Original Paper

Annals of Nutrition & Metabolism

Ann Nutr Metab 2011;58:141–149
DOI: 10.1159/000327912

Received: September 16, 2010
Accepted after revision: March 30, 2011
Published online: May 25, 2011

Weight Change, Blood Pressure, Lipids and Glycemic Control among Patients with Type 2 Diabetes

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Key Words
Blood pressure · Diabetes mellitus, type 2 · Glycemic control · Lipids · Weight change

Abstract
Background/Aim: Although weight loss in patients with type 2 diabetes is very important, available data on the effects of long-term weight change on blood pressure (BP), lipids and glycemic control in these patients are limited. The aim of this study was to assess the long-term impact of weight change on BP, plasma lipids and glycemic control among patients with type 2 diabetes receiving routine care. ***Methods:*** During the mean [standard deviation (SD)] follow-up period of 9.2 (3.4; range 2–15) years, 7,712 patients with type 2 diabetes were examined to determine changes in weight, BP, plasma lipids and glycemic control using a linear mixed-effects model for repeated measures. The mean (SD) age of participants was 51.3 (10.5) years with a mean (SD) duration of diabetes of 6.3 (6.3) years at initial registration. ***Results:*** The change in fasting plasma glucose and glycosylated hemoglobin (HbA_{1c}) from baseline to the last follow-up examination was significantly more favorable in those patients who gained weight during follow-up than in those who lost weight or whose weight remained stable. Systolic and diastolic BP and lipids also rose more significantly in the group with weight gain. ***Conclusions:*** Although this population of type 2 diabetes in Iran had negligible weight change over mean 9.2 years, this weight gain was associated with an increase in BP and plasma lipids, but also an improvement in glycemic control.

Introduction

Weight, in association with age, is the strongest indicator of blood pressure (BP), dyslipidemia and type 2 diabetes in virtually all societies and ethnic groups, and in both genders [1]. The majority of patients with type 2 diabetes are considered overweight or obese and will eventually require insulin to achieve a target blood glucose value [2, 3]. Weight loss in these patients reduces BP, improves glucose control and blood lipids, and decreases the risk of cardiovascular disease [4–7]. For this reason, at the time of diagnosis of type 2 diabetes, much attention is directed toward modifying patients' lifestyle and major diabetes risk factors including obesity, BP and cholesterol level, to prevent complications. However, the long-term results of weight-loss programs are disappointing, with patients often regaining most of the weight they initially lost. Moreover, insulin initiation is associated with weight

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gain [8–10]. Weight gain is associated with adverse changes in plasma lipids and BP and increases the risk of heart attack and stroke [11–14]. There is a dearth of information available on the impact of long-term unintentional weight change on BP, plasma lipids and glycemic control among patients with type 2 diabetes receiving routine care.

This study used data that had been collected routinely over a mean 9-year period from a clinical information system for diabetes at the Isfahan Endocrine and Metabolism Research Center, Iran, to assess the effects of long-term unintentional weight change on BP, lipids and plasma glucose in patients with type 2 diabetes receiving routine care.

Patients and Methods

Participants and Data Collection

The recruitment methods and examination procedures of the Isfahan Endocrine and Metabolism Research Center outpatient clinics have been described before [15]. In summary, clinical data are collected for all consecutive patients at the first attendance and at review consultations (usually annually) using standard encounter forms. These include an examination of the ocular fundus and lens, the limbs and BP, and the measurement of height, weight, fasting plasma glucose (FPG), glycosylated hemoglobin (HbA_{1c}), urine protein, triglyceride, cholesterol and serum creatinine levels. The clinician compiles a list of problems and smoking is reported via a questionnaire completed by the patient on demography, family history, and smoking.

Generally, newly diagnosed patients are referred to qualified nutritionists for evaluation; if necessary, a lifestyle and weight management program is recommended. All newly diagnosed patients attend weight-related health education classes free of charge.

Participants

Between 1992 and 2008, a total of 13,411 patients with type 1 and type 2 diabetes were registered in the system. However, this study used data for only 7,712 of these patients, i.e. 2,946 (38.2%) men and 4,766 (61.8%) women with type 2 diabetes who had had at least one subsequent review since registration at baseline. The tenets of the Declaration of Helsinki were followed, institutional ethical committee approval was granted, and an informed consent form was signed by each participant.

