Clinical Benefit of a Short Term Dietary Oatmeal Intervention in Patients with Type 2 Diabetes and Severe Insulin Resistance: A Pilot Study

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Key words
- insulin resistance
- carbohydrate-days
- adiponectin
- leptin

Abstract

Aims/hypothesis: To evaluate the potential effectiveness of 'carbohydrate days' as a dietary intervention to overcome insulin resistance in type 2 diabetes.

Materials and Methods: Patients (n = 14) with uncontrolled type 2 diabetes and insulin resistance as defined by a dosage of more than 1 IU/day*kg BW were consecutively enrolled in this prospective study. Primary outcomes were daily insulin requirement and mean blood glucose levels which were evaluated before, after, and 4 weeks after the intervention.

Results: All patients had a metabolic syndrome, 75% had microvascular and 57.1% macrovascular complications. Hospital setting and diabetes adapted diet alone led to improved glycemic control with a mean blood glucose 158 ± 47 mg/dl. Intervention with two days of oatmeal diet further decreased mean blood glucose to 118 ± 37 mg/dl ($p < 0.05$). This was associated with a significant reduction of insulin dosage by 42.5% (before: 145 ± 68.9 U/d, after 83 ± 34.2 U/d, $p < 0.001$) as well as a significant reduction (−26.4%, $p < 0.01$) of serum leptin levels.After the four weeks outpatient period, insulin dosage remained significantly decreased (83 ± 20.2 U/kg*d, $p < 0.01$). Glycemic control was comparable (mean blood glucose141 ± 20.78 mg/dl) to glucose levels within the hospital setting. Adiponectin levels increased significantly by 53.8% ($p < 0.05$).

Conclusions: In this uncontrolled pilot study, hospital admission and diabetes adapted diet followed by oatmeal intervention achieved a ~40% reduction of insulin dosage required to achieve controlled glucose levels. This effect was conserved after a 4 week outpatient phase with normal diet.

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Introduction

Insulin resistance is a central feature of type 2 diabetes [1]. Chronic hyperglycemia is associated with adverse outcomes [2] and the development of micro- and macrovascular complications [3]. An established intervention to improve insulin resistance and glucose control in patients with type 2 diabetes (T2DM) is the use of a diet rich in complex carbohydrates and dietary fiber. The basic principle of this dietary intervention termed 'carbohydrate days' was first introduced in 1903 by Carl von Noorden [4]. While still applied in clinical practice today, to our best knowledge there is no published scientific evaluation regarding the effectiveness of this approach in patients with uncontrolled T2DM.

Therefore, we designed a pilot study to evaluate the efficiency of short term oatmeal-'carbohydrate days' on markers of insulin resistance and glucose metabolism in an inpatient clinical setting and after a follow up of four weeks. We analyzed adipocytokines and free fatty acids which are associated with insulin resistance [5, 6].

Research Design and Methods

We designed a prospective cohort study with consecutive inclusion of patients in an inpatient clinical setting. Inclusion criteria for the study presented here were: a. T2DM, b. inappropriate glucose control (mean blood glucose >200 mg/dl or HbA1c >8%), c. insulin dependency and d. insulin-resistance by a daily insulin dose of more than one unit per kilogram body weight [7]. Primary outcomes were daily insulin requirement and mean blood glucose. The study was approved by the local ethics committee.

At study entry the insulin-dose was adjusted in a two day run in phase to achieve adequate glycemic control. During this phase, all patients received a diabetes-adapted diet with a macronutrient content of 50–55% carbohydrates, 15–20% protein and 30% fat at an energy intake of ~1,500 kcal daily. Thereafter, the dietary intervention was performed for 2 days with 15 carbohydrate units of oatmeal. This diet has a macronutrient content of 63% carbohydrates 12% protein, 7% fat and 16.2 g of fiber (30% soluble and 70% insoluble) at an energy content of 1,100 kcal per day. Within this phase, insulin dosage was reduced by 40%. Further reduction by an average of 10% was necessary on day two of oatmeal to prevent hypoglycemia. The intervention was completed with one day of normal diabetes-adapted diet for final titration of the insulin dosage. During run in phase, intervention and the final adjustment correction of insulin dosage was individualized to achieve pre-prandial blood glucose levels < 150 mg/dl.

Fourteen patients affected by the metabolic syndrome (NCEP ATPIII) with abdominal obesity (BMI 36.9 ± 9.3 kg/m^2), arterial hypertension and severe insulin resistance (**Table 1**) were included. Average age was 60.1 ± 10.1 years with a long history of diabetes (15.7 ± 9.3 years). 71.1% (10/14) were females; 75% had microvascular complications and 57.1% of the patients suffered from macrovascular complications. Nine participants were followed up after 4 weeks in an outpatient setting.

Blood samples were collected after an overnight fast on the first day of oatmeal, directly and 4 weeks after intervention. Data of preprandial blood glucose self monitoring were used for analysis. HbA1c was measured by the Bio-Rad's Micromat™ II (Bio-Rad, Munich, Germany). A RIA method was used for analysis of leptin [8]. Adiponectin was determined by an EIA (Mediagnost, Reutlingen, Germany). Cholesterol, HDL, LDL, triglycerides and free fatty acids were measured by routine laboratory. All values are given as mean ± sd. Statistical analysis was performed by Wilcoxon testing in comparison to baseline values (Pre). A p value of < 0.05 was considered to be statistically significant.

