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Modified Food Selection Improves Obesity-Related Metabolic Disturbances Independent from Weight Loss

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Abstract: Dietary therapy has been shown to be important to reduce weight and other risk factors for CVD if a high-risk pattern is present. We investigated if modified food selection improved obesity-related metabolic disturbance independently from weight loss in a prospective cohort study. After a comprehensive 4-week residential period which stressed healthy food, physical training, and stress management, patients were followed for one year. The most common diagnoses besides obesity were hypertension, type-2 diabetes and dyslipidemia. A dietary questionnaire was completed at the first visit and after one year. Weight loss resulted in lower blood glucose (B-Glu) Odds Ratio (OR) = 2.45, $p<0.001$, serum triglyceride (S-TG) OR = 2.80, $p<0.001$ and serum urate (S-Urate) OR = 2.62, $p<0.001$. With less fat on bread body weight was reduced (OR = 2.46, $p<0.01$), and with less candy S-HDL was increased (OR = 1.72, $p<0.01$) and S-Urate was decreased (OR = 2.10, $p<0.001$). A decrease in S-Urate was not found associated with more fruit and berries (OR = 0.48 $p<0.05$), less cheese (OR = 0.38, $p<0.05$) or less milk (OR = 0.50 $p<0.05$). Less coffee was associated with decreased systolic blood pressure (SBP) OR = 1.85, $p<0.05$. Modified food selection was associated with improved risk factor levels independently from weight loss.

Keywords: Food, intervention, metabolic syndrome, obesity, weight loss.

INTRODUCTION

To improve health – e.g., by tackling the increasing problem of obesity and related metabolic disorders –- risk factors can be reduced by making changes in food consumption, both amount and type, and by increasing physical activity [1-4]. Lifestyle interventions have strong impact on CVD risk factors [1, 2, 5-7]. A combination of dietary changes, energy restriction and increased level of physical activity seems to be effective in the long run, and often more pronounced in the short term [8, 9].

During recent years the influence from macronutrients, e.g., high protein or high carbohydrate diets, has been in focus for weight loss and CVD risk factors. Both high carbohydrate and high protein diets improve CVD risk with weight loss, although the weight loss per se causes these improvements [10]. Comparable effects on long-term weight loss may be achieved with diets differing in glycemic load [11, 12].

The DASH diet reduces blood pressure and modifies biomarkers of disease risk [2]. Exercise and healthy diet are known to improve carbohydrate metabolism and glycemic control [13, 14]. Also, energy restriction with body weight loss improves glycemic control in obesity and mild type-2 diabetes [15]. Obesity-related disturbances are thus alleviated by reducing body weight [16]. However, there is an increasing interest in the effects of different types of diets and food groups, a complement to the focus on single macronutrients [17-19]. Protective effects from whole-grain, low-fat dairy products, vegetables, and fruit have been presented [20-23]. This study assessed whether a modification in the selection of single foods could be associated with improvements in obesity-related disturbances after adjusting for weight loss, sex and age one year after a 4-week comprehensive intervention program.

MATERIALS AND METHODOLOGY

Population and Intervention

Patients (n=995) were referred during 1984-1987, from physicians working in primary health care and in hospitals in Västerbotten, Sweden to the Vindeln Patient Education Center (VPE-center). They had multiple health problems, e.g., hypertension, type-2 diabetes and dyslipidemia, in addition to obesity [24]. No differences in mean body weight or level of metabolic disturbance were seen at the baseline between the study group (n=599) and those subjects who did not accept the invitation (n=396) after one year. To be included, they had to be physically able to take part in a full-time schedule. The 4-week residential comprehensive program consisted of group sessions that addressed nutrition, physical activities, stress relief, smoking cessation, etc. [25]. A dietician, a physician, and a physiotherapist gave individualized advice about energy restriction and physical training at the end of the course at the Centre, to be maintained in the habitual environment. Daily energy intake was restricted to 6,000–7500 kJ (~1,500 kcal) per day, achieved by prescribing a diet with a low-fat content and a low energy density. The goals for this study were to assess the associations between patterns of food selection and metabolic parameters related to obesity at admittance and after one year. Patients were invited to a four-day refresher course after one year to remind them about the importance of addressing lifestyle with both proper food choices and physical activity.