Procedures

Predictors of BP, lipids and HbA_{1c} change were assessed using the following data from the patient's registration consultation: gender, age at diagnosis (i.e. at the time this was first recorded by a physician on the participant's chart), current age (at the time of the examination), educational level, duration of diabetes (the time between diagnosis and the baseline examination), body mass index (BMI), smoking status (never, current), HbA_{1c} (measured by spectrophotometer), FPG (measured by the glucose oxidase method; Clinical Chemistry Analyzer Liasys, Rome, Italy), proteinuria (measured by precipitation with 3% sulfosalicylic acid and determination of turbidity by measuring absorbance at a wavelength of 550 nm with a spectrophotometer), serum creatinine, triglyceride, cholesterol, high-density lipoprotein cholesterol (HDL; measured using standardized procedures), and low-density lipoprotein cholesterol (LDL; calculated by the Friedewald equation [16]) levels.

Height and weight were measured using standard apparatus, with the subjects in light clothes and without shoes. Weight was measured to the nearest 0.1 kg on a calibrated beam scale. Height was measured to the nearest 0.5 cm and assessed at baseline only. A physician measured the systolic and diastolic BPs of the participants (after they had been seated for 10 min) using a mercury sphygmomanometer and standard techniques. All clinical and laboratory measurements at baseline and follow-ups were made using the same standardized protocol.

Definitions

Criteria for the classification of underweight, normal weight, overweight and obesity used in the study were based on BMI as follows: underweight <18.5, normal weight 18.5–24.9, overweight 25–29.9, and obesity ≥30. Less than 1.0% of the subjects were classified as underweight, so this category was combined with the normal-weight group for analysis. Percent weight change was determined by taking the difference between the baseline and last-measured weight and dividing it by the patient's baseline weight. There was no severe weight fluctuation during the study period. Individuals were grouped into 3 categories of weight change: (1) weight reduction, (2) stable weight, serving as the referent category, and (3) weight gain. Patients were classified as having had a clinically significant weight reduction if their weight at the last follow-up visit was at least 4% lower than the baseline weight. Those who had gained or lost less than 4% in body weight were classified as stable. Those who had gained ≥4% in body weight were classified as having gained weight [17]. Smoking was estimated from a self-report and categorized as current and non-smokers. Smoking status was assessed at baseline only. The physician defined the type of diabetes according to the American Diabetes Association criteria [18].

Statistical Analysis

The statistical methods used included Student's t test, analyses of variance (ANOVA), χ^2 test, a linear mixed-effects model for repeated measures and a general linear model. Paired t tests were used to test whether changes in continuous variables between baseline and the last follow-up were significantly different from zero. Equivalently, for categorical variables, changes in proportions between baseline and the last follow-up were tested against the null hypothesis of no change (zero) using McNamar's test. A linear mixed-effects model for repeated measures was used to investigate the time course of HbA_{1c}, FPG, BP and plasma lipids [19]. For each outcome variable, a model with time (baseline and follow-ups) as the repeated measure factor was constructed. HbA_{1c}, FPG, BP and cholesterol were included in the model as fixed effects. Age at baseline, gender and smoking were included as covariates. An individual's identification number was included as a random effect to account for the variability due to individual differences between subjects. All tests for statistical significance were 2-tailed and performed assuming a type I error probability of <0.05. Analysis was performed using SPSS software for Windows© (SPSS Inc., Chicago, Ill., USA).

Table 1. Characteristics of 7,712 patients with type 2 diabetes mellitus at baseline and last follow-up visit

