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Low Glycemic Index and Load, Hypo Caloric Diet as an Effective Treatment for Obesity and Hyperlipidemia in Girls with Metabolic Syndrome

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Abstract

Objective: Considering the multiple complications of childhood obesity and metabolic syndrome (MS) at an early age, successful interventions are desperately needed. The aim of the study is to assess the effectiveness of a hypocaloric, low Glycemic Load (GL) and low Glycemic Index (GI) diet on the improvement of obesity and MS-related parameters.

Methods: Fifty obese girls, aged 7-16 years, were randomly recruited from the Obesity Clinic of the First Department of Pediatrics, of the University of Athens. Half of the girls were randomly prescribed a 3-month hypocaloric dietary intervention emphasizing on portion control and low GL foods, versus no intervention in the control group. The dietary advice was according to the principles of the Mediterranean diet. Physical activity was kept constant. Anthropometric measurements, fasting blood lipids, glucose and prevalence of MS were assessed before and after the 3-months.

Results: The girls in the intervention group exhibited a significant decrease in BMI, BMI z-score, waist circumference, total cholesterol and LDL compared to the control group (all $p<0.05$) and a 17% decrease in the incidence of MS. The decrease in total carbohydrate intake was the only dietary parameter significantly correlated to the decrease in BMI z- score in this population ($p=0.049$). The decrease in GI of the diet was positively correlated with a decrease in diastolic blood pressure (DBP). No other dietary components were found to be associated to the improvement of the MS parameters ($p>0.05$).

Conclusions: This study demonstrates the efficacy of a hypocaloric-low GI/GL diet, incorporating adequate protein and healthy fat, in improving parameters of MS in obese children and adolescents. It suggests a positive role of the reduction in total carbohydrate intake and GI to the decrease in BMI z-score and DBP respectively. Further research is needed to confirm these results in the long-term.

Keywords: Glycemic index; Hypocaloric diet; Obesity; Hyperlipidemia; Metabolic syndrome; Insulin resistance

Introduction

Recent evidence suggests that the prevalence of obesity in children and adolescents has been leveling off during the last few years in developed countries [1-4]. However, the prevalence of overweight and obesity still remains at high levels and presents a public health issue [5,6]. The close relationship of insulin resistance, impaired glucose tolerance and obesity has initiated research aiming to find effective nutritional ways for the treatment of excess adiposity and the Metabolic Syndrome (MS) [7].

The latest review from the Cochrane Library [8] addressing interventions for treating obesity in children included 64 Randomized Controlled Trials (RCTs) out of which 6 were focusing on diet. Successful dietary interventions in decreasing overweight in children and adolescents include: restricting energy intake to 1000-1500 kcal/day using the Traffic light diet for the whole family and enhancing the increase of healthy food i.e. fruit and vegetables, a positive behavioral change [9]; the prescription of a 1400 or 1600 calorie diet, with frequent follow-up sessions[10,11] or a diet of 1750 kcal/day for extremely obese adolescents with a 2 year follow-up [12], a community based behavior-modification intervention involving revising food diaries weekly via phone calls for 6 months [13] and combined dietary-behavioral-physical activity approach involving the whole family, using a nutrient balanced hypocaloric diet [14].

Apart from energy restriction, which is the basis of all previously mentioned successful interventions, few diets differing in their macronutrient content and quality have been examined for their effectiveness in weight loss and maintenance in children. There is preliminary evidence in children and adolescents for the effectiveness of a low Glycemic Load (GL) diet as a promising alternative to a low fat standard diet for the reduction of BMI and fat mass, although most studies are in adults. In a 1 year clinical intervention and follow-up study in 14 obese adolescents, the reduced GL diet resulted in a greater decrease in mean BMI, fat mass and smaller increase in insulin resistance as compared to the low fat diet group [15]. BMI and body weight were also significantly reduced to a greater extent in 64 obese children following a low-GI diet for 4 months compared to 43 following the low-fat diet, in a non-RCT trial [16]. The low GI-GL diets being used involve an ad-libitum approach, emphasizing on the consumption of low GI foods (i.e. GI<55 i.e. nonstarchy vegetables, legumes, milk and fruits that generally have a low GI), with instructions to eat to satiety and snack when hungry, macronutrient goals of 45% to 50%

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carbohydrate, 20% to 25% protein and 30% to 35% fat and a low GL as a result of the combination of low GI and the 45-50% of energy from carbohydrate.

The Glycemic Index (GI) is a term proposed in 1981 by Jenkins, used to categorize carbohydrate containing foods according to their effect on blood sugar levels. Initially it was developed to be used in the treatment of diabetes. Along with GI, Glycemic Load (GL) was introduced in order to take into account the serving size of the food eaten. GL is defined as the product of GI with the quantity of available carbohydrate consumed divided by 100 [6].

