A prospective clinical pilot-trial comparing the effect of an optimized mixed diet versus a flexible low-glycemic index diet on nutrient intake and HbA\textsubscript{1c} levels in children with type 1 diabetes

Jan Marquard\textsuperscript{1,*}, Anna Stahl\textsuperscript{2}, Christian Lerch\textsuperscript{3}, Mareen Wolters\textsuperscript{4}, Maike Grotzke-Leweling\textsuperscript{1}, Ertan Mayatepek\textsuperscript{1} and Thomas Meissner\textsuperscript{1}

\textsuperscript{1} Department of General Pediatrics, University Children’s Hospital Dusseldorf, Duesseldorf, Germany
\textsuperscript{2} German Diabetes Center, Leibniz Institute for Diabetes Research, Duesseldorf, Germany
\textsuperscript{3} Department of General Practice, Cochrane Metabolic and Endocrine Disorders Group, University Hospital Dusseldorf, Duesseldorf, Germany

Abstract

Background: Low-glycemic index (GI) diet vs. high-GI diet improves glycemic control, but it is not clear whether a low-GI diet is superior to an optimized mixed diet (OMD).

Methods: This was a 12-week parallel-group pilot-trial including 17 children with type 1 diabetes. A separate dietary education into the allocated diet (OMD vs. low-GI) was performed. Nutrition was recorded by means of a three-day dietary record.

Objectives: The primary objective was to determine the macro- and micronutrient composition of the different diets, the secondary objective was to determine the short-term effect on HbA\textsubscript{1c} levels.

Results: In the low-GI group carbohydrate intake decreased, fat intake increased by trend. In the OMD group fat and energy intake decreased. No changes of HbA\textsubscript{1c} levels between the groups were observed.

Conclusion: OMD could have positive effects in overweight and obese diabetic children, since a reduction in fat and energy intake can be achieved. The findings of this pilot-trial suggest that OMD could be superior to a low-GI diet.

Keywords: diet; HbA\textsubscript{1c}; nutrition; type 1 diabetes.

Introduction

In addition to insulin treatment nutritional management is one of the cornerstones of type 1 diabetes care and education (1, 2). The basic aims of nutritional management in children with diabetes according to the International Society for Pediatric and Adolescent Diabetes (ISPAD) are to provide sufficient and appropriate energy intake and nutrients for optimal growth, development and good health. Moreover, to achieve and maintain an appropriate body mass index (BMI) and to strike a balance between food intake, metabolic requirements, energy expenditure and insulin action profiles to attain optimum glycemic control. In general, there is a recommendation of having three balanced meals a day with additional healthy snacks; the total daily energy intake should be distributed as 50%–55% of carbohydrate, 30%–35% of fat and 10%–15% of protein (3). The strong recommendation for children and young people to undertake regular physical activity is as important as the nutritional management. These recommendations partly correspond to dietary instruction based on the food pyramid of the United States Department of Agriculture (4) and the recommendations given in the optimized mixed diet (OMD) by the Research Institute of Child Nutrition in Dortmund, Germany (FKE) (5). Nutritional advice should ideally be adapted to cultural, ethnic and family traditions and the psychosocial needs of the individual child (1). Ultimately the ISPAD dietary recommendations are based upon general healthy eating principles suitable for all children and families and are focused on counting carbohydrates and matching insulin doses to the grams of carbohydrate consumed. Yet, there is currently no universal approach to the optimal dietary strategy for diabetes (3). The recommendation implies that different carbohydrates have the same effect on blood glucose, but use of the glycemic index (GI) has been shown to provide additional benefit to glycemic control over that observed when total carbohydrate is considered alone (6–9). The rate of carbohydrate absorption after a meal, as quantified by GI, has effects on postprandial endocrine and metabolic responses. After eating a high GI meal, initial high blood glucose and insulin levels were found, followed by reactive hypoglycemia, counter regulatory hormone secretion and elevated serum free fatty acid concentrations (10). In case of patients with diabetes, these pathophysiological conditions could impair the glycemic control. In contrast, a low-GI meal causes a slower and more sustained blood glucose response.

