Applied nutritional investigation

A meal replacement regimen improves blood glucose levels in prediabetic healthy individuals with impaired fasting glucose

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ABSTRACT

Objective: The aim of this study was to investigate the effect of a 6-wk intervention with either lifestyle intervention (increased physical activity and a low-calorie diet) or a meal replacement regimen on glycemic control in patients who are prediabetic and have impaired fasting glucose.
Methods: Forty-two overweight or obese men and women (age 54 ± 8 y; weight 95.1 ± 11.9 kg; body mass index [BMI] 32.8 ± 2.89 kg/m^2) were included in this randomized controlled clinical trial. Patients in the lifestyle group (LS; n = 14) received dietary counseling sessions (fat-restricted low-calorie diet) and instructions on how to increase physical activity. Patients in the meal replacement group (MR; n = 28) were instructed to replace two daily meals with a low-calorie, high soy-protein drink with a low glycemic index.
Results: Both interventions resulted in a significant decrease in body weight and BMI, although the reduction was more pronounced ($P < 0.05$) in the MR group. In both groups, glucose concentrations decreased significantly (LS: -12 mg/dL, $P < 0.01$; MR: -11 mg/dL, $P < 0.01$), and mean glucose levels returned to the normal range. Insulin (LS: -1 μU/mg [not significant]; MR: -6.3 μU/mg, $P < 0.01$) and homeostasis model assessment of insulin resistance (HOMA-IR; LS -0.92, $P < 0.01$; MR: -2.1, $P < 0.01$) were also significantly lower following both interventions; again improvements were more pronounced in the MR group (insulin: $P < 0.05$; HOMA $P < 0.01$)
Conclusion: It can be concluded that meal replacement is an effective intervention for rapid improvement of elevated fasting glucose and increased insulin concentrations, these being important biomarkers of the prediabetic state. The 6-wk intervention has shown that the effect of meal replacement on fasting blood glucose was comparable to the effect of lifestyle intervention. The alterations in BMI, insulin, and HOMA-IR were significantly more pronounced following the meal replacement regimen.

Introduction

Formal guidelines suggest that individuals showing increased fasting glucose concentrations (>100 mg/dL) that do not meet the criteria for diabetes mellitus (>126 mg/dL) should be diagnosed with prediabetes [1]. Additionally, the presence of impaired glucose tolerance (IGT; 2-h values in the oral glucose tolerance test of 140–199 mg/dL and an HbA$_{1c}$ range of 5.7%–6.4%) also identifies individuals with prediabetes. In these individuals, the postprandial phase is characterized by a large and more prolonged increase in blood glucose concentrations. It is estimated that approximately 10% of the adult population in Western societies have prediabetes [2]. Although individuals with prediabetes are healthy and per definition not diabetic, there is good scientific evidence to suggest they have an increased risk for the conversion to type 2 diabetes mellitus (T2DM) [3].

It has been demonstrated that the reconversion from the prediabetic state to normoglycemia may substantially reduce the risk for the development of T2DM and its associated complications [4]. Furthermore, it has been shown that the prediabetic state also is associated with early forms of neuropathy, nephropathy, or retinopathy [5]. Therefore, there is general agreement that individuals with prediabetes should be treated by therapeutic lifestyle interventions (TLC) or, in the case of malcompliance with TLC, by pharmacotherapy [6].

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The Diabetes Prevention Program and other clinical trials have shown that prediabetic conditions and insulin resistance (IR) can be improved [7]. Increasing evidence suggests that the risk for T2DM can be substantially reduced if one is physically active, loses weight, and makes wise food choices [8]. It has been demonstrated that meal replacement regimens are associated with fast weight loss and improvements in metabolic risk factors [9–11]. A recent Medline search showed that the effect of meal replacement on glycemic control and measures of IR has not been fully investigated in individuals with prediabetes. Therefore, in this study, the influence of a very-low-calorie meal replacement regimen by a soy-protein drink on changes in fasting glucose and insulin levels and the homeostasis model assessment of insulin resistance (HOMA-IR) were investigated. The effects of the meal replacement regimen were compared with those of a lifestyle intervention with a fat-restricted, low-calorie diet in combination with increased physical activity.

Methods

Pre-obese and obese men (n = 16) and women (n = 26) (age 54 ± 8 y; weight 95.1 ± 11.9 kg; body mass index [BMI] 32.8 ± 2.89 kg/m^2) with increased fasting blood glucose levels (>100 mg/dL and <126 mg/dL) were selected for this randomized parallel-group design investigation.

Patients with T2DM, clinically significant illnesses, or those who took anti-diabetic or lipid-lowering drugs were excluded. The present data set represents a subset from three studies that were all performed as randomized controlled trials with an identical design. All participants completed a comprehensive medical examination and routine blood tests. Written informed consent was provided by all participants, and the study protocol was approved by the Ethical Committee of the University of Freiburg. Participants were initially randomized into three equal groups as described previously [10]. In the first 6 wk, two groups received the same intervention (meal replacement [MR]) and were therefore pooled for analysis (MR group n = 28). This was feasible because the guided exercise program that was intended for one of the MR groups was not started before the end of the 6-wk period. The lifestyle (LS) group received lifestyle education only (LS group n = 14). The lifestyle education was designed in a way that participants in the LS group had the same negative energy balance as those in the MR group.

