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Title page

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Beneficial effects of replacing diet beverages with water on Type 2 diabetic obese women following a hypo-energetic diet - a randomized, 24 week clinical trial

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Abbreviations:

- Analysis of variance: ANOVA
- Cognitive behavioral therapy: CBT
- Diet beverages: DBs
- Fasting plasma glucose: FPG
- Glycated hemoglobin: Hb A_{1C}
- Homeostasis model assessment of insulin resistance: HOMA-IR
- Hour: h
- Liter: l
- Mole: mol
- Standard deviation: SD
- Sugar sweetened beverages: SSBs
- Total cholesterol: TC
- Triglyceride: TG
- 2 hour post prandial glucose: 2hpp
- Waist circumference: WC

Abstract

Aims: To compare the effect of replacing diet beverages (DBs) with water or continuing to drink DBs, in Type 2 diabetes during a 24 week weight loss program. The primary endpoint was the effect of intervention on weight over 24 weeks. The main secondary endpoints included anthropometric measurement, glucose and fat metabolism during the 24 weeks.

Methods: 81 Overweight and obese women with type 2 diabetes, who usually consumed DBs in their diet, were asked to either substitute water for DBs or continue drinking DBs five times per week after their lunch for 24 weeks (DBs group), while they were on a weight loss program.

Results: Compared with the DBs group, the Water group had a greater decrease in weight (Water: -6.40 ± 2.42 kg; DBs: -5.25 ± 1.60 kg; *P* =0.006), BMI (Water: -2.49 ± 0.9 2kg/m^2; DBs: -2.06 ± 0.62 kg/m^2; *P* =0.006), FPG(Water: -1.63 ± 0.54 mmol/l; DBs: -1.29 ± 0.48 mmol/l, P=0.005), fasting Insulin (Water: -5.71 ± 2.30 m IU/ml; DBs: -4.16 ± 1.74 m IU/ml, P=0.011), HOMA IR (Water:-3.20 ± 1.17; DBs: -2.48 ± 0.99, P=003) and 2h post prandial glucose (Water: -1.67 ± 0.62 mmol/l; DBs: -1.35 ± 0.39 mmol/l; P=0.027) over the 24 weeks. However, there was no significant group * time interaction for waist circumference, lipid profiles and HbA_{1C} within both groups over 24 weeks.

Conclusion: Replacement of DBs with water after the main meal in patients with type 2 diabetes obese adult women may lead to more weight reduction during a weight loss program.

Introduction:

There is evidence that the risk of developing type 2 diabetes is associated positively with BMI (1, 2). Obesity also complicates the management of type 2 diabetes by increasing insulin resistance and blood glucose concentrations (3). In contrast, weight reduction is an effective goal for overweight/ obese type 2 diabetes in order to improve glycemic control (4).

In the last decades, the amount of energy consumed in beverages has increased, providing a significant source of daily energy intake (5). Also, to promoting weight gain, a higher intake of sugar sweetened beverages (SSBs) is associated with the development of metabolic syndrome and an increased risk of type 2 diabetes (6). On the other hand, diet beverages (DBs) are of interest as dietary tools which offer sweet taste without energy (7-9).

Nutritionists usually advise individuals who wish to lose weight to raise their water consumption (10, 11). Conversely, many obese and diabetic patients believe that they can drink DBs during a diet plan without any deleterious effects on their weight and diabetes management (12). A previous review indicated that DBs might be the ideal use of intense sweeteners in the setting of a weight control plan, while they have been shown to be associated with some modest weight loss (13). Thus, it would be expected that Type 2 diabetic patients could consider DBs in order to help them to lose weight and control their blood glucose.

Nevertheless, SSBs and DBs intake were associated with a significantly higher risk of type 2 diabetes (14) and a subsequent observational study revealed that consumption of DBs was significantly associated with an increased risk for type 2 diabetes (15). More experimental study is needed to determine the effect of DBs consumption on the management of diabetes and metabolic syndrome.

Recently, we investigated the effect of replacing DBs with water, on promoting weight reduction in obese adults without diabetes who were on a hypo-energetic diet (16). The Water group had a greater decrease in weight and insulin resistance over the 24 weeks of study compared with DBs group. Due to beneficial effects of substitution of DBs with water in overweight/ obese women, it would be interesting to repeat this protocol in those with Type 2 diabetes.

Thus, the purpose of this study was to investigate the effects of replacing DB consumption with water during a comprehensive 24-wk weight-loss program on body weight as a primary outcome, along with abdominal adiposity, carbohydrate and lipid metabolism as secondary outcomes, in overweight and obese women with Type 2 diabetes.

