Impact of Weight Loss on Metabolic Control in Obese non-insulin Dependent Diabetic Patients: A Correlational Study

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ABSTRACT

Background: *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 diabetes mellitus patients.* ***Subjects and methods:*** *Forty obese non-insulin dependent diabetes mellitus patients participated in this study and divided into two equal groups; the training group received diet regimen, exercise training and medical treatment. Where the control group received only medical treatment. Measurements of body mass index (BMI), leptin and glycated hemoglobin (HBA_1c) were taken before starting of the study and repeated at the end of the study (after three months).* ***Results:*** *There was a significant decrease in values of BMI, leptin and HBA_1c of the training, while the results of the control group were not significant. There was a significant difference between both groups.* ***Conclusion:*** *In obese non-insulin dependent diabetic patients, BMI, leptin and HBA_1c could be considered as a valuable marker for assessment of metabolic control which is improved by weight loss. Serum leptin might be a marker for maintaining weight loss.*
Key words: *Metabolic control, Obesity, leptin, Diabetes and Weight reduction.*

INTRODUCTION

Diabetes mellitus is a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, specially the eyes, kidneys, nerves, heart and blood vessels[3].

Prevention of weight gain must be a part of any obesity treatment as even a relative small weight loss produces a significant health gains[19]. There is a strong evidence that weight loss in overweight and obese individuals improves risk factor for diabetes[22]. 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[17].Obesity is the result of a long standing imbalance between energy intake and energy expenditure aided by a complex biologic system that regulates appetite[5].

Leptin is produced by adipose tissues, signals body fat content to the hypothalamus. Serum leptin is usually elevated in obese humans and is decreased with weight loss[16]. 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[13].

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[21].

Low caloric diets are effective in improving glycemic control and blood lipids through weight loss in overweight non insulin dependent diabetic patients[14].Prospective studies on diabetes have been shown that improved glycemic control is associated with sustained decreased rates of retinopathy, nephropathy and neuropathy[2].

The level of glycated hemoglobin (GHb) in a blood sample provides a glycemic history of the previous 120 days (the average erythrocyte life span) .Also; GHb most accurately reflects the previous 2-3 months of glycemic control[8].

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[4].Hyperleptinaemia have been demonstrated to correlate with hyperphagia, insulin resistance and other markers of metabolic syndrome including obesity, hyperlipidemia and hypertension[24].Leptin has been proposed to potentially contribute to obesity related hypertension[18].

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

SUBJECTS, MATERIAL AND METHODS

Subjects

Forty obese non-insulin dependent diabetic patients of both sexes were selected, their age ranged from 45-56 years, their body mass index (BMI) ranged 31-37 Kg/m^2. This study was conducted at Kaser El-Aini Hospital in the Rehabilitation and Fitness Department. After obtaining consent; patients were randomly allocated by means of a random numbers to one of two equal groups.

Equipments and measurements

1-Glass tubes containing few milligram of K2EDTA an anticoagulant material.
2-Centrifuge to separate plasma.
3-Commercial Kites to measure leptin hormone by ELISA and glycated hemoglobin (HBA_1c) using colorimetric method.
4-Freezer to store the samples.
5-Weight and height scale (Metro type – England) was used to measure weight and height to calculate the body mass index (BMI). Body mass index was calculated by dividing the weight in kilograms by the square of the height in meters (Kg/m^2). According to the WHO classification, a BMI of <18.5 kg/m^2 is under weight, 18.5-24.9 kg/m^2 is normal 25-29.9 kg/m2 is overweight. A BMI of > 30 kg/m^2 is classified as obese and this group was further divided into moderate obesity (30-34.9 kg/m^2), sever obesity (35-39.9 kg/m^2) and very sever obesity ($\leq$40 kg $/m^2$)[11].
6-Treadmill (Enraf Nonium, Model display panel Standard, NR 1475.801, Holand) was used in performance of walking exercise.

Measurements of body mass index (BMI), leptin and glycated hemoglobin (HBA_1c) were taken before starting of the study and repeated at the end of the study (after three months).

Statistical Analysis

The mean values of body mass index (BMI), leptin and glycated hemoglobin (HBA_1c) obtained before and after three months in the control and the training 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 glycated hemoglobin (HBA_1c).

PROCEDURES

The sample was divided into two equal groups

Group 1(The experimental group): received diet regimen, exercise training and medical treatment. Each subject participated in:

1-The bicycles ergometer training: The session began with 5 minutes of aerobic exercise in the form of stretching exercise and walking in places (warm-up). Then the subject started the bicycle ergometer training for 40 minutes with an intensity of 65% of maximal heart rate for one month and increased gradually for 85% of maximal heart rate during the third month of the program. The workload was gradually reduced over 5 minutes (Cool down), three sessions per week.

2-Diet regimen: The diet regimen was applied in association with the exercise training; the diet regimen was to limit calories given to each subject to be 1000 kcal/day.

Group 2 (The control group): received only medical treatment and asked to maintain their ordinary life style.