Lifestyle education consisted in group sessions in which the participants were informed about the importance of physical activity for weight loss and improvement of metabolic risk factors. Furthermore, they were instructed on how to increase physical activity and individual information was provided regarding the amount that should be attained to increase energy expenditure (∼300–400 kcal/d). Additionally, they were advised on ways to change their habitual diet to a low-calorie, fat-reduced diet according to the guidelines of the German Nutrition Society (DGE). This diet consisted of approximately 55% to 60% energy from carbohydrate, 25% to 30% from fat, and 15% from protein (1200–1500 kcal/d for women and 1500–1800 kcal/d for men). Participants assigned to the MR group were instructed to replace two daily meals with a commercially available soy-yogurt-honey preparation (Almased®), known to have a low glycemic index [12] and a high content of bioactive genisteins [13]. This diet contained about 1000 kcal/d for women and 1200 kcal/d for men. Data collected at enrolment and after 6 wk were body weight, height, BMI (kg/m^2), fasting blood glucose, and fasting insulin from which the HOMA-IR was calculated. Hemoglobin (Hb)A$_{1c}$ was not investigated, because it is less suited to detect relatively subtle changes in patients with prediabetes in a period of only 6 wk [1].

Normality of all variables was tested before statistical analyses using the Kolmogorov-Smirnov test procedure. Testing for changes between the two examinations was performed by the paired-sample *t* test. The unpaired-sample *t* test was used to establish significant differences between the two groups at both examinations. All *P*-values were two-sided and a *P*-value of ≤0.05 was considered statistically significant. Analysis was conducted using SPSS software (version 20).

Results

All 42 participants completed the study and compliance and adherence to the recommendations were good in both groups; none of the individuals stated being unable to fulfill the requirements of the study protocol.

Initial body weight of those in the LS group (n = 14) was higher than in the MR group (n = 28). However, this difference

Table 1
Baseline and postintervention levels of target variables

	Intervention	
	Lifestyle	Meal replacement
	Mean (± SD)	Mean (± SD)
Height (cm)	172 (± 12)	169 (± 9)
Body weight-2 (kg)	93.34* (± 11.36)	87.98† (± 10.84)
BMI-1 (kg/m^2)	32.83 (± 2.31)	32.88 (± 3.18)
BMI-2 (kg/m^2)	31.46† (± 2.29)	30.86† (± 3.20)
Glucose-1 (mg/dL)	109 (± 8)	109 (± 5)
Glucose-2 (mg/dL)	97† (± 10)	98† (± 7)
Insulin-1 (μU/mL)	10 (± 4.1)	13.9 (± 6.5)
Insulin-2 (μU/mL)	9.00‡ (± 5.25)	7.60† (± 4.38)
HOMA-1	3.46 (1.52)	3.90 (2.23)
HOMA-2	2.54† (1.50)	1.84† (1.15)

BMI, body mass index; HOMA-IR, homeostasis model assessment of insulin resistance

Significance within groups Lifestyle vs. Meal replacement
* *P* < 0.05.
† *P* < 0.001.
‡ Not significant.

was not significant. Additionally, because BMI did not differ between the groups, it was not of clinical relevance (Table 1).

Both groups showed a significant decrease in body weight and BMI, although the reduction was more pronounced (*P* < 0.05) in the MR group (Fig. 1). In both groups, glucose concentrations decreased significantly (LS: −12 mg/dL, *P* < 0.01; MR: −11 mg/dL, *P* < 0.01) and mean glucose levels returned to the normal range. Insulin (LS: −1 μU/mg [not significant]; MR: −6.3 μU/mg, *P* < 0.01) was significantly lower following both interventions; again the improvements were more pronounced in the MR group (insulin *P* < 0.05; HOMA *P* < 0.01).

Discussion

The main finding of the present study was that the MR regimen induced a significant reduction in both fasting blood glucose and insulin concentrations as well as in HOMA-IR. With respect to fasting glucose, the effect was comparable to lifestyle education. In contrast, the effect of the MR intervention on body weight, insulin, and HOMA-IR was more pronounced in the MR group. There is broad scientific consensus that the prediabetic state should be treated with comprehensive lifestyle inventions or even drug therapy if lifestyle is not desired or applicable [3,14]. It is estimated that the conversion rate from prediabetes to T2DM is approximately 10%, although the numbers may vary as a function of diagnostic criteria or ethnicity [3]. A number of large intervention trials have convincingly demonstrated the potential of lifestyle interventions on decreasing the conversion rate from prediabetes to T2DM. In the DPPOS (Diabetes Prevention Program Outcomes Study), the risk for developing diabetes was 56% lower for participants who had returned to normal glucose regulation than for those who consistently had prediabetes [4]. Interestingly, the risk remained significantly reduced, even if the reversion to normal glucose levels was only transient [4]. Therefore, it could be speculated that the individuals in our trial are likely to have a significantly lower conversion rate to T2DM in the future.