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Physical and Biochemical Variables

The physical examination was performed on the first or second day of the visit. A medical journal was set up for each patient admitted, and all data, including for the follow-up period, were collected at the Centre. The BMI (kg/m^2) was calculated, and systolic blood pressure (SBP) and diastolic blood pressure (DBP) (mmHg) were measured as a mean of three BP measurements obtained in a sitting position.

At the start of the program, all patients fasted before blood samples were drawn in the morning. The samples were analyzed according to standardized routine procedures of the Department of Clinical Chemistry, University Hospital, Umeå, Sweden. The levels of B-Glu (mmol/l), S-TG (mmol/l), S-Chol (mmol/l), S-HDL (mmol/l), and S-Urate (mmol/l) were determined using routine methods on a Hitachi 717 multianalyser (Boehringer Mannheim Diagnostica, Mannheim, Germany).

Food Questionnaire and Selections

When the patients were admitted to the VPE Center, questionnaires (995) were used to gather information about their selection of raw vegetables (frequency), fruit and berries (frequency), milk (frequency and type), cheese (frequency), candies (frequency), fat (amount and type), bread (type), coffee (cups), sugar in coffee or tea (lumps), salt (frequency), cookies and cakes (frequency). Patients completed questionnaires again at the 4-day follow-up a year later (n=599, 60%).

Questions about time spent eating and smoking habits were also evaluated (data not presented in this report). An individual patient could have changed in one or more of 14 dietary questions, but a healthy choice in one question did not necessarily indicate a healthy choice in another question. A healthy food selection corresponded to more raw vegetables, fruit and berries, whole-grain bread, low-fat margarine, less full-cream milk or less amount of milk, fat on bread, candy, sugar in coffee, cookies and cakes, table salt, coffee, and alcoholic beverages.

Statistics

Multiple logistic regression analysis, with changed risk factor level over one year as dependent variables, was performed and adjusted ORs (95% CI) were calculated for food choices and alcohol intake over one year. Each model was adjusted for baseline pattern for the food selected (dichotomized), age, sex, BMI at baseline, BMI change and baseline value for the risk factor studied. For S-HDL, baseline cholesterol change in S-Chol was included.

The analyses were carried out using the SAS program pack 9.1.3 [26]. Proc GLM in the SAS program was used. Multiple comparisons were made using the Bonferroni

Table 1. Personal Data, Risk Factors and Main Diagnoses for the whole Cohort and Study Group and for the Subjects Not Admitted to the Follow Up. DM = Diabetes Mellitus. IHD/PMI = Ischemic Heart Disease/Post-Myocardial Infarction

	The whole Cohort	Subjects not admitted at 1 yr [1]	Study group			
			Baseline	1 yr	Diff	
	(n=995)	(n=396)	(n=599)	(n= 599)		*P*-value
Age, yrs	49.7 (10.1)	48.1 (10.9)	50.8 (9.5)			
Men/Women, %	44 / 56	41 / 59	45 / 55			
BMI, kg/m^2	31.9 (5.0)	32.3 (4.8)	31.6 (5.1)	30.3 (4.7)	- 1.3 (2.3)	<0.001
SBP, mmHg	144 (19)	142 (19)	145 (19)	136 (17)	- 8.8 (17.2)	<0.001
B-Glucose, mmol/l	6.8 (3.4)	6.7 (3.4)	6.8 (3.3)	6.5 (2.7)	- 0.26 (2.44)	0.0091
S-TG, mmol/l	2.4 (1.7)	2.4 (1.7)	2.5 (1.8)	2.2 (1.5)	- 0.25 (1.22)	<0.001
S-HDL, mmol/l	1.3 (0.4)	1.3 (0.4)	1.3 (0.4)	1.3 (0.4)	+ 0.02 (0.26)	0.177
S-Urate, mmol/l	344 (85)	345 (85)	344 (86)	332 (86)	- 12 (60)	<0.001
Main diagnosis, %						
Hypertension	42 %	36 %	46 %			
Type-2 DM	19 %	20 %	19 %			
IHD/PMI	5 %	5 %	5 %			
Dyslipidemia	7 %	6 %	8 %			
Obesity	26 %	32 %	21 %			
Other diagnoses	1 %	1 %	1 %			

All values are mean and (SD).
[1]Values are not significantly different from that of the study group at baseline.

method [27]. In the multiple regressions, age, sex, and BMI at baseline and changes in BMI over one year together with the level of the metabolites at baseline were controlled for. Adjustments were also made for the baseline food selection. Each question was coded and turned into indicator variables. Data that were lacking in the questionnaires were considered as missing. The study was approved by the Regional Ethical Review Board in Umeå, Sweden (Dnr 05-177M) and registered as a Lifestyle intervention trial (no. ISRCTN79355192).