Characteristics	Baseline	Last follow-up visit[1]	Difference (95% CI)
Age, years	51.3 (0.12)	60.4 (0.23)	–9.1 (–8.7, –9.4)*
Weight, kg	69.7 (0.14)	70.7 (0.14)	–1.0 (–1.08, –0.8)*
Height, cm	159.5 (0.10)	–	–
BMI	27.7 (0.05)	28.0 (0.05)	–0.3 (–0.37, –0.24)*
Weight change, kg	–	1.0 (0.07)	–
Systolic BP, mm Hg	122.4 (0.21)	133.4 (0.25)	–11.0 (–11.4, –10.5)*
Diastolic BP, mm Hg	75.1 (0.13)	83.2 (0.13)	–8.1 (–8.4, –7.8)*
Fasting blood glucose, mg/dl	201.3 (0.89)	170.9 (0.78)	30.4 (28.4, 32.5)*
HbA_{1c}, %	9.0 (0.04)	7.9 (0.03)	1.1 (1.01, –1.19)*
Creatinine, mg/dl	0.95 (0.01)	1.0 (0.01)	–0.05 (–0.1, –0.06)*
Triglyceride, mg/dl	229.2 (1.90)	198.6 (1.51)	30.6 (27.1, 33.9)*
Cholesterol, mg/dl	223.0 (0.62)	207.8 (0.59)	15.2 (13.9, 16.4)*
LDL, mg/dl	125.7 (1.33)	108.3 (1.06)	17.4 (14.5, 20.4)*
HDL, mg/dl	45.2 (0.43)	42.1 (0.33)	3.1 (2.3, 4.0)*
Gender, %			
Men	38.2	–	–
Women	61.8	–	–
Therapeutic regimen, %			
Diet	21.1	10.8	10.3 (9.2, 11.4)*
Oral agent	65.1	55.4	9.7 (8.2, 11.2)*
Insulin	13.8	33.8	–20.0 (–21.3, –18.7)*
Weight change, %			
Loss (≥4%)	–	20.9	–
Stable	–	50.2	–
Gain (≥4%)	–	28.8	–
Weight category, %			
Normal weight (BMI 18.5–24.9)	27.8	26.1	1.7 (0.3, 3.1)*
Underweight (BMI <18.5)	1.0	0.8	0.2 (–0.1, 0.5)
Overweight (BMI 25–29.9)	43.1	43.4	–0.3 (–1.8, 1.3)
Class I obesity (BMI 30–34.9)	21.8	22.4	–0.6 (–1.9, 0.7)
Class II obesity (BMI 35–39.9)	4.9	5.6	–0.7 (–1.5, –0.03)*
Class III obesity (BMI ≥40)	1.3	1.5	–0.2 (–0.5, 0.2)
Obesity (BMI ≥30)	28.1	29.7	–1.6 (–3.1, –0.2)*
Overweight and obesity (BMI ≥25)	71.2	73.1	–1.9 (–3.3, –0.4)*

Data are mean. * $p < 0.001$ between baseline and follow-up. [1] Follow-up period ranged from 2 to 15 years.

Results

Characteristics

Patients had a mean (SD) duration of diabetes of 6.3 (6.3) years and a mean age of 51.3 (10.5) years at baseline. The average time of follow-up in years was 9.2 (3.5; range 2–15). The average number of follow-up visits was 14.2 (14.1; range 2–103). At baseline, 29.0% of men and 3.2% of women were smoking. The mean (SD) BMI was 26.1 (3.9) in men, and 28.6 (4.7) in women.

At baseline, 40.5% (95% CI 38.7, 42.2) of the men and 22.8% (95% CI 21.6, 24.0) of the women had normal weight. Nearly two thirds of the patients were overweight or obese (BMI ≥25) (70.4%; 95% CI 69.4, 71.4). Overall, 61.0% men and 77.2% women were overweight or obese, 14.9% men and 35.3% women were obese (BMI ≥30), 1.4% of men and 0.7% of women were underweight (BMI <18.5), and 0.4% of men and 1.9% of women were morbidly obese (BMI ≥40).

Population characteristics at baseline and at the last follow-up visit are presented in table 1. At the last clinic visit, patients had higher weight, BMI, creatinine and BP, and had lower FPG, HbA_{1c}, triglyceride, cholesterol, LDL and HDL levels than at baseline ($p < 0.001$). Frequency of insulin use was higher at the last clinic visit, with 89.2% of all patients using hypoglycemic medication by then.

Table 2. Age-adjusted comparison of baseline variables for the weight change group in 7,712 patients with type 2 diabetes mellitus