Materials and Methods

Study participants

Obese female adults with diabetes were selected between April 2015 and June 2015 from the participants attending NovinDiet Clinic, Tehran, Iran to lose weight and control diabetes. Inclusion criteria were female, 18-50y of age, BMI = 27 -35 kg/m², $6.5 < Hb_{A1C} < 7.2$ and only taking Metformin to control their diabetes , self-reported habitual consumers of DBs who were willing to introduce a dietary change to lose weight which might include changing beverage consumption.

All participants were required to be nonsmokers, free of established cardiovascular diseases, stroke, liver diseases, kidney diseases, depression, cancer or autoimmune disease. Subjects included those who were able to keep an adequate 4- day food record and who demonstrated readiness to participate safely in daily physical activity (PA).

Exclusion criteria were pregnancy or lactation during the previous 6 months or planned pregnancy in the next 6 months, weight loss ≥10% of body weight within the 6 month before enrollment in the study, taking medication to lower lipids/ cholesterol or that could affect metabolism or change body weight.

The study was approved by the Ethical Committee of The Digestive Research Institute, Tehran University of Medical Science. All subjects provided their signed consent prior to study enrollment. This trial was registered at http:/www.clinical trials.gov/ as NCT02412774.

Randomization and Intervention

The study was a 2-arm, single-blind, randomized clinical trial. Eligible participants were randomly assigned after baseline measures by using a computer-generated random-numbers method by the project coordinator with allocation concealed from the participants and dietitians until randomization was revealed to the study participants at the initial intervention clinic appointment.

Eighty-one participants who were eligible for the study were randomly assigned to one of the 2 groups. All had a 2-wk any artificial sweetener products including diet beverages washout period before intervention. The groups were the Water group in which subjects replaced habitual post lunch (main meal) intake of DBs with a glass of water (250 ml) and in the DBs group subjects were instructed to continue to drink DBs once a day (250ml), after their main meal (lunch) 5 times a week. Both groups were free to drink water as beverage at other times, but were not allowed to have DBs consumption. In addition, both groups were asked not to drink DBs or water during the lunch meal and also not to add low calorie sweeteners to beverages such as tea or coffee. To control the effects of menstrual cycle on measurements, participants started the study at the same phase of their menstrual cycle. Bi-weekly visits to the dietitian were required in order to promote adherence to the hypo-energetic diet and beverage substitution.

Dietary and activity programs

NovinDiet Clinic is a private weight loss clinic which uses an integrated approach (dietary, behavioural, exercise and medical treatments). Subjects who participated in this study did not pay clinic fees, were provided the diet beverages for DBs group and water for the Water group over the study. In this study the program was designed to enable weight loss of 7-10% of starting body weight, at a rate of 0.5-1 kg/week over 24 weeks. The individual diet programs were based on the individual's food diary records, with gradual adjustment to bring their diet in line with the NovinDiet protocol. PA was encouraged; the objective was to gradually increase activity levels to achieve 60 minutes of moderate activity on five days/ week. Predominant behavior change strategies applied included stages of change, goal setting, self-monitoring with food diaries and PA (17, 18).

At bi-weekly sessions, resources were provided as home booklets for each subject to record adherence to the diet protocol. During the intervention period, subjects completed the feedback form regarding their adherence to the diet. Subjects also had access to a website, weekly internet magazines, and one to one telephone/ online support from a consultant, if needed.

Outcomes

To assess the effect of replacing DBs with water outcomes were collected at the baseline, 12 weeks and 24 weeks (except height which was taken only at the screening visit).

Anthropometric measurements

Body weight was taken to the nearest 0.1 kg using a digital calibrated scale (Omron Health Care, Hoofdorp, Netherland), whilst subjects wore light clothing, without shoes. Body height was measured to the nearest 0.1 cm by using a wall mounted stadiometer (SECA, Hamburg, Germany) while participants were barefoot and in a free-standing position. Waist circumference (WC) was measured with a rigid measuring tape and recorded to the nearest 0.5 cm. WC was measured at the smallest horizontal circumference between the ribs and iliac crest (the natural waist), or, in case of an indeterminable waist narrowing, halfway between the lower rib and the iliac crest (19). BMI was calculated from measured weight in kilogram divided by the square of height in meters.