The benefit of a pure low-GI diet in diabetic patients is controversially discussed (11). There is evidence that a low-GI diet vs. a high-GI diet reduces glucose excursions and improves glycemic control in pediatric diabetic patients (8, 12) but it is not clear whether a low-GI diet is superior to an optimized mixed diet including vegetables, fruits, intact whole grains...
and legumes that, in general, also have a low-GI rank. Up to now, most of research studies compared low-GI diets with high GI diets or carbohydrate exchange diets (8). Gilbertson et al. showed in 2001 that a flexible dietary instruction based on the food pyramid with an emphasis of low-GI foods improves HbA1c levels without increasing the risk of hypoglycemia and enhances the quality of life among children with diabetes. In 2009, Rovner et al. presented their data, where subjects wore a continuous blood glucose monitoring system and completed diet diaries on two days (on the first day participants consumed usual meals, on the second day low-GI meals). During the low-GI day, mean daytime blood glucose values, blood glucose area above 180 mg/dL and high blood glucose index were lower compared to the usual mean day.

Critics of the low-GI diet believe that it may limit food choice and increases fat intake (11).

The primary objective of our study was to determine the macro- and micronutrient composition of OMD vs. a low-GI diet in pediatric patients with type 1 diabetes; secondary objectives were to determine the short-term effect on HbA1c levels within 3 months and the contentment of the families with the allocated diet. In the current study we tested the hypothesis that the macro- and micronutrient composition of OMD is superior to a low-GI diet in children with type 1 diabetes.

Patients and methods

Trial design

This was a 12-week single-center, open-label, parallel-group pilot-trial performed between August 2007 and December 2007 in the University’s Children’s Hospital in Duesseldorf, Germany. The trial was conducted in agreement with the Declaration of Helsinki. The protocol was approved by Local Ethical Committee, the patients and their parents gave written informed consent.

Eligible patients and their parents were asked by letter attending the trial; furthermore an informative meeting was performed. Families who were interested to participate in the study were invited to the first visit. On this visit, an instruction in the 3-day dietary record was performed for all patients and their parents together. Prior to the intervention, the first 3-day dietary record was completed, thus documenting the previous food patterns. On the second visit, data of body dimension and HbA1c levels were collected. To reduce baseline imbalance, the intervention group was assigned using minimization according to age, gender, BMI, duration of diabetes and HbA1c values (13). An education regarding the allocated study diet (OMD or low-GI) was performed. At a time of 1, 2 and 3 months after beginning of the intervention, a 3-day dietary record was documented, followed by the third and last visit where data of body dimension and HbA1c levels were collected again.

In addition, a questionnaire regarding contentment with the allocated diet was answered at the end of the study by parents and children together. Figure 1 summarizes the trial profile of this study.

Participants

Children with type 1 diabetes were selected using the following criteria: 1) age between 6 and 14 years, 2) diagnosis of type 1 diabetes for longer than 1 year, 3) treatment with an intensive conventional insulin therapy (ICT), 4) no additional dietary restrictions, 5) exclusion of other chronic diseases, 6) no medications that would affect appetite.

Interventions: diet education

Instructions for the dietary record and diet education were conducted by the research dietician in group session for children alone, parents alone and children and parents together. The duration per session was approximately 90 min. Diet education was performed in the form of a presentation and an active practice. Suggestions for recipes were delivered to the families.

Optimized mixed diet

The OMD is a flexible diet plan; instead it is a setting that helps families to implement a healthy diet in their daily lives. In OMD “recommended” foods can be separated from “tolerated” foods. The “recommended” foods cover the nutritional intake of 100%, but only about 90% of energy required. Thus, approximately 10% of total energy intake can be recovered by food like sweets, sweetened beverages or other snacks. This calculation is based on reference values for energy intake including moderate physical activity (5).

Flexible Low-Glycemic Index diet

The low-GI diet in this study was based on the dietary recommendations of OMD but focuses on other priorities. Table 1 shows detailed information of OMD and low-GI diet, which were used in this study.

Dietary record

The dietary record was adopted from “The Eating study” as a KiGGS Module (EsKiMo) (14), a module of the German Health Interview and Examination Survey for Children and Adolescents (KiGGS) (15). Food intake was assessed using dietary records on three consecutive days; the selection of weekdays was free.