Results

After two days of diabetes adapted diet mean blood glucose was 158 ± 47 mg/dl (**Table 1**) at an insulin dose of 1.4 ± 0.5 U/kg*d. Consecutive treatment with oatmeal for two days significantly reduced the insulin dosage by 42.5% ($p < 0.001$). This was associated with a significant improvement of mean blood glucose (118 ± 37 mg/dl, $p < 0.05$) and paralleled by a significant reduction (−26.4%) of serum leptin levels. Adiponectin levels, however, remained unaffected.

Despite returning to regular diet within the 4 weeks of the outpatient period, patients showed a persistent improvement of glycemic control and significantly reduced insulin doses (−39.3%, $p < 0.01$). HbA1c showed a trend for reduction (8.6–8.2%, $p = 0.09$). Adiponectin levels increased significantly by 53.8% ($p < 0.05$). The lipid profile yielded small significant reductions of cholesterol and triglycerides in the acute setting. Free fatty acids did not change within the study and remained elevated (~15–17% above limit).

Table 1 Metabolic changes by "oatmeal-days"

	Pre	After	At 4 Weeks
mean blood glucose [mg/dl]	158 ± 47.3	115 ± 36.7*	141 ± 20.78
mean daily insulin [IE/d]	145 ± 68.9	83 ± 34.2***	83 ± 20.2**
cholesterol [mg/dl]	180 ± 39.9	162 ± 31.4*	180 ± 43.0
LDL [mg/dl]	110 ± 35.4	96 ± 28.2	105 ± 46.4
HDL [mg/dl]	31 ± 7.1	30 ± 5.9	35 ± 11.9
triglycerides [mg/dl]	237 ± 131.09	177 ± 76.77**	201 ± 66.0
free fatty acids [mmol/l]	0.8 ± 0.23	0.9 ± 0.35	0.8 ± 0.2
leptin [ng/ml]	33 ± 16.3	24 ± 11.5**	28 ± 16.2
adiponectin [μg/ml]	3.4 ± 1.8	3.7 ± 1.7	5.2 ± 2.8*
HbA1c [%]	8.6 ± 0.8	–	8.2 ± 0.5

Blood sampling was performed directly before (Pre, n = 14), after two days of oatmeal (After, n = 14) and after 4 weeks (At 4 weeks, n = 9). Mean blood glucose was calculated by summarizing pre-meal blood glucose levels divided by the number of performed measurements. Data are given as means ± standard deviation. (p-value: * < 0.05, ** < 0.01 and *** < 0.001)

Discussion

In this pilot study, the two day oatmeal intervention achieved a ~40% reduction of insulin dose accompanied with almost normalization of mean blood glucose. Although the intervention lasted only for 2 days we observed a lasting significant reduction of insulin dosage and ameliorated mean blood glucose in the follow up 4 weeks after hospital dismissal. The pathophysiological grounds by which this effect is achieved remain obscure. Several possible mechanisms appear involved 1. the dietary intervention was hypocaloric, 2. intake of saturated fat was reduced and 3. intake of fiber was increased. Improvement of insulin resistance by these mechanisms has been demonstrated in long term interventional as well as epidemiological studies [9–11].

Similar results with short term interventions have been demonstrated by Weickert et al. Their diet enriched with 30 g of the insoluble fraction of dietary oat fibre for 24 hours improved markers of insulin sensitivity in healthy women [12]. Furthermore, they showed that an intervention with oat fibre for 3 days in overweight and obese women improved insulin sensitivity as measured by the euglycemic-hyperinsulinemic clamp [13]. Consistent with our observations, the latter study demonstrated a delayed effect on insulin sensitivity.

The improvement of insulin resistance as indicated by reduced insulin dose and mean blood glucose was associated with an acute reduction of leptin and a 53.8% increase of adiponectin after 4 weeks. This rise may be a cause for the persistent improvement of insulin sensitivity [14, 15]. Interestingly, levels of free fatty acids did not change within the different phases of the study. All subjects demonstrated elevated levels through out the course of the study. This is consisting with findings in poorly controlled T2DM patients after an intervention with three days of insulin-induced normoglycemia [16].

We are aware that our pilot study has several limitations. We showed systematically in a descriptive manner that a short term intervention consisting of a hypocaloric carbohydrate rich diet successfully improved glycemic control and reduced the subsequently needed insulin dosage in patients with uncontrolled type 2 diabetes up to 4 weeks. Furthermore, the lost of follow-up in our study may have generated a selection bias. Our study was not designed to dissect the possible mechanisms by which these

effects may have been achieved. Due to the lack of a control group we cannot assess the specific contribution of oatmeal alone. Further studies are necessary to validate and explore the concept of carbohydrate days for treatment of insulin resistance in insulin dependent T2DM patients.

Competing Interests:

"None to declare"

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