Blood sample measurements

Blood samples of all subjects were taken after overnight (8-10 h) fasting, between 07:00 and 09:00, at baseline, 12 and 24 weeks for biochemical, cellular and hormonal measurements. Fasting blood samples were collected by venipuncture according to a standard protocol. Blood samples were taken while the subjects were in a sitting position, according to the standard protocol, and were centrifuged at 2000g at room temperature within 30–45 min. Antecubital venous blood samples for two-hour postprandial plasma (2hpp) glucose were taken 2 hours after ingesting 75g of glucose according to the standard method(20). Fasting plasma glucose (FPG) and 2hpp plasma glucose levels were measured using the enzymatic colorimetric method. Insulin was measured by using a radioimmunoassay with ^{125}I-labeled human insulin and a human insulin antiserum in an immunoradiometric assay (IRMA) (Biosource, Dorest, Belgium) with a gamma-counter system (Gamma I; Genesys). Insulin resistance was evaluated by homeostasis model assessment of insulin resistance (HOMA-IR) (21).

Glycated hemoglobin (Hb A_{1C}) was measured by a colorimetric method after an initial separation by ion exchange chromatography (Biosystem, Barcelona, Spain).

Biochemical analysis of the serum total cholesterol (TC), triglyceride (TG), and high-density lipoprotein (HDL) cholesterol was carried out on a Selectra E auto analyzer (Vita Laboratory, Netherlands) following standard procedures of the Pars Azmoon diagnostic kits (Iran). The LDL cholesterol was calculated using the Friedewald formula(22).

LDL cholesterol = TC – HDL cholesterol + (TG ÷ 2.2)

Self-reported dietary assessment

Energy and macronutrient intake at baseline, weeks 11 and week 23 was analyzed by Nutritionist IV software (version 4.1; Hearst).

Statistical analyses

Baseline values of cardiovascular risk factors (including weight, waist circumference, LDL-c, HDL-c, TC, FPG, TG, fasting insulin, HOMA IR, Hb_{A1C}, 2hpp glucose data) were compared between the Water and DBs groups using unpaired *t*-tests.

At baseline, distribution was normal for all variables. All participants who were randomly assigned and completed an initial assessment were included in the final results by using an intention-to-treat analysis. Multiple imputations with the use of linear regression were used to impute missing values from 24 wk and were based on the assumption that data were missing at random.

The primary analysis was an intent to treat linear mixed effect, which assessed at 12 and 24 weeks. These models, which included time, treatment, a time by group interaction and the respective baseline value as principal explanatory variables for all 81 participants. The per-protocol analysis was also done for the outcomes .the results from per-protocol analysis were also similar to those of the intent to treat analysis in direction and significance. Statistical significance was set at $p \leq 0.05$. All data are presented as mean ± SD unless otherwise stated. Associations between variables were assessed by simple correlational analyses (Pearson's *r*). All statistical analyses were performed using SPSS 22.0 for Windows (SPSS Inc., USA).

The primary outcome addressed in this study was the difference in body weight loss during the 24 week weight loss program. The power calculation was based on the previous studies (16, 23) ($\alpha = 0.05$, power = 0.85), which were performed based upon expected differences in weight loss between weight loss diet groups (2.0 ± 2.5 kg) to determine the targeted final sample size ($n = 56$). Anticipating a dropout rate of 30% the sample size required was 80.

Results

Sample characteristics

124 patients with type 2 diabetes, who believed that they were eligible and expressed an interest in participating in the study, were evaluated for eligibility by a physician. After evaluation, 81 subjects were recruited and 65 subjects completed the 24-week intervention (with 80% retention rate, **Figure 1**). The remaining 81 subjects gave written consent and then randomly 41 subjects were allocated to the water and 40 to the DBs group. After starting the intervention, a total of 11 subjects dropped out because they did not wish to continue or they moved away from the area. 2 subjects left the study as they became pregnant. The remaining 3 subjects did not give any reason for their withdrawal.

At baseline, there were no statistically significant differences in age, physical characteristics or biochemical measurements between the groups or between those who completed or did not complete the study once recruited (**Table 1**).

Body weight

As shown in **Table-2**, there was a significant weight reduction in each group after 24 weeks ($P<0.001$). There was also a significant difference in weight reduction between the two groups after 24 weeks ($P=0.006$, **Figure 2**).

BMI and Waist circumference

BMI reduction in each group was in the expected direction with significant effects over 24 weeks for both groups ($P< 0.001$). However, the decline in BMI was greater in the water group than the DBs group after 24 weeks ($P=0.006$).

In both groups, waist circumference had decreased after 24 weeks of intervention ($P<0.001$) with no significant difference in WC effects between the two groups after the intervention ($P=0.833$).

Glucose metabolism measurement

Fasting plasma glucose, fasting serum insulin, 2 hour postprandial (2hpp) glucose, Hb A_{1C} and HOMA-IR all decreased over time in both groups ($P < 0.001$). Also between group differences were significant for all variables (Table 2).