RESULTS

This study included forty obese non-insulin dependent diabetic patients divided into two equal groups; the training group received diet regimen, exercise training and medical treatment. Where the control group received only medical treatment. Measurements of body mass index (BMI), leptin and glycated hemoglobin (HBA_1c) were taken before starting of the study and repeated at the end of the study (after three months).

Table (1) and figure (1) show the difference between pre and post test values of BMI, HBA_1c and leptin in the training group. There was a significant reduction in BMI, Leptin and in HBA_1c (P value <0.05).

Table (1): Show the difference between the pre and post values of BMI, leptin and glycated hemoglobin (HBA_1c) in the training group

	Mean ±SD		T-value	Significance
	Pre	Post		
BMI (kg /m^2)	36.42±3.25	32.15±2.89	-7.45	Sig
Leptin (ng/ml)	41.67±3.80	35.32±3.14	-6.82	Sig.
HBA_1c (%)	8.57±1.16	6.88±0.78	-5.68	Sig.

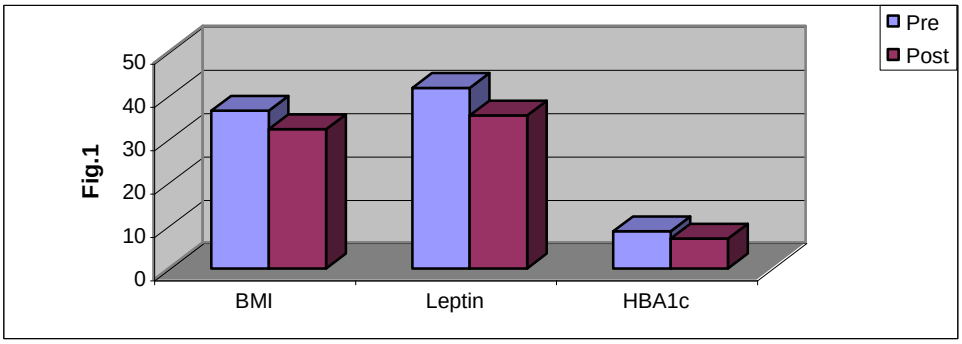

Fig. (1): Show the difference between the pre and post values of BMI, leptin and glycated hemoglobin (HBA_1c) in the training group.

Table (2) and figure (2) show the difference between pre and post test values of BMI, HBA1c and leptin in the control group. There was a non-significant change in BMI, Leptin and HBA1c (P value<0.05).

Table (2) and figure (2): Show the difference between the pre and post values of BMI, leptin and glycated hemoglobin (HBA_1c) of the control group.

	Mean ±SD		T-value	Significance
	Pre	Post		
BMI (kg /m^2)	36.42±3.25	35.98±2.76	-0.87	Non Sig
Leptin (ng/ml)	41.67±3.80	40.85±3.24	-0.92	Non. Sig.
HBA_1c (%)	8.57±1.16	8.14±0.88	-0.84	Non Sig.

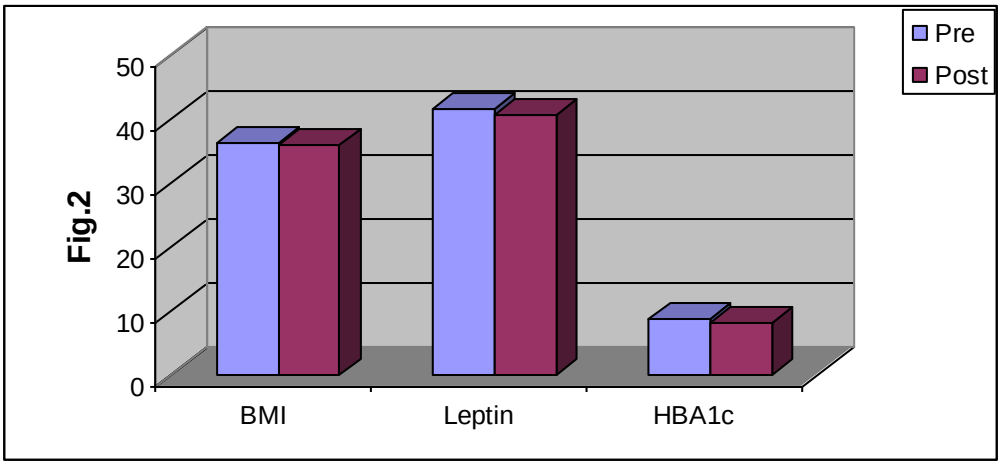

Fig. (2): Show the difference between the pre and post values of BMI, leptin and glycated hemoglobin (HBA_1c) of the control group.

Table (3) and figure (3) show the difference between the post test values of BMI, leptin and HBA_1c between the training and the control group. There was a significant difference between both groups (P value <0.05).

Table (3) and figure (3): Show the difference between the training and the control groups in BMI, leptin and glycated hemoglobin (HBA_1c) after three months.