The following data were collected in the dietary record: date, time and location of consumption, portion size, detailed product information (e.g., brand name, fat content, fortification) and preparation (e.g., raw, boiled, and deep-fried). Energy and nutrient intake was estimated with the same methods as in EsKiMo. Portion sizes were identified using a German picture book adapted from the EPIC-SOFT Picture Book (16), by means of packaging size and household measurements or by weighing. The calculation of average daily energy and nutrient intakes from the dietary records was done using the EsKiMo nutrient database. This database included the German Nutrient Database (BLS version II.3; Max Rubner Institut, Karlsruhe, Germany), which is a standard instrument for the assessment of nutritional surveys in Germany, and additional branded foods and fortified foods [see (17) for more details]. The individual energy, macro- and micronutrient and water intakes were calculated using the 3-day dietary record at each point of time. The dietary records were completed four times (at month 0, 1, 2 and 3), and phone calls were made weekly to ensure compliance.

Nutritional Quality Index

For the assessment of the total micronutrient intake, the Nutritional Quality Index (NQI), which is composed of Intake Quality Scores (IQS), was used (18). The IQS of a vitamin or mineral is the individual average daily intake in percent of the German reference value (19) (100% at most). The NQI takes the intakes of vitamin A, vitamin D, vitamin E, vitamin K, thiamine, riboflavin, niacin, pyridoxine, folate, pantothenic acid, biotin, vitamin B12, vitamin C, potassium, sodium, phosphor, magnesium, iron and zinc into account. The NQI was calculated as harmonic mean using the following formula:
NQI = \[\frac{N}{(1/IQS_1) + (1/IQS_2) + \ldots + (1/IQS_N)}\] with \(N\) = number of micro-nutrient and \(n = 1, 2, \ldots, N\).

HbA\(_{1c}\)

Serum HbA\(_{1c}\) (DCCT aligned) was measured at a local laboratory with an immunoturbidimetric immunoassay by Roche Diagnostics\(^\circledR\) (Mannheim, Germany).

**Efficacy measures**

The primary efficacy outcome measure was the macro- and micro-nutrient composition of OMD and low-GI diet as measured by change in the macro- and micronutrient composition from baseline to endpoint. Endpoint was defined as completion of the last dietary record at study end (12 weeks). Secondary outcome measures were (a) glycemic control as measured by change in HbA\(_{1c}\) from baseline to endpoint and (b) contentment with the allocated diet at endpoint.

**Table 1** Dietary advice. Dietary advice given to the children and families randomized to the OMD or flexible low-GI diet at entry of the study.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Optimized-mixed diet</th>
<th>Flexible low-glycemic index diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 rules</td>
<td>“3 rules”</td>
<td>Avoid consuming</td>
</tr>
<tr>
<td></td>
<td>Plenty of plant fruits (vegetables, fruits, cereals)</td>
<td>Carbohydrate carriers (pasta, rice)</td>
</tr>
<tr>
<td></td>
<td>Moderately animal food (milk, dairy products, meat, sausage, eggs)</td>
<td>Sweets</td>
</tr>
<tr>
<td></td>
<td>Occasionally fat and sugar rich food (sweets)</td>
<td>Light bread and biscuits made with white flour</td>
</tr>
<tr>
<td>Number of meals</td>
<td>5 a day</td>
<td>Free</td>
</tr>
<tr>
<td>Grains</td>
<td>&gt;50% whole grain</td>
<td>Whole grain only</td>
</tr>
<tr>
<td>Beverages</td>
<td>Calorie poor or free at any time</td>
<td>Calorie poor or free at any time</td>
</tr>
</tbody>
</table>
Statistical analyses

Variables were described by means and standard deviations. For primary and secondary efficacy measures the Wilcoxon signed-rank test was used to assess the related samples. The Mann-Whitney U-test was used to assess differences between the OMD- and low-GI group (independent samples). Statistical significance was defined as p≤0.05. Statistical analyses were performed using SPSS (version 11.5.1, 2002).

Results

Patient disposition and baseline characteristics

Patient disposition is shown in Figure 1. A total of 210 children with type 1 diabetes were assessed for eligibility for the study. 70 patients were eligible, a total number of 17 children and their parents agreed to participate, and were enrolled, one patient of the low-GI group was withdrawn from the study after 2 and 3 months (72±20 g/day baseline, 54±10 g/day at 2 months, p=0.02; 58±15 g/day at 3 months, p=0.05) was observed. In the low-GI group, an increase in relative fat intake was observed by trend, but it was not statistically significant (±2.5±3%, p=0.17). Fiber intake did neither in the OMD nor the low-GI group change.