RESULTS

Patients and Diagnoses

The change in level of metabolites at one year was compared to the baseline for each individual, and thereby each patient acted as his or her own control (Table **1**). One fifth of the study group had obesity as the main diagnosis and they had a low prevalence of an additional diagnosis (Table **1**). The aim with the therapy in this group was to prevent the progression of metabolic disturbance associated with obesity. Body mass index (BMI = kg/m^2) in this group at the time of admission (35.1±4.7 kg/m^2) was also higher than in subjects with type-2 diabetes (30.4±4.9; p<0.001) or hypertension (31.5±5.2; p<0.001).

Body Weight Loss

Mean body weight loss at one year was 4.0±5.8 kg (BMI change = –1.3 ±2.3), a number that corresponds to 4.2±5.7% of initial body weight. Women lost 4.1±6.1 kg (3.7±6.0 %) and men 4.4±5.5 kg (4.3±5.2 %).

The difference for each metabolite over one year is presented in Table **1**. The multiple logistic regression analysis with BMI change as the dependent variable and each of the risk factors as the independent variables with adjustments for age, sex, BMI and the risk factor at baseline are presented in Table **2**. There was a high correlation between the level of the metabolites at baseline and its change over time. These correlations are referred to as regression towards the mean. Age and sex were also associated with a change in S-Urate.

Modified Food Selection

To evaluate effects of food selection on changes in obesity-related metabolic variables, each risk factor change was used as the dependent variable with age and sex, BMI at baseline, change in BMI and baseline-values for every single metabolite and food pattern included as independent variables in each model.

As seen in Table **3**, using less fat on bread was associated with weight loss (OR=2.461 (1.378-4.395) (p<0.01). Eating more whole-grain bread and more vegetables was almost significantly associated with weight loss (OR=1.746 (0.977-3.121) (p<0.06) and 1.681 (0.933-3.030) (p<0.08), respectively. A reduction in coffee consumption (reduced from >7 cups a day) reduced SBP. More vegetables but not less cookies and cakes reduced S-TG. Less fat on bread, increased intake of low-fat margarine/improved fat quality or less candy increased S-HDL. More fruit and berries, less milk or cheese limited the possibility to reduce S-Urate. A decreased frequency of candy or alcohol decreased S-Urate.

DISCUSSION

A weight loss of 4–5 kg, or about 4% of the initial body weight, was associated with decreased B-Glu, S-TG, and S-Urate levels after adjustment for age, sex and BMI. With this moderate weight loss, important improvements of CVD risk factors were still shown. The impressive decrease of SBP (-8.8 mmHg) indicates the importance of multiple lifestyle interventions. However, exercise and diet-induced weight loss may be additive in the effect on high blood pressure [1].

Other lifestyle intervention trials show reduced SBP and blood lipids at a weight loss between 5 and 10% of the baseline weight [28,29]. The metabolic response per se from a negative energy balance seems to be important, rather than the level of weight loss or the glycemic load [11]. Weight loss elicits physiological improvements – making it difficult to conclude about the effects from macronutrients and/or different food items.

We performed a multiple logistic regression analysis to control for weight loss in the test of associations between altered food selection and obesity-related disturbances. The strength of each change, e.g., the level of risk besides age and sex, and progression of the disease, has to be considered to understand the effect of dietary changes on obesity-related disturbances.