There was a significant difference in fasting plasma glucose level changes between the two groups after 24 weeks ($P=0.005$). In terms of 2hpp, during the 24 weeks of intervention between group changes was significant ($P=0.027$).

There was a significant difference in insulin resistance between the two groups over 24 weeks ($P =0.003$) but no significant improvement in HbA_{1C} in the water group compared with the DBs group over the 24 weeks ($P =0.149$).

Furthermore, Fasting serum insulin concentration decreased significantly over time, with significant differences between the two groups after 24 weeks ($P=0.011$).

Food intake measurement

At baseline, there was no significant difference in energy intake. Estimated energy intake measurements showed a significant reduction over time in both groups ($P < 0.001$ for time effect). As shown in Table 3, there was a significant group*time interaction for total energy intake over 24 wk ($P = 0.005$).

In addition, macronutrient intake measurements showed no significant differences between the 2 groups at baseline. However, there was a greater carbohydrate deficit in the water group than in the DB group during the 24 wk of intervention (group * time interaction, $P < 0.001$, Table 3)

Discussion

The purpose of the present study was to compare the effects of DBs and water consumption after lunch, as a main meal, on weight loss and also characteristics of carbohydrate and lipid metabolism in overweight and obese women with type 2 diabetes attending a weight loss program for 24 weeks. The results of present study showed that drinking water may lead to more weight loss, a greater improvement in fasting plasma glucose, insulin sensitivity, measured by HOMA IR and 2hpp glucose levels compared with consumption of DBs in women with Type 2 diabetes.

To our knowledge, this study was the first randomized controlled trial in women with Type 2 diabetes which has assessed the impact of excluding DBs consumption on weight loss, during a voluntary weight reduction program, for 24 weeks.

Weight gain and obesity are strongly related to the increased risk of type 2 diabetes while moderate weight loss improves glycaemic control (1). All of the subjects in our weight loss plan had a significant weight loss. This would have been predicted given the characteristics of the prescribed treatment plan which included energy restriction, PA instruction and regular patient visit and consultation in the clinic. In other rigorous clinic-based behavioral lifestyle adjustment programs, 5–10% weight losses have been reported at 6 months (24-26) which is similar to the weight losses reported in our study. These comprehensive weight loss methods are more constantly effective in comparison with others recommending small but theoretically sustainable lifestyle changes that can be made to improve health (27). Furthermore, the present study showed a major reduction in waist circumference and significant improvements in cardio metabolic risk characteristics in both groups over 24 weeks, as would be predictable given the weight loss observed. Although the results indicated a significant effect of replacing DBs with water on weight loss during 24 weeks, it seems that the 24 weeks of intervention was not enough to reveal any significant effects on waist circumference (WC) as a related metabolic variable. Further longer term studies measuring metabolic effects, including WC, and more accurate assessment of body fat change using DEXA Scanning would be required.Previous intervention studies have attempted to investigate the effects of water and DBs consumption on weight loss with inconsistent results. In a recent study, the effects of either water or DBs consumption in comparison to SSBs, without any hypoenergetic diet, and only having group behavioural counselling to promote adherence to beverage substitution were compared(28). The authors failed to find any significant differences in weight loss between water and DBs. In another study(29), drinking water and diet beverage was compared in subjects undergoing cognitive behavior therapy only, with no specific dietary restrictions. The result of this study showed a greater impact on weight loss with DBs compared with water. On the other hand, in a study by Dennis et al. (30), subjects who were randomly assigned to drink pre-meal water lost about 2 kg more weight than subjects on an hypoenergetic diet alone. It should be noted that the protocol of the last study (30) was not similar to our study in that subjects in both groups had either water or DBs after their meal rather than before the meal, which is more representative of normal behaviour in this group. Furthermore, none of these studies involved obese or overweight subjects with Type 2 diabetes. Following our recent study (16) indicating the beneficial effects of replacing diet beverages with water on weight loss and insulin sensitivity of obese and overweight adults, our goal was to investigate whether these effects may be seen in women with Type 2 diabetes.

In our current study, participants drinking water after their lunch over 24 weeks lost 1.16 kg more than those in the DBs group, which is in agreement with the result of our previous study(16) where the overweight/ obese but otherwise healthy women in the water group lost 1.2 kg more than the DBs group. In contrast, our results are inconsistent with other studies which indicated either no significant change in effects on weight loss between water and DBs (28) or reported greater impact on weight loss with DBs compared with water(29). Nevertheless, it should be mentioned that these studies had different experimental designs, for example not including any weight loss plan(28) or have cognitive behavioral therapy alone for weight loss during a shorter period of 12 weeks(29). Also, the volume of beverage, the time of drinking and the type of participants were different in these studies.