Over the whole observation period there were no changes observed in micronutrient intake as measured by the Nutritional Quality Index.

Glycemic control

After 3 months of intervention there were no differences in HbA1c levels between the OMD- and low-GI group and within the groups (Table 3). During the observation period there were no variations in ICT.

Questionnaire regarding contentment with allocated diet

In the OMD group 22% of families, in the low-GI group 29% reported a limitation of previous eating habits (p=0.84). There was a trend for spending more money on food in the OMD group, but it was not statistically significant (33% additional cost reported in OMD, in low-GI 0%, p=0.30). The additional cost was due to consuming more organic food. In the OMD group all families (100%) reported to continue implementation of dietary advice in the future, in the low-GI group 86% of families were motivated to continue the low-GI diet (p=0.68).

Study group preintervention vs. patients not enrolled

There were no differences in age, sex and BMI-SDS between all patients of the study group (OMD and low-GI together) preintervention and the eligible patients not enrolled. Patients of the study group had significant lower HbA1c levels compared with patients not enrolled (7.2±0.6% in study group; 7.7±0.7% in patients not enrolled, p=0.02).

Discussion

The low-GI diet was associated with a decrease in carbohydrate intake and increase in percent energy from fat intake by trend. OMD was associated with a decrease of fat intake and overall energy intake. No significant changes in HbA1c levels between the two study groups were observed in this pilot study.

Previous studies have shown benefits of low-GI diets, particularly an improvement in HbA1c levels when compared...
However, the question arises whether a low-GI diet is superior to OMD which is recommended by ISPAD. In general, most vegetables (except potatoes), most fruits, intact whole grains, and legumes have a low-GI rank, whereas more refined and processed foods, such as white bread, typically have a high-GI rank. Buyken et al. could demonstrate that OMD is characterized by a low dietary GI (20). Our study figured out that there were no significant changes in HbA₁c levels between the two study groups. The lack of HbA₁c improvement in our study could be explained by a short observation period. Gilbertson et al. could demonstrate an improvement in HbA₁c levels in the low-GI group not before 12 months of intervention (8). The fact of significant improvement in HbA₁c levels in Gilbertson’s study in the low-GI group could also be explained by consuming more health promoting food like whole grains, fruits and vegetables because the low-GI diet was also based on the food pyramid. Another point which might explain the fact of a missing HbA₁c improvement is the fact that the study patients started with already good HbA₁c levels compared with the patients not enrolled, suggesting that the study patients were generally more motivated concerning treatment of diabetes.

Baseline data of macro- and micronutrient intake of study patients showed that they had already health promoting nutrition habits, reflected in low fat and protein intake, high carbohydrate intake and no excessive energy intake. The carbohydrate distribution in mono-, di-, and polysaccharides reflects also health promoting nutrition habits. Therefore, it could be...
difficult to improve HbA1c levels through dietary advice when nutrition is already comparatively health promoting.

In the OMD group, but not in the low-GI group, a significant decrease in energy intake could be observed after 3 months. This could be regarded as a benefit of OMD especially in overweight and obese diabetic patients.

Probably implementation of change in diet is even more difficult in diabetic children than a daily insulin therapy. Our study showed that motivated children are ready to switch nutrition. Therefore, it must be discussed if OMD could be recommended especially for children with limited adherence. In comparison to low-GI diet, there are fewer restrictions in OMD, particularly sweets and sweetened beverages are allowed in small amounts. Perhaps this could improve adherence. Critics of the low-GI diet believe that it might restrict food variety and increase fat intake (21).

In micronutrient intake, no significant changes were observed. Baseline Index Data of the Nutritional Quality Index was at 79.5%, hence in a normal range [79% median in EsKiMo study (14)]. One could have expected an increase of the NQI especially in the OMD group, but there were no significant changes. Actually, OMD is designed to supply 100% of the recommended micronutrient intake; it has to be discussed in how far an implementation of the recommendations of the German Nutrition Society is possible in practice.

