. Physical activity may lower leptin concentrations not only due to decreased body fat mass but potentially through an increase in leptin sensitivity [24].

Increased physical activity leads to improvement in insulin resistance and increase in muscle oxidative capacity which are likely contribute to the beneficial effects of exercise training on insulin action [25]. Physical activity in obese non-insulin dependent diabetes mellitus decreased blood glucose level through improving insulin sensitivity and decreasing deposition of total fat and intra-abdominal fat. Also, physical activity is negatively associated with insulin concentration as a defense mechanism [26].

Exercise promotes favorable energy balance and reduced visceral fat deposition through enhanced basal metabolism and activity levels while counteracting age and disease –related muscle wasting.Exercise training improves insulin sensitivity and glycemic control, increases muscle mass, strength and endurance [27].

It was found that physical exercise promotes utilization and lowering of blood glucose. This improvement in insulin action was attributed to the increase in insulin sensitive glucose transporter on the plasma membrane and oxidative enzymes in skeletal muscle [28] and [29].

Management of the obese diabetic patient involves glycemic control and weight reduction. Lifestyle modifications with diet and exercise are essential part of the management of the diabetic obese patient As Weight loss leads to improvement in the glucose tolerance, insulin sensitivity, reductions in lipid levels [30].

The two most important factors contributing the development of NIDDM are obesity and physical inactivity. Current therapies for NIDDM focus primarily on weight reduction. Weight reduction program (diet restriction and exercise) induced significant reductions in body weight and serum leptin levels and improvements in lipoprotein profile and glucose control in a study conducted on 35 obese NIDDM patients for 12 weeks men [31].

CONCLUSION

Lifestyle intervention programs encompassing exercise and healthy diets are an option for the treatment and management of obese diabetic patients and have long been known to exert beneficial effects on whole-body metabolism, in particular leading to enhanced insulin-sensitivity and metabolic control.

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