The results of our latest study may have arisen because the effect of replacement of DBs with water may lead to better adherence to the weight loss diet in the Water group. It has been hypothesized that artificial sweeteners may raise the hedonic desire for sweetened and more energy dense foods (31-33). Also in our current study, the effect of replacement of DBs with water on weight loss reflected better adherence to the weight-loss diet in the water group. The greater reduction in energy intake in water group compared with DBs group resulted in more weight loss in this group than DBs group. Moreover, more reduction of carbohydrate consumption in the water group than in the DBs group might support greater weight loss in the water group. However, in order to elucidate the mechanism that might explain the better weight loss in the Water group compared with the DBs group, longer term studies are required.

Like our study on healthy overweight/obese women (16), our present study in women with Type 2 diabetes revealed a better improvement in fasting insulin sensitivity, (HOMA IR), in the Water group over the 24 weeks. there was also a beneficial impact of on fasting glucose and Hb_{A1C} in the Water group, although our previous study in women without diabetes(16) did not show any effects on these carbohydrate metabolism characteristics. But these outcomes seen on diabetic patients were consistent with the results of the recent epidemiological study indicating daily diet beverage consumption was associated with impaired glucose control(32). These results may have clinical implications, showing that if overweight/ obese people with Type2 diabetes use a weight loss plan, they may have better improvements in glycemic characteristics and weight loss if they drink water instead of DBs. These findings would reinforce the recommendations given in popular weight loss programs that the obese and overweight patients who are keen to lose weight should increase their water intake (10, 11). On the other hand, most obese people consider that they can drink diet beverages during a low- energy diet without any harmful effects on their weight management, and whilst they do still lose weight, the magnitude of the weight loss may be greater if they avoid DBs completely. Whilst the present study is consistent with the current guideline for increasing water consumption for better diabetes control, our results do not entirely support the recommendations indicating no deleterious effects of diet beverage on diabetes control(34). Since the consumption of diet soda is higher among people with diabetes than those without (35), the potential implications of studies such as ours needs further investigation.

The main strength of this study is that it was a randomized, outpatient clinical trial, whilst participants were selected from participants wished to lose weight and control their blood sugar and included middle-aged overweight and obese women who were able to comply with weight-loss plan; hence, they demonstrated that they were motivated to adhere to the weight-loss diet protocol (36). Thirdly Subjects who participated in this study did not pay clinic fees and were provided the diet beverages for DBs group and water for the Water group which were incentive for regular by-weekly visits with the dietitian when compliance could be encouraged in both groups.

On the other hand, there are some limitations. First of all, even though the sample size providing sufficient power to distinguish statistically significant effects in the key outcome variables, the sample was not representative of the general population, mainly as it did not include men. In addition, due to the possible effects of the time of the beverage consumption, we only asked the participants to drink either water or diet beverages after the lunch in order to cover this confounding factor. Also we did not record the fluid intake of participants as it may influence satiety. Moreover the energy expenditure was not verified which would affect weight loss. Lastly, although our weekly follow up by phone call and fortnight clinic visit to measure dietary compliance of the subjects, the present study

only relied upon subjective report of storing and consuming the water and DBs which is not as accurate as objective methods for measuring their compliance.

In conclusion, replacing DBs with water consumption would appear to impact beneficially on weight loss, BMI, FPG and insulin sensitivity in overweight and obese women with Type 2 diabetes following a weight loss diet. However, longer term studies are essential to see what would happen in long term in such patients.

Author contributions:

Experiments in this study were conducted in NovinDiet Clinic, Tehran. AM: contributed to the initial study design, study protocol setup, data collection, data analysis, and writing of the first draft of the manuscript; HRF: designed the research, conducted the research, contribution to data interpretation, revision of the manuscript and provided medical supervision; MAT, IAM: refined the study design and contributed to data interpretation and redrafting of the manuscript.RM and AD: provided advice and consultation for the study design, conducted the research. All authors read and approved the final manuscript. HRF is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 1. Baseline characteristics before the intervention*

	water group(n=41)	DBs Group(n=40)
Age (y)	34.15 (6.99)	35.45 (7.45)
Body wt (kg)	83.92 (4.42)	84.70 (7.43)
Height (cm)	159.83 (2.83)	159.65 (3.08)
BMI (kg/m²)	32.86 (1.67)	33.19 (2.25)
WC (cm)	103 (5)	102 (7)
Married	78%	82%
TC (mmol/l)	4.78 (0.43)	4.75 (0.37)
HDL-C (mmol/l)	1.13 (0.19)	1.13 (0.17)
LDL-C (mmol/l)	2.73 (0.51)	2.71 (0.38)
TG (mmol/l)	2.02 (0.27)	1.97 (0.25)
FPG (mmol/l)	8.49 (0.90)	8.48 (1.03)
2hppG (mmol/l)	8.82 (1.14)	8.76 (1.22)
HA1C (%)	6.97 (0.77)	6.95 (0.20)
Insulin (mU/l)	19.99 (4.07)	19.84 (4.07)
HOMA-IR	7.59 (1.93)	7.50 (1.89)

* Group difference, $P > 0.05$.