Concerning the contentment with the allocated diet, there were no statistically significant differences between low-GI and the OMD group. Furthermore, the GI has been criticized as being a concept that is too complex for pediatric diabetes management and has limited clinical utility, also it is not realistic for children to estimate the GI of every food they consume (22).

It must be pointed out that this study was performed as a pilot study and the number of cases was limited. By using the sample mean outlier could have affected the outcome. However, we decided to use the mean because all values of the study were in a plausible range and should be included in the analysis.

The study results indicate that OMD, which is characterized by foods with low GI rank, seems to be easier implemented by children because of fewer limitations than in low GI diet. In particular, OMD could have positive effects in overweight and obese diabetic children, since a reduction in fat and energy intake can be achieved which could reduce the risk of cardiovascular diseases. In summary, these findings suggest that OMD could be superior to a low-GI diet. Long-term studies with larger numbers are now indicated.

### References


### Table 3

Baseline and outcome measures for patients assigned to OMD and low GI diet groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline measures</th>
<th>3 Months</th>
<th>p-Value Low-GI</th>
<th>p*-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study diet</td>
<td>Baseline measures</td>
<td>3 Months</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OMD</td>
<td>Low-GI</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n = 9)</td>
<td>(n = 7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>7.4 ± 0.6</td>
<td>7.0 ± 0.5</td>
<td>7.3 ± 0.5</td>
<td>0.04</td>
</tr>
<tr>
<td>BMI-SDS</td>
<td>0.12 ± 0.07</td>
<td>0.42 ± 0.4</td>
<td>0.32 ± 0.7</td>
<td>0.07</td>
</tr>
<tr>
<td>Energy intake, kcal/day</td>
<td>1767 ± 2300</td>
<td>1847 ± 281</td>
<td>1532 ± 286</td>
<td>0.05</td>
</tr>
<tr>
<td>Fiber intake, g/day</td>
<td>20.4 ± 21</td>
<td>21.3 ± 3</td>
<td>23.8 ± 1.9</td>
<td>0.21</td>
</tr>
<tr>
<td>Carb intake abs., g/day</td>
<td>214 ± 34</td>
<td>236 ± 46</td>
<td>191 ± 20</td>
<td>0.17</td>
</tr>
<tr>
<td>Fat intake abs., g/day</td>
<td>61.6 ± 5.5</td>
<td>63.5 ± 7</td>
<td>61.8 ± 5</td>
<td>0.86</td>
</tr>
<tr>
<td>PE from Carb, %</td>
<td>72 ± 2.5</td>
<td>70 ± 19</td>
<td>58 ± 15</td>
<td>0.05</td>
</tr>
<tr>
<td>PE from fat, %</td>
<td>20.7 ± 4</td>
<td>19.1 ± 4</td>
<td>19.2 ± 4</td>
<td>0.24</td>
</tr>
<tr>
<td>Protein intake abs., g/day</td>
<td>60 ± 10</td>
<td>64 ± 16</td>
<td>57 ± 12</td>
<td>0.26</td>
</tr>
<tr>
<td>PE from protein, %</td>
<td>17.7 ± 3</td>
<td>17.5 ± 3</td>
<td>19 ± 2</td>
<td>0.09</td>
</tr>
<tr>
<td>Water intake, l/day</td>
<td>1.7 ± 0.4</td>
<td>1.8 ± 0.3</td>
<td>1.9 ± 0.6</td>
<td>0.21</td>
</tr>
<tr>
<td>Nutritional Quality Index</td>
<td>79.5 ± 10</td>
<td>79.5 ± 13</td>
<td>75.9 ± 14</td>
<td>0.68</td>
</tr>
</tbody>
</table>

Data are mean±SD. p: Mann-Whitney U-test for two independent samples, used to assess differences between OMD and low-GI group. p*: Wilcoxon signed-rank test for two related samples, used to assess differences within one group (OMD or low-GI); between baseline and 3 months values. OMD, optimized-mixed diet; low-GI, low-glycemic index diet; BMI-SDS, body mass index standard deviation score; Carb, carbohydrate; abs, absolute; MS, monosaccharide; DS, disaccharide; PS, polysaccharide; PE, percent energy.