Most intervention trials up-to-date have focused on treating obesity, with few measuring other metabolic parameters related to MS such as insulin resistance or hyperlipidemia [13-15]. Lately, there has been an increase in interest for the treatment of MS as an adjunct to obesity in children [17,18]. The former study is in Hispanic children, aged 7-15 years, suggesting that low fat and low GL diets are equally effective in improving BMI, insulin resistance, systolic BP and waist circumference. The latter compares the Dietary Approaches to Stop Hypertension (DASH) diet to usual low fat dietary advice, with the DASH diet resulting in a greater decrease in hypertension and prevalence of MS [17,18].

The purpose of the study is to investigate further in our population of Mediterranean origin i.e. obese Greek girls, the effectiveness of a hypocaloric low GI/GL diet in achieving changes in BMI and parameters of the MS.

Methods

Fifty obese girls, aged 7-16 years, who were regularly followed in the Obesity Clinic of the Division of Endocrinology, Diabetes and Metabolism of the First Department of Pediatrics of the University of Athens, Aghia Sofia Children's Hospital were voluntarily and randomly recruited to participate in the intervention study [19]. Children were included in the study only after their parents had provided their written informed consent. The girls were randomly assigned either to the intervention group (n=25), and received a 3-months hypocaloric, low GL/GI diet, or to the control group (n=25), who received no intervention. All participants were followed for 3 months.

The inclusion criteria were being obese, not receiving any chronic medication and not following a diet for the last 6 months. The presence of the full MS was not an inclusion criterion, as it varies according to the severity of obesity and insulin resistance and our sample included a range of obese children, varying in insulin sensitivity, and did not focus only on the severe cases [19]. In addition, our aim was to observe the effectiveness of the intervention in the improvement of each of the parameters of the MS separately, even before the clustering of three or more factors occurs.

One girl out of the 25 of the intervention group was excluded due to incomplete data collection regarding her blood results i.e. attrition rate was 96% for the intervention group. In the control group 3 girls dropped out from the 25 included i.e. attrition rate 88%. These girls refused the second blood draw. All children were assessed for their pubertal stage. Eight girls out of 24 in the intervention group were at Tanner breast stage I, 6 girls at stages II and III, and 10 girls at stages IV and V. In the control group, 7 girls were at Tanner stage I, 6 at stages II and III and 9 at stages IV and V.

The definition of obesity was made according to Cole et al. [20], where obese is a child with a BMI percentile resulting to BMI of 30 at age 18, using the BMI percentiles for the Greek population [21].

The term Metabolic Syndrome (MS) has been used to describe a clustering of factors linked to obesity-especially central obesity- that is correlated with a significantly increased risk of Type 2 diabetes and cardiovascular disease. For the purpose of this study the MS definition used, as in Weiss et al. [19] was based on the modified National Cholesterol Education Program's Adult Treatment Panel (ATPIII) [22] adapted using our national percentile curves, and included: obesity as defined by Cole et al. [20], hypertension, defined as a systolic or diastolic BP>95th percentile for age and sex [23]; high triglycerides, defined as levels >90th percentile for age, sex and ethnicity, based on the Greek population percentiles [24]; low *HDL* defined as <10th percentile based on the Greek population percentiles; *impaired glucose metabolism expressed either as Impaired Glucose Tolerance (IGT)* diagnosed by a 2 hour value greater than 140 and less than 200 mg/dl in the Oral Glucose Tolerance Test (OGTT) or *Impaired Fasting Glucose (IFG)* based on a fasting glucose greater than 100 mg/dl [25]. The 2 hour value of the OGTT has been widely used in latest research as part of the diagnostic criteria for metabolic syndrome due to its high correlation with insulin resistance, even when fasting glucose may be within the normal range [26,27].

At the initial visit anthropometric measurements were assessed, including weight, height, blood pressure, waist circumference and a fasting blood sample was obtained. The blood sample was analyzed for triglycerides, total cholesterol, HDL, LDL and glucose. An Oral Glucose Tolerance Test (OGTT) was performed for all subjects at baseline. At follow-up, an OGTT was requested from all subjects of the intervention group and for the subjects of the control group with pathological OGTT at baseline.

Girls in the intervention and control groups were asked, with the help of their parents, to keep a 3 day food diary for their initial and last visit for the change in the diet to be assessed. Plastic food models were used to better estimate portion sizes. Girls in the control group received no intervention until the next reassessment and a visit was scheduled with the dietitian 3 months later. All girls were instructed to keep their physical activity, i.e. times per week of moderate- vigorous exercise, constant.

Dietary intervention

In the intervention group, during the first meeting the nutritional education for a hypocaloric- low GL/GI diet took place using the low-GL food pyramid [28]. Families were encouraged to make acceptable gradual changes to their diet, choosing more of the foods at the base of the pyramid, ie. Non-starchy vegetables, fruit, legumes and limiting foods at the top of the pyramid ie white bread, potatoes, phyllo pastry pies, cookies, sweets, sugary cereal. A weekly menu was given for them to use as guidance, with instructions on how to vary the type of meat, fish, legumes and mixed dishes in order to include a variety of foods. The macronutrient composition of the diet was to achieve 40-45% of energy from carbohydrates, 35%-40% from lipids and 20% from protein. The diet was planned to be 500 calories less than their energy requirements for age for the 10 year olds or above and less than 300 kcal for age for the 7-10 year olds, as estimated using Schofield equations [29].