Data are presented as mean (SD)

Diet beverages: DBs, Waist circumference: WC, Total cholesterol: TC,
Triglyceride: TG, Fasting plasma Glucose: FPG, 2 hour post prandial glucose:
Glycated haemoglobin: HA1C,
Homeostasis model assessment of insulin resistance: HOMA-IR

Table 2. Anthropometric and blood measurement characteristics in Water and DBs Groups at baselien,12 and 24-week interventions*

	Water Group(n=41)			DBs Group(n=40)			P for time × group†
	Baseline	week 12	week 24	Baseline	week 12	week 24	
Weight, kg	83.92 (4.42)	79.96 (4.86)	77.52 (4.95)	84.70 (7.43)	81.25 (7.03)	79.45(6.99)	0.006
BMI, kg/m²	32.86 (1.67)	31.32 (2)	30.36(2.06)	33.19 (2.25)	31.84 (2.13)	31.14(2.12)	0.006
WC, cm ‡	103 (5)	99 (7)	97(7)	103 (7)	99 (7)	97(6)	0.832
TC, mmol/l ‡	4.78 (0.43)	4.52 (0.45)	4.29(0.41)	4.75 (0.37)	4.49 (0.37)	4.31 (0.33)	0.119
HDL-C, mmol/l ‡	1.13 (0.19)	1.23 (0.18)	1.33(0.17)	1.13 (0.17)	1.25 (0.18)	1.33(0.16)	0.319
LDL-C, mmol/l ‡	2.73 (0.51)	2.49 (0.49)	2.22(0.46)	2.71 (0.38)	2.44 (0.40)	2.24(0.35)	0.07
TG, mmol/l ‡	2.02 (0.27)	1.77 (0.28)	1.63(0.27)	1.97 (0.25)	1.75 (0.24)	1.62(0.19)	0.639
FPG, mmol/l	8.49 (0.90)	7.76 (0.82)	6.86(0.77)	8.48 (1.03)	7.85 (0.96)	7.19(0.81)	0.005
2hpp, mmol/l	8.82 (1.14)	7.91 (0.87)	7.15(0.70)	8.76 (1.22)	8.03 (1.06)	7.40(1.01)	0.027
Hb A1C,% ‡	6.97 (0.77)	6.16 (0.99)	5.80(0.82)	6.95 (0.20)	6.81 (0.17)	6.53(0.16)	0.149
Insulin, m U/l	19.99 (4.07)	16.75 (4.03)	14.27(3.81)	19.84 (4.07)	17.36 (3.43)	17.36(3.43)	0.011
HOMA-IR	7.59(1.93)	5.80(1.62)	4.39 (1.37)	7.50 (1.89)	6.05 (1.39)	5.01(1.20)	0.003

* Data are presented as mean (SD) for the 81 participants

† P values are for Water relative to DBs group (time × Group interaction) by a linear mixed model analysis with repeated measures.

‡ Significant main effect of time, $P < 0.001$

Diet beverages: DBs, Waist circumference :WC, Total cholesterol: TC,Triglyceride: TG,Fasting plasma glucose: FPG

Glycated hemoglobin: Hb A1C, 2 hour post prandial: 2hpp,Homeostasis model assessment of insulin resistance: HOMA-IR