Other intervention studies, which focus on multiple lifestyle changes, show similar results to those in our study [5-7, 16]. Even greater effects have been shown 6 months after a lifestyle intervention with a loss of 8% of body weight and 10 mmHg decreases in SBP [8]. A weight loss of 4% was achieved in addition to improved cardiovascular function

Table 2. The Association Between Weight Change and Changes in Risk Factors Over One Year

Variables	n	OR (95% CI)	*P*-value
SBP, mmHg ↓	567	1.331 (0.811–2.182)	0.2577
B-Glu, mmol/l ↓	498	2.452 (1.495–4.021)	0.0004
S-TG, mmol/l ↓	555	2.804 (1.759–4.469)	<0.0001
S-Chol, mmol/l ↓	563	1.271 (0.803–2.011)	0.3067
S-HDL, mmol/l ↑	558	1.366 (0.865–2.159)	0.1813
S-Urate, mmol/l ↓	550	2.615 (1.630–4.196)	<0.0001

Each calculation was adjusted for age, sex, BMI and the risk factor at baseline. For S-HDL, S-Chol at baseline and change over one year are included.

Table 3. Association Between Changed Risk Factor Levels (Dependent Variables) and Altered Food Selection

Changed pattern	N	BMI (kg/m^2)	SBP (mmHg)	B-Glu (mmol/l)	S-TG (mmol/l)	S-HDL (mmol/l)	S-Urate (mmol/l)
		↓	↓	↓	↓	↑	↓
Raw vegetables ↑	539	1.681 0.933-3.030	0.792 0.471-1.330	0.757 0.465-1.233	1.650 * 1.003-2.714	1.019 0.640-1.622	1.338 0.829-2.160
Fruit and berries ↑	551	0.772 0.369-1.616	1.001 0.530-1.890	0.806 0.429-1.514	0.616 0.329-1.154	0.873 0.486-1.567	0.482* 0.262-0.887
Amount of milk ↓	526	0.847 0427-1.682	1.803 0.990-3.285	0.720 0.401-1.293	0.929 0.521-1.657	1.350 0.780-2.335	0.501 * 0.284-0.884
Full-cream milk ↓	525	1.325 0.757-2.318	0.798 0.486-1.310	1.297 0.800-2.104	1.282 0.794-2.070	1.080 0.690-1.690	0.938 0.590-1.491
Amount of cheese ↓	485	1.061 0.487-2.310	1.169 0.617-2.216	1.038 0.567-1.900	1.052 0.569-1.944	1.298 0.732-2.304	0.383 * 0.205-0.717
Whole-grain bread ↑	493	1.746 0.977-3.121	1.033 0.616-1.731	1.242 0.770-2.004	1.186 0.730-1.928	1.088 0.691-1.713	1.203 0.748-1.934
Fat on bread ↓	483	2.461 ** 1.378-4.395	1.228 0.763-1.977	0.738 0.471-1.156	1.394 0.873-2.227	1.581* 1.032-2.424	1.128 0.724-1.756
Low-fat marga-rine ↑	503	1.471 0.848-2.552	0.681 0.425-1.091	0.845 0.531-1.344	1.111 0.703-1.755	1.655 * 1.070-2.558	1.203 0.769-1.881
Candies ↓	516	1.099 0.645-1.872	0.955 0.603-1.511	1.155 0.740-1.803	0.850 0.549-1.317	1.722 ** 1.131-2.622	2.099 *** 1.349-3.265
Sugar in coffee ↓	553	0.925 0.426-2.012	0.798 0.393-1.620	0.799 0.399-1.601	0.584 0.288-1.185	1.112 0.577-2.141	0.636 0.326-1.243
Cookies and cakes ↓	511	1.292 0.788-2.118	0.716 0.462-1.109	1.063 0.698-1.618	0.639* 0.418-0.976	1.090 0.735-1.618	1.221 0.811-1.837
Table salt ↓	527	1.351 0.722-2.529	1.423 0.811-2.495	0.731 0.426-1.256	0.863 0.503-1.481	1.070 0.648-1.767	0.884 0.523-1.496
Coffee ↓	522	0.895 0.473-1.695	1.851* 1.017-3.372	1.670 0.958-2.912	0.782 0.455-1.342	0.783 0.472-1.300	1.141 0.667-1.953
Alcohol ↓	505	0.833 0.480-1.447	1.511 0.907-2.519	1.084 0.671-1.752	1.239 0.770-1.994	1.405 0.893-2.211	1.645* 1.026-2.640

Each calculation was adjusted for baseline pattern of the variable, age, sex, BMI at baseline, BMI change and baseline value for the risk factor studied. For S-HDL, baseline cholesterol and change in S-Chol was included.* $p<0.05$ ** $p<0.01$ *** $p<0.001$.