Characteristics	Weight change		
	stable	gain (≥4%)	loss (≥4%)
Number	3,874 (50.2)	2,222 (28.8)	1,616 (20.9)
Age at registration, years	51.5 (0.17)	51.1 (0.22)	51.2 (0.26)
Age at diagnosis, years	45.2 (0.17)	44.2 (0.22)	45.5 (0.26)***, a
Follow-up, years	9.1 (0.06)	9.4 (0.07)	9.2 (0.09)**, a
Number of follow-up visits	10.3 (0.21)	20.8 (0.28)	14.3 (0.33)***, a, b
Duration of diabetes, years	6.3 (0.10)	6.9 (0.13)	5.7 (0.15)***, a, b
Height, cm	159.5 (0.15)	158.3 (0.19)	159.3 (0.23)***, a, b
Weight, kg	70.6 (0.19)	67.0 (0.26)	72.4 (0.30)***, a, b
BMI	27.8 (0.07)	26.8 (0.10)	28.5 (0.11)***, a, b
Systolic BP, mm Hg	122.4 (0.29)	121.0 (0.38)	123.3 (0.44)***, a, b
Diastolic BP, mm Hg	75.0 (0.18)	74.4 (0.24)	75.6 (0.28)**, b
Fasting blood glucose, mg/dl	198.0 (1.22)	215.2 (1.60)	192.4 (1.87)***, a, b
HbA_{1c}, %	8.7 (0.06)	9.5 (0.07)	8.7 (0.08)***, a, b
Creatinine, mg/dl	0.96 (0.02)	0.93 (0.02)	0.93 (0.02)
Triglyceride, mg/dl	232.2 (2.63)	219.1 (3.43)	237.7 (4.03)**, a, b
Cholesterol, mg/dl	221.5 (0.86)	225.1 (1.12)	223.5 (1.31)*, a
LDL, mg/dl	131.8 (1.37)	134.7 (1.42)	129.3 (1.86)
HDL, mg/dl	45.1 (0.46)	44.9 (0.47)	45.1 (0.62)
Gender, %			
Men	40.3	34.8	37.9***, a, b
Women	59.7	65.2	62.1***, a, b
Smokers, %	13.5	11.0	13.7*, a, b
Education, %			
Primary or below	75.5	80.3	78.2***, a, b
Secondary	14.8	12.7	12.9***, a
Matriculation or above	9.7	7.0	8.9***, a, b
Treatment status, %			
Diet	22.0	18.2	25.5***, a, b
Oral agent	66.1	60.5	67.5*** a, b
Insulin	11.9	21.3	7.0***, a, b
Normal weight (BMI <25), %	27.3	36.5	21.7***, a, b
Overweight (BMI 25–29.9), %	44.2	41.2	43.2***, a, b
Obesity (BMI ≥30), %	28.4	22.3	35.1***, a, b

Data represent mean with SE in parentheses (with the exception of number with the percentage in parentheses). Age-adjusted means were calculated using general linear models.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ comparison across all 3 groups.

[a] Comparison of weight-gain and stable-weight groups. [b] Comparison of weight-gain and weight-loss groups. Weight loss and weight gain are defined by losing or gaining 4% or more of baseline weight, respectively. Stable weight is gaining or losing less than 4% in body weight.

Mean HbA_{1c} was 9.0% at baseline and 7.9% at the last follow-up, decreasing by a mean of 1.1% ($p < 0.001$).

Table 2 compares the age-adjusted baseline characteristics of the 3,874 (50.2%) participants with stable weight, 2,222 (28.8%) with weight gain and 1,616 (20.9%) with weight loss. The 3 groups were significantly different with respect to gender, treatment, baseline weight and BMI, BP, duration of diabetes, FPG, HbA_{1c}, follow-up, the number of follow-up visits, triglyceride and cholesterol levels. Those with weight gain had a higher number of follow-up visits, longer duration of diabetes, as well as higher levels of FPG and HbA_{1c}. Body weight at baseline was lower and insulin use at baseline was higher in those who subsequently gained weight.

Table 3. Age-adjusted comparison of absolute change from baseline by the weight-change group in 7,712 patients with type 2 diabetes mellitus