	Mean ±SD		T-value	Significance
	Training	Control		
BMI (kg /m^2)	32.15±2.89	35.98±2.76	3.03	Sig
Leptin (ng/ml)	35.32±3.14	40.85±3.24	3.89	Sig.
HBA_1c (%)	6.88±0.78	8.14±0.88	3.50	Sig

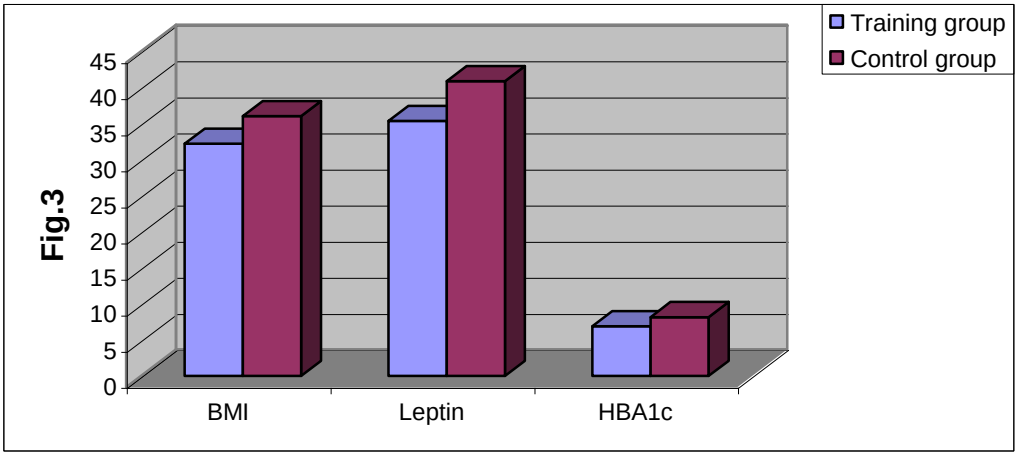

Fig.3

Tables (4,5): Show the Pearson's correlation coefficients test value and the relationship between the grade of BMI, leptin and glycated hemoglobin (HBA_1c) in the training and control group .There was a Strong inverse relationship between these variables in both groups.

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

Test	Pearson's value	Relationship to glycated hemoglobin (HBA_1c [%])
BMI (kg /m^2)	0.93	Strong inverse relationship
Leptin (ng/ml)	0.94	Strong inverse relationship

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

Test	Pearson's value	Relationship to glycated hemoglobin (HBA_1c [%])
BMI (kg /m^2)	0.93	Strong inverse relationship
Leptin (ng/ml)	0.94	Strong inverse relationship

DISCUSSION

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

Measurements of body mass index (BMI), leptin and glycated hemoglobin (HBA_1c) were taken before starting of the study and repeated at the end of the study (after three months).

The results of this study indicated that there was a significant decrease in values of glycated hemoglobin (HBA_1c), BMI and leptin of the training, while the results of the control group were not significant. There was a significant difference between both groups. Also, there was a strong inverse relationship

between the grade of BMI, leptin and glycated 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[7].

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[23].

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 [9] . 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[28].

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[15].

Leptin is recognized to play an integral role in endocrine regulation of metabolism. It is clearly evident that leptin is decreased during calorie restriction[14]. Higher serum leptin levels have been reported in obese non – diabetic subjects. Hyperleptinaemia have been demonstrated to be correlated with hyperphagia, insulin resistance, other markers of metabolic syndrome including obesity, hyperlipidaemia and hypertension[24]. The serum leptin levels were reduced after weight reduction as Plasma leptin concentrations correlated with BMI[27].

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[10].

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[6].

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[31]. 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[20].

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[25].

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[29,30].

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[1].

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[26].

In Conclusion, in obese non-insulin dependent diabetic patients, BMI, leptin and HBA1c could be considered as a valuable marker for assessment of metabolic control which is improved by weight loss. Serum leptin might be a marker for maintaining weight loss.

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الملخص العربى

استجابة التحكم فى التمثيل الغذائى لإنقاص الوزن لدى مرضى السكر البدناء دراسة ارتباطيه

تهدف الدراسة الى معرفة فوائد انقاص الوزن لمرضى السكر البدناء على مستوى التحكم فى التمثيل الغذائى من خلال قياس معامل كتلة الجسم و مستوى هرمون الليبتين ، نسبة الدهون ومستوى الهيموجلوبين السكرى ، أشتملت الدراسة على أربعين مريضا تراوحت أعمارهم بين45-56سنة وتم تقسيمهم الى مجموعتين متساويتين المجموعة الأولى تلقت تمارين هوائية وبرنامج غذائى بالأضافة الى العلاج الدوائى فى حين تلقت المجوعة الثانية (المجموعة الصابطة) العلاج الدوائى فقط .تم أجراء التحاليل قبل بدء الدراسة و بعد ثلاثة شهور فى نهاية الدراسة. أظهرت النتائج انخفاض ذو دلالة إحصائية فى معامل كتلة الجسم و مستوى هرمون الليبتين و مستوى الهيموجلوبين السكرى فى المجموعة الاولى فقط فى حين لم تظهر المجموعة الضابطة تحسن ذو دلالة إحصائية ووجد فروق ذات دلالة إحصائية بين المجموعتين .لذا يوص باتباع برنامج لإنقاص الوزن لمرض السكر البدناء.