already after two months [9]. After 14 months, moderately low-fat intake, rather than very low fat intake, improved CVD risk factors, and this could be explained by better adherence to the dietary strategies [30]. In our study a reduced amount of fat on bread, indicating less energy density of the diet, was associated with weight loss and increased S-HDL. Whole-grain cereals can reduce the risk of type-2 DM [31] and reduce visceral adipose tissue [20]. Both of those effects of whole-grain cereals, blood glucose reduction and body weight loss, may reduce the risk of developing type-2 DM. However, in our study we did not find any effect of increased intake of whole-grain bread on the studied CVD risk factors.

Modified food selection and increased physical training were the main goals at the VPE-center. It has been shown that low fat milk intake may prevent insulin resistance syndrome [21]. It has also been shown in the DASH study that a low fat diet, besides salt restriction and intake of low-fat milk products, reduces BP [2, 32]. However, changing from high fat to low-fat milk in the present study did not reduce body weight or any of the risk factors studied. On the contrary, we found that a reduced milk intake hindered a decrease in S-Urate. This suggests that further studies are needed on the effect of milk intake on CVD risk factors. The most impressive BP reductions in the present study were seen with a reduced alcohol intake (12.5±17.6 mmHg). Numerous dietary factors can influence BP [2, 32, 33]. By reducing alcohol in the obese, high-risk condition, we found a decreased S-TG and an almost significant decrease in SBP and S-Urate after adjusting for weight loss and other confounders. Weight loss and reduced alcohol intake are two therapeutic goals in treating patients with gout, and these results are of interest also in the obese condition. Because S-Urate is a risk factor for morbidity and mortality (especially in metabolic syndrome), and because weight loss and changed food selection (more fruit, less candy, less alcohol) can influence the degree of S-Urate reduction, these results need to be evaluated further. S-Urate should then be considered either as an end product from purine metabolism or as an antioxidant. More fruit and vegetables are described as one way to improve health [34]. We found that an increased intake of fruit and berries was less likely to be associated with a decrease in S-Urate levels. It is shown that S-Urate increases with a high consumption of apples, six per day [35]. As fruit is more frequently consumed than berries, and since fruit contains more fructose than berries, we think the changes in S-Urate may have been due to changes in fruit intake. However, no studies have investigated this question. Thus, it seems to be important to study the effects of vegetables separated from those of fruit when S-Urate is evaluated in connection with obesity. Due to the recommendations to increase intake of whole-grain bread, fruit and vegetables, the carbohydrate intake was probably increased. Portion sizes of meat, fish and chicken, etc. were kept normal and therefore, the protein intake was probably reduced and the relative contributions of protein and carbohydrates (P/CHO-ratio) was probably also reduced after the intervention.

It is well known that obesity is positively related to S-TG and inversely related to S-HDL [36]. As S-HDL levels are associated with both age and sex, this could have contributed to the lesser influence of dietary changes on S-HDL. By reducing amount of candy and fat on bread, but also improving fat quality, S-HDL will increase. It has been shown in another study that nutrition education and dietary counselling strategies, in addition to physical activity prescription, should be followed-up closely to maintain increased S-HDL and decreased S-TG levels [37]. Katan *et al.* (1997) discussed whether a high carbohydrate diet should be recommended for everyone, due to the fact that S-TG might increase and S-HDL decrease with such a diet [38].

The dietary treatment offered at VPE-Center had impressive effects on obesity-related metabolic disturbances over one year, and improved metabolic profiles were associated with changed selections for a healthy food pattern. More vegetables, less fat on bread, more whole-grain bread, and less candy are all important recommendations to achieve benefits. The question about the amount of fruit in a weight-loss regime needs to be studied further in both clinical and epidemiological studies, but the advice to reduce alcohol seems to be effective. The importance of improved selections of food, to choose "the healthy alternatives", is necessary for improving obesity related disturbances.

CONCLUSION

The multiple logistic regressions showed that improved food selection was associated with weight loss and improved obesity-related risk factors for CVD. Furthermore, the improved risk factors occurred independently from the weight loss. Both a reduction of candy and increased intake of fruit and berries contributed to a change in S-Urate, but in opposite directions. With improved fat quality, less fat on bread and less candy, S-HDL increased.

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