Characteristics	Weight change		
	stable	gain (≥4%)	loss (≥4%)
Number	3,874 (50.2)	2,222 (28.8)	1,616 (20.9)
Weight, kg	−0.07 (0.06)	7.9 (0.08)	−6.2 (0.09)[***, a, b]
BMI	−0.11 (0.03)	2.8 (0.04)	−2.2 (0.05)[***, a, b]
Systolic BP, mm Hg	10.1 (0.33)	15.7 (0.44)	7.5 (0.52)[***, a, b]
Diastolic BP, mm Hg	7.9 (0.21)	9.8 (0.27)	6.6 (0.32)[***, a, b]
Fasting blood glucose, mg/dl	−25.2 (1.53)	−48.7 (1.92)	−16.4 (2.28)[***, a, b]
HbA_{1c}, %	−0.8 (0.07)	−1.6 (0.07)	−0.8 (0.09)[***, a, b]
Creatinine, mg/dl	0.06 (0.02)	0.1 (0.02)	0.06 (0.02)[*, a, b]
Triglyceride, mg/dl	−26.8 (2.53)	−27.4 (3.2)	−45.3 (3.8)[***, b]
Cholesterol, mg/dl	−11.9 (0.92)	−20.0 (1.16)	17.0 (1.38)[***, a]
LDL, mg/dl	−15.6 (2.44)	−21.5 (2.36)	−13.1 (3.21)
HDL, mg/dl	−3.4 (0.73)	−3.5 (0.70)	−2.1 (0.96)
Treatment status, %			
Diet	−9.7	−11.5	−13.4[***, a, b]
Oral agent	−2.7	−26.5	−2.7[***, a, b]
Insulin	12.4	38.0	16.1[***, a, b]
Normal weight (BMI <25), %	0.9	−21.2	18.4[***, a, b]
Overweight (BMI 25–29.9), %	0.5	0.8	−1.0[***, b]
Obesity (BMI ≥30), %	−1.2	20.4	−17.4[***, a, b]

Data represent mean with SE in parentheses (with the exception of number with the percentage in parentheses). Age-adjusted means were calculated using general linear models.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ comparison across all 3 groups.

[a] Comparison of weight-gain and stable-weight groups. [b] Comparison of weight-gain and weight-loss groups. Weight loss and weight gain are defined by losing or gaining 4% or more of baseline weight, respectively. Stable weight is gaining or losing less than 4% in body weight.

Weight Change

Weight change was, on average, minimal. Between baseline and the last clinic visit, a mean (SE) of 1.0 (0.07) kg was gained in the study group as a whole. Large changes in weight were infrequent; less than 7% of participants lost or gained 15 kg or more during follow-up, 19.0% of participants lost at least 5 kg and 7% gained 5 kg or more.

The weight-gain group showed a mean weight of 67.0 kg at baseline and gained weight until the end of follow-up, reaching a mean of 74.9 kg (11.8% gained). In the weight-loss group, the mean baseline weight was 72.4 kg and decreased to 66.2 kg until the end of follow-up (8.6% lost).

Plasma Lipids

Plasma cholesterol rose at the last follow-up in those having lost weight, but fell in those with stable weight or weight gain. The plasma triglyceride level decreased in each group but the decrease was more marked in those with weight loss. Plasma HDL and LDL fell during follow-up in each group, and the change was not statistically different between the groups (table 3). In a linear mixed-effects model for repeated measures, the addition of the time course of cholesterol and triglyceride appreciably altered the relationship and plasma cholesterol and triglyceride levels rose with weight gain. Subjects with more weight gain tended to have higher cholesterol and triglyceride levels.

Glycemic Control

Both HbA_{1c} and FPG were higher in the weight-gain group at baseline, when those with weight gain and those with stable weight and weight loss were compared. However, the change in HbA_{1c} and FPG from baseline to the last follow-up was significantly more favorable in those with weight gain. Baseline insulin therapy was also higher in those who subsequently gained weight, compared with those losing or maintaining weight. In the weight-

Table 4. Age-, gender- and multivariate-adjusted mean HbA_{1c}, FPG, BP and lipids according to weight change at the last follow-up visit in 7,712 patients with type 2 diabetes mellitus