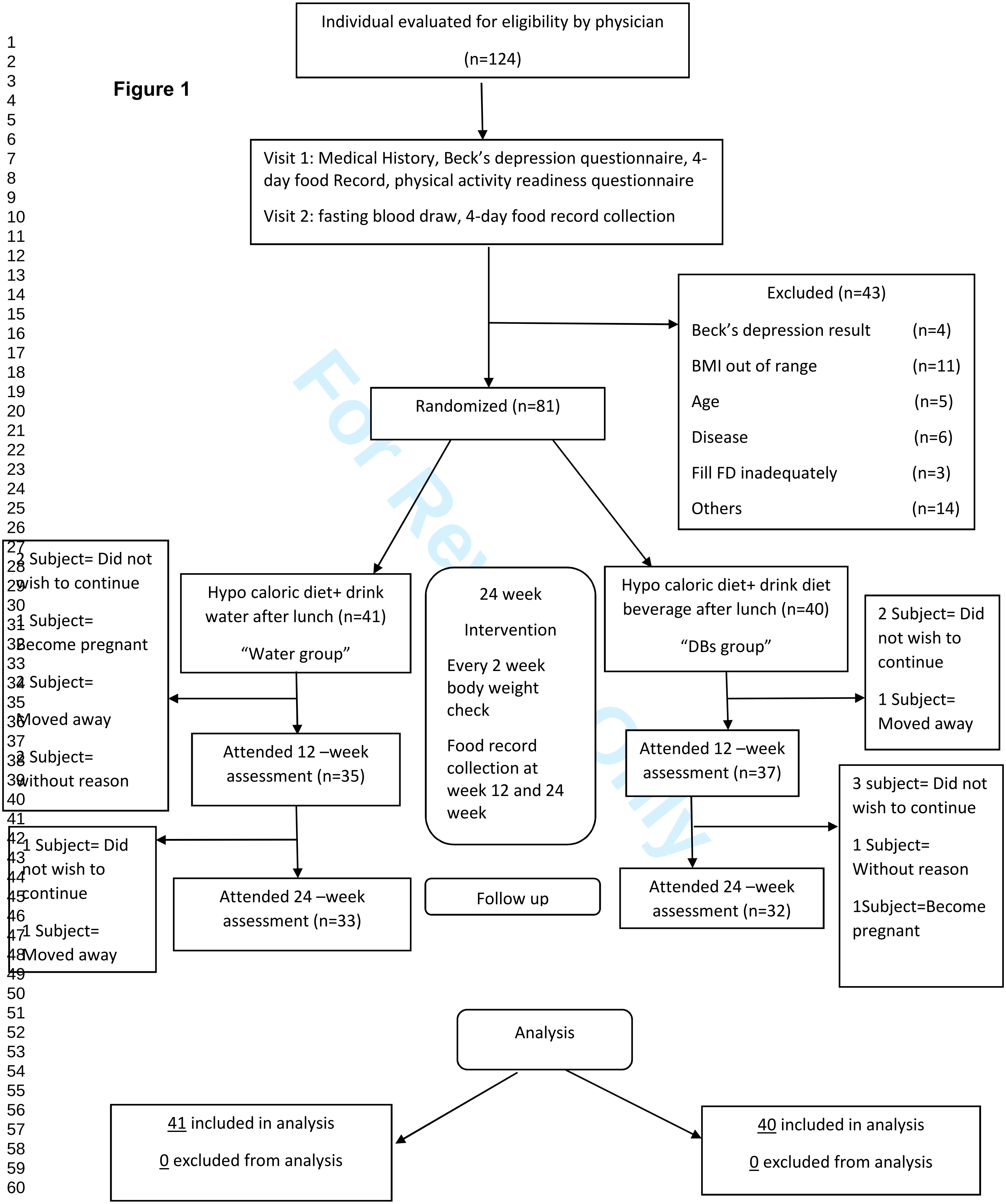
Table 3. Self-reported dietary intake in Water and DBs Groups before and after the 24-week interventions*

Intake	Water Group(n=41)		DBs Group(n=40)		P for time × group†
	Baseline	week 24	Baseline	week 24	
Total Energy (kcal)	2202(173)	1785(146)	2157(275)	1827(302)	0.005
Protein (g)	81.2(8.7)	79.6(9.4)	80.4(13.9)	80(15.6)	0.240
Protein (%)	14.8(2)	17.9(1.6)	14.9(2.1)	17.5(1.8)	
Fat (g)	86.2(11.7)	63.8(8.1)	82.6(16.6)	61.1(12)	0.675
Fat (%)	35.1(2.8)	32.1(2.3)	34.4(4.3)	30.1(2.4)	
Carbohydrate (g)	275.4(20.9)	223(17.6)	273.1(34.5)	239.1(38.6)	<0.001
Carbohydrate (%)	50.1(1.7)	50(2.5)	50.7(3.2)	52.4(2.4)	
Fiber(g)	20.7(5.3)	22.2(5.3)	20.8(3.1)	22.2(3.2)	0.280

* Data are presented as mean (SD) for the 81 participants

† P values are for Water relative to DBs group (time × Group interaction) by repeated-measures two way ANOVA