Apart from the weight loss, the effect of MR on fasting glucose concentrations and in particular on insulin levels and HOMA-IR also could be explained by the specific components of soy that are contained in the MR. Clinical studies that examined the effects of soy foods and soy proteins on elevated glucose and
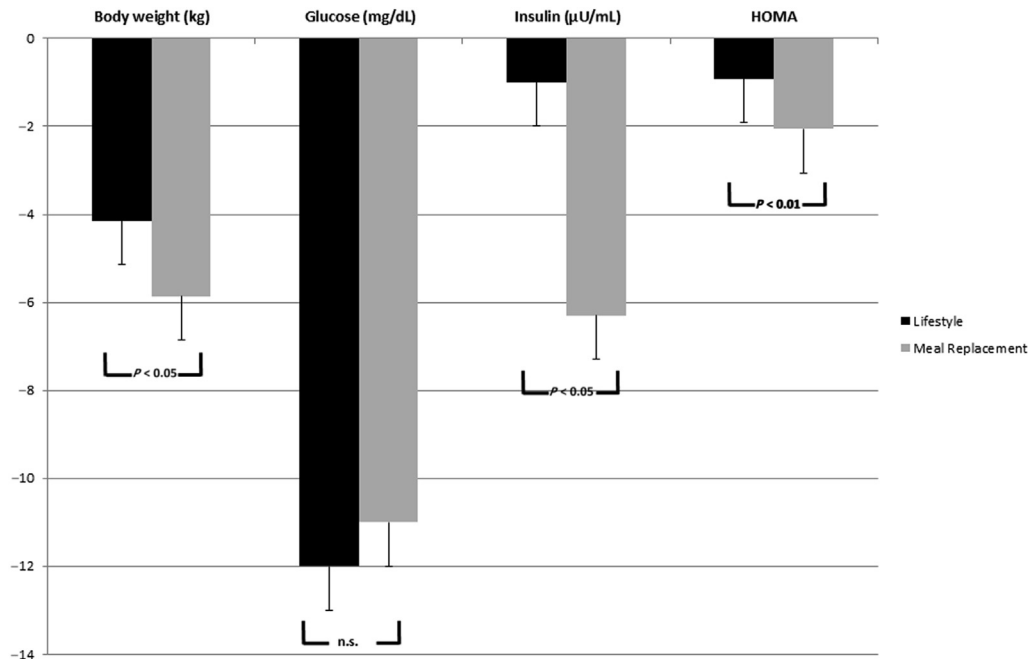
Fig. 1. Changes in target variables (6 wk minus baseline value). Black bars: decrease in target variables following the lifestyle intervention. Gray bars: decrease in target variables following the meal replacement regimen. HOMA, homeostasis model assessment; n.s., not significant.

insulin levels produced encouraging, although somewhat inconsistent results.

Soy-protein consumption revealed a beneficial effect in cases of prediabetes [15]. Observational studies in Asians indicated a very significant inverse dose-dependent association between soybean intake and the risk for diabetes, particularly with fermented soybean products [16–18]. There is also experimental evidence suggesting that soy protein improves IR and lipid levels by activating peroxisome proliferator–activated receptors (PPARs) [19,20]. One study demonstrated that consumption of a high-isoflavone, soy-protein diet improves glucose tolerance, IR, hepatic cholesterol, and triglyceride concentrations in obese Zucker rats [19]. In cell culture studies, these investigators further showed that isoflavone-containing soy extracts and individual soy isoflavones increased the gene expression of PPARs, suggesting that the beneficial effects of soy protein on glucose and lipid metabolism may be mediated by PPAR activation. Another study [21] demonstrated that soy-protein feeding in rats decreased hepatic triglyceride levels and epididymal adipose tissue weight. These changes were associated with increased activity and mRNA levels of several skeletal muscle enzymes involved in fatty acid oxidation. Moreover, PPAR-γ coactivator PGC1-α and PPAR-α mRNA levels also were found to be elevated, suggesting that soy-protein intake stimulates skeletal muscle fatty acid oxidation by activating PPAR pathways leading to a reduced accumulation of body fat [21].

Altogether, the direct interaction of bioactive soy ingredients with glucose control mechanisms on a cellular level may help to understand the beneficial influence of soy proteins on glycemic control in individuals with prediabetes.

Lifestyle intervention programs also can significantly reduce the incidence of T2DM in individuals with prediabetes [3,22]. In one study [22], diabetes was found in 9 individuals in the intervention group (n = 103) and 18 in the control group (n = 110). These data clearly show that lifestyle changes that improve glycemic control in healthy individuals lower the risk for diabetes [4].

Conclusion

Results from this study have demonstrated that both lifestyle intervention by increased physical activity and a hypocaloric low-fat diet, and meal replacement using a soy-protein formula, decrease fasting glucose levels by approximately 10%. Therefore, the meal replacement regimen as applied has the potential to restore individuals with prediabetes to normal glucose regulation.

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