	Weight change		
	stable	gain (≥4%)	loss (≥4%)
Number	3,874 (50.2)	2,222 (28.8)	1,616 (20.9)
HbA_{1c}			
Age-adjusted	7.8 (0.05)	7.9 (0.06)	7.9 (0.07)
Age/gender-adjusted	7.8 (0.05)	7.9 (0.06)	7.9 (0.07)
Multivariate-adjusted	7.9 (0.05)	7.7 (0.06)	8.0 (0.07)*, a, b
FPG			
Age-adjusted	171.8 (1.15)	166.1 (1.45)	174.7 (1.72)***, a, b
Age/gender-adjusted	172.1 (1.15)	165.8 (1.45)	174.6 (1.72)***, a, b
Multivariate-adjusted	171.4 (1.19)	166.3 (1.52)	176.6 (1.75)***, a, b
Systolic BP			
Age-adjusted	132.5 (0.33)	136.7 (0.44)	130.9 (0.51)***, a, b
Age/gender-adjusted	132.6 (0.33)	136.6 (0.44)	130.9 (0.51)***, a, b
Multivariate-adjusted	132.9 (0.35)	136.5 (0.46)	130.6 (0.52)***, a, b
Diastolic BP			
Age-adjusted	83.0 (0.18)	84.3 (0.24)	82.3 (0.28)***, a, b
Age/gender-adjusted	83.0 (0.18)	84.2 (0.24)	82.3 (0.28)***, a, b
Multivariate-adjusted	83.0 (0.19)	84.7 (0.25)	81.8 (0.28)***, a, b
Cholesterol			
Age-adjusted	208.9 (0.86)	205.3 (1.07)	206.3 (1.28)*, a
Age/gender-adjusted	209.3 (0.84)	204.8 (1.06)	206.1 (1.26)**, a
Multivariate-adjusted	206.4 (0.84)	209.5 (1.07)	205.8 (1.23)*, b
Triglycerides			
Age-adjusted	204.6 (2.21)	191.8 (2.76)	192.0 (3.29)***, a
Age/gender-adjusted	205.0 (2.20)	191.4 (2.76)	191.9 (3.29)***, a
Multivariate-adjusted	201.7 (2.20)	197.2 (2.81)	190.4 (3.23)*, a, b

Data represent mean with SE in parentheses (with the exception of number with the percentage in parentheses). All means were calculated using general linear models. Multivariate mean adjusted for age, gender, follow-up visits, duration of diabetes, treatment, FPG, cholesterol, triglyceride, systolic BP and BMI.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ comparison across all 3 groups.

[a] Comparison of weight-gain and stable-weight groups. [b] Comparison of weight-gain and weight-loss groups. Weight loss and weight gain are defined by losing or gaining 4% or more of baseline weight, respectively. Stable weight is gaining or losing less than 4% in body weight.

gain group, the number of patients taking insulin was 38% compared to 12% in the stable and 16% in the weight-loss groups. During follow-up, the insulin dose rose in each group but the change was significantly more marked in the weight-gain group (table 3).

Blood Pressure

Both systolic and diastolic BP were similar between groups at baseline. Both rose during follow-up in each weight change group, but the change was significantly more marked in the weight-gain group (table 3).

Age-, gender- and multivariate-adjusted mean (SE) HbA_{1c}, FPG, systolic and diastolic BP, cholesterol and triglyceride values at the last follow-up visit within each weight change category are displayed in table 4. In a multivariate model, the additional adjustment for other time-dependent covariates slightly decreased mean HbA_{1c} in the weight-gain group compared to the model adjusted for age alone or age and gender. Mean HbA_{1c} ($p < 0.05$) and FPG ($p < 0.001$) levels were lower in those who gained weight compared to those who lost or maintained weight. Mean systolic and diastolic BP levels were slightly higher in those who gained weight compared to those who lost or maintained weight. Mean triglyceride levels were slightly lower in those who gained weight compared to those with stable weight.

In the linear mixed-effects model for repeated measures modeling, weight showed a significant negative association with FPG ($\beta = -0.0133$, $p < 0.001$) and HbA_{1c} ($\beta = -0.272$, $p < 0.001$) and a positive association with systolic BP ($\beta = 0.193$, $p < 0.001$). Systolic BP was also positively associated with diastolic BP ($\beta = 0.151$, $p < 0.01$), triglyceride ($\beta = 1.160$, $p < 0.001$) and cholesterol ($\beta = 0.092$, $p < 0.01$). We found a 0.01 mg/dl decrease in the FPG level and 0.27% decrease in HbA_{1c} for every 1 kg of weight gain, whereas a 0.19-mm Hg increase in systolic and 0.15-mm Hg increase in diastolic BP for every 1 kg weight gain was found during the follow-up period.

Discussion

During a mean 9.2-year follow-up of patients with type 2 diabetes receiving routine care, improved glycemic control was accompanied by weight gain. In contrast, weight gain was associated with a rise in BP and plasma lipids. This is the first study to describe the effects of long-term unintentional weight change on BP, lipids and glycemic control in Iranian patients with type 2 diabetes receiving routine care.