Figure 1


Individual evaluated for eligibility by physician
(n=124)
Visit 1: Medical History, Beck's depression questionnaire, 4-day food Record, physical activity readiness questionnaire
Visit 2: fasting blood draw, 4-day food record collection
Excluded (n=43)
Beck's depression result (n=4)
BMI out of range (n=11)
Age (n=5)
Disease (n=6)
Fill FD inadequately (n=3)
Others (n=14)
Randomized (n=81)
2 Subject= Did not wish to continue
1 Subject= Become pregnant
1 Subject= Moved away
2 Subject= without reason
Hypo caloric diet+ drink water after lunch (n=41)
"Water group"
24 week
Intervention
Every 2 week body weight check
Food record collection at week 12 and 24 week
Hypo caloric diet+ drink diet beverage after lunch (n=40)
"DBs group"
2 Subject= Did not wish to continue
1 Subject= Moved away
Attended 12 –week assessment (n=35)
Attended 12 –week assessment (n=37)
3 subject= Did not wish to continue
1 Subject= Without reason
1Subject=Become pregnant
1 Subject= Did not wish to continue
1 Subject= Moved away
Attended 24 –week assessment (n=33)
Follow up
Attended 24 –week assessment (n=32)
Analysis
41 included in analysis
0 excluded from analysis
40 included in analysis
0 excluded from analysis

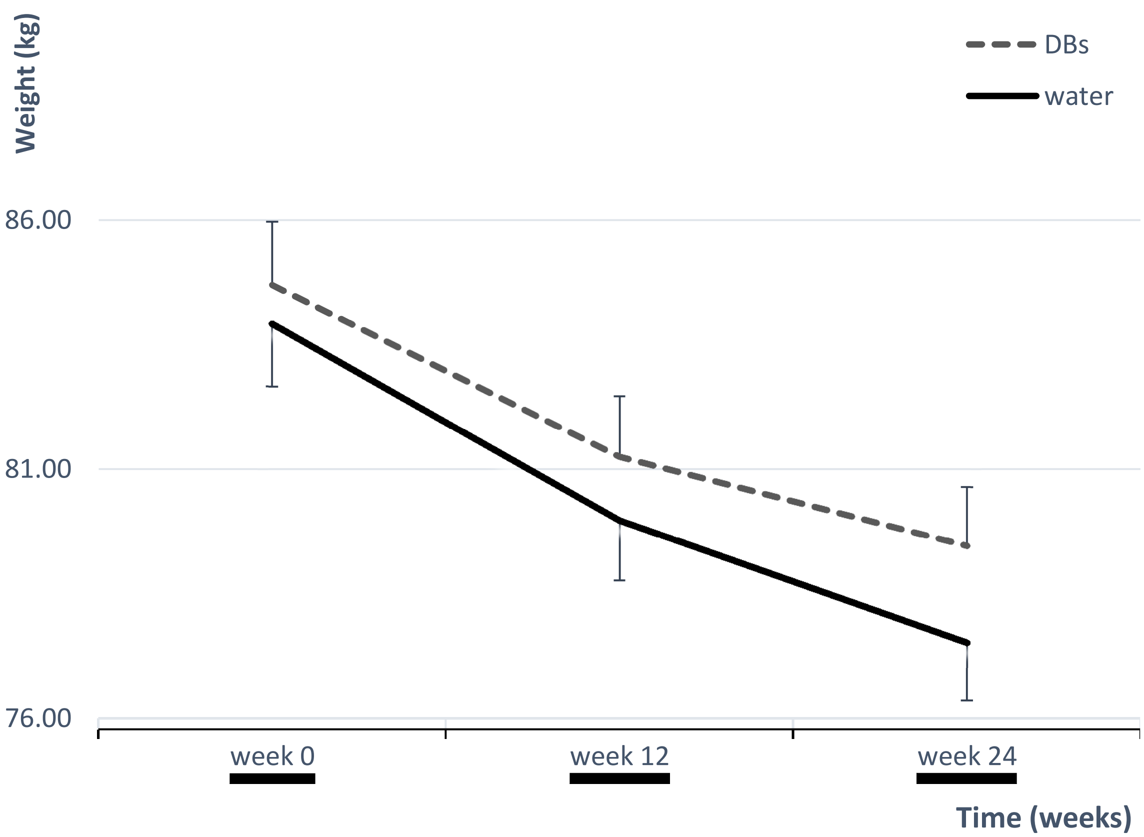


Figure 2 Mean (SE) weight at baseline, 12 and 24 wk of energy restriction with either drinking water (Water; *n* = 41) or diet beverages (DBs; *n* = 40) in all participants, regardless of attrition. *P* < 0.001 for the main effect of time.There was also a significant difference in weight reduction between the two groups after 24 weeks (P=0.006), based on linear mixed effects models.