Few studies have assessed the impact of long-term unintentional weight change on BP, lipids and glycemic control in persons with type 1 and type 2 diabetes, and the results are inconsistent. Some studies have reported an inverse association between changes in HbA_{1c} and changes in weight [11, 20, 21], whereas in other studies, those who lost weight had improved glycemic and BP control compared to groups with stable weight or weight gain [4–7]. The interactions between the metabolic state, antidiabetic treatment and changes in weight are complex in type 2 diabetes and obesity is a strong risk factor for its development [1, 2]. On the other hand, weight loss is in itself associated with reduced insulin resistance and improved glucose metabolism [5–7]. Initiation of insulin therapy for patients with type 2 diabetes is associated with weight gain [22]. Improved glycemic control may increase body weight, possibly as a result of daily insulin use, as we observed. The combined effects of insulin treatment, weight gain and improved glycemia complicate the interpretation of association between weight change and HbA_{1c} in these patients. We observed that in the weight-gain group, a greater percentage of patients used insulin which may have resulted in better glycemic control. The observation that a change in HbA_{1c} from baseline to follow-up was significantly more marked in those who had gained weight may be due to changes in the frequency and/or amount of the insulin dose, whereby (1) participants who gained weight were subsequently put on hypoglycemic medication resulting in a decrease in HbA_{1c} and/or (2) participants who were put on insulin had lower HbA_{1c} but gained weight as a result of insulin use. In Iran, sulfonylureas and insulin (NPH and regular) are the most often-used medication in the treatment of patients with type 2 diabetes. Weight gain is a known side effect of this type of medication. The number of patients taking insulin at the last follow-up visit was increased up to 20% compared to baseline (table 1). These findings revealed that, as expected, better glycemic control was accompanied by weight gain.

Exogenous insulin has been shown to be a risk factor for cardiovascular disease [23]. Diabetic patients using insulin have been found to have a higher risk for the development of hypertension [24]. Our findings were generally in agreement with those of the Diabetes Control and Complications Trial, in which patients with type 1 diabetes were followed for an average of 6.2 years [11]. Among conventionally treated patients, those in the top quartile of weight gain had higher levels of total cholesterol, LDL and systolic BP when compared with patients in the lowest or second lowest quartiles. Among intensively treated patients, those in the top quartile of weight gain had higher levels of triglycerides, total cholesterol, LDL and systolic BP, and reduced HDL compared with patients in the lower quartiles. In contrast to our findings, in the Pittsburgh Epidemiology of Diabetes Complications study [25], marked weight gain was not associated with a deterioration in plasma lipids in those who had improved HbA_{1c} levels, while similar to our findings weight gain was associated with a rise in BP irrespective of glycemic control.

Although interventional studies have consistently shown that intentional weight reduction produces short-term improvement in BP, lipids and HbA_{1c} [4–6, 26–29], no published data describe the effect of long-term unintentional weight changes after the diagnosis of type 2 diabetes in patients receiving routine care.

The strengths of this study include the prospective design, large sample size, long-term follow-up, and measuring weight with well-functioning, validly calibrated scales, as well as detailed information on potential confounding factors such as smoking, body size, duration of diabetes, fasting blood glucose, HbA_{1c}, systolic and diastolic BP, and total cholesterol. Selection and information bias were unlikely because of the prospective design and high rate of follow-up. Our data were collected during routine clinical care representing varying time intervals;

thus, weight and other measurements may not have been as precise or complete as they would be during a clinical trial. Our study was limited by possible selection bias by restricting the study to patients who remained alive during the whole study period. Our study also did not document the adherence to insulin therapy or other medication and differences in adherence may have affected our results. Individuals in the different categories of weight change are likely to differ in several aspects, such as physical activity, certain lifestyle and dietary factors. We could not rule out the possibility of residual confounding because of unmeasured or inaccurately measured covariates, e.g. information on physical activity, fat distribution and a history of smoking was not collected in the study. It was, nevertheless, a real-life study that reflected unintentional weight change patterns and their association with BP, plasma lipids and glycemic control. In addition, this study provided new data from Iran, a developing country, which has been underrepresented in studies in the past.

In conclusion, this study showed that in patients with type 2 diabetes receiving routine care, improved glycemic control was associated with weight gain. This is supported by the greater increase in the insulin dose in the group that gained weight.

Acknowledgements

This work was supported partially by a grant from the Isfahan Endocrine and Metabolism Research Center, Iran. The authors are grateful to Mr. Majid Abyar for computer technical assistance.

Disclosure Statement

There were no conflicts of interest.

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