Regarding the type of foods encouraged, lean sources of protein were recommended such as fish, chicken and red meat with reduced fat content, reduced or low fat cheese and legumes. The source of fat encouraged was olive oil i.e. monounsaturated fatty acids, by including 2 tablespoons in the daily menu, generally one per person used for the salad and one per serving for cooking the meal (which brings the % fat to 35-40%), thus following the Mediterranean diet and giving advice which may be more realistic for this population. Reduced GI grains i.e. wholegrains were recommended in moderation, as well as fruit as a snack. Non-starchy vegetables were instructed to be eaten ad libidum.

The families in the intervention group followed one nutrition counseling every 2 weeks within the first month and once a month for the next 2 months. In the follow-up sessions, weight and height were measured and a 24 hour diet recall was taken to assess their adherence to the diet, agreeing on specific goals. Families in the control group continued with their usual habits and both groups were reassessed at 3 months, repeating all measurements of the initial visit.

The analysis of the food diaries was performed using The Food Processor ESHA-SQL 10.1. For the composite Greek dishes missing, the Greek tables for composition of foods were used and GI values missing were estimated using the macronutrient composition of foods and the methodology described in the Methodology for adding glycemic load values used in Epidemiologic Studies [13,30].

Ethical issues

The study's protocol has been approved by the ethical committee of the Children's Hospital and children and families were voluntarily involved in the study. The children were included in the study only after a written informed consent has been obtained by their parents or guardians.

Statistical analysis

The analysis of the data was performed using SPSS 21.0, using as level of significance p-values less than 0.05. T-test, Mann Whitney test and Wilcoxon test were used depending on whether the variable under investigation had a normal distribution or not. Data were also analyzed using Spearman test in order to examine the possibility of an association between the difference before and after dietary intervention in the variables already mentioned in association to difference in GL and GI of the diet.

Results

At the initial visit, the two groups did not significantly differ for age, BMI, BMI z-score, total cholesterol, LDL, waist circumference, triglycerides, but did differ for SBP, DBP, glucose and HDL with the participants of the intervention group demonstrating the worse metabolic profile at baseline (Table 1). Comparing the diets of the intervention versus control group at baseline, no significant differences were observed for energy, carbohydrate, protein, fat, GI and GL and in % energy intake from macronutrients (Table 2).

After 3 months, the intervention group achieved a significant within and between group decrease regarding the total energy intake, grams and % of carbohydrate intake, GI and the GL of the diet and a significant *increase* in the % protein intake ((p<0.05). In addition, it achieved an almost significant between group decrease in grams of protein intake (p<0.06) and an almost significant within group decrease in grams of fat intake (p<0.06).

As a result, the hypocaloric-low GI/GL intervention resulted in a statistically significant decrease in *BMI,* BMI z-score, waist circumference, total cholesterol and *LDL* (Table 3) as compared to controls. In addition, there was a significant within group decrease in SBP in the intervention group. Consequently, MS resolved in 4 out of the 10 subjects who exhibited it initially, showing a 16.7% decrease in MS due to the intervention. The control group, however, showed the opposite results, with MS resolving in 1 out of 4 subjects that exhibited it initially and 3 subjects developing it (9.1% increase in prevalence of MS).

	Control group (N=22)	Intervention group (N=24)	p-value
Age	10.9	11.0	>0.05
BMI (kg/m^2)	26.4	28.7	0.165
BMI z-score	3.0	2.6	0.350
SBP (mmHg)	110	115	*0.010*
DBP (mmHg)	67.5	75	*0.004*
WC (cm)	87.5	92	0.076
Glucose (mg/dl)	84	92.5	*0.013*
TC (mg/dL)	168	166	0.996
LDL (mg/dL)	101	108	0.675
HDL (mg/dL)	50	43	*0.045*
TG (mg/dL)	67	82	0.086

Table 1: Comparison of the difference between groups at the Initial visit. **Abbreviations:** BMI: Body Mass Index; SBP: Systolic Blood Presssure; DBP: Diastolic Blood Pressure; WC: Waist Circumference; TC: Total Cholesterol; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; TG: Triglycerides.

	Baseline Intervention (median) (N=24)	3 month Intervention (median) (N=24)	Baseline Control (median) (N=22)	3 month Control (median) (N=22)
GI	56.1	52.1^{1,3}	56.3	56.5
GL	95.5	68.1^{1,3}	103	107.8
Energy (kcal)	1737	1439^{1,3}	1766	1784
Carbohydrate (gr)	190	147^{1,3}	195	199
Fiber (gr)	13.6	12.5	12.5	12.4
Protein (gr)	73	67^{1,4}	72.5	72
Fat (gr)	77	68 ^{2}	73.5	74
Carbohydrate %	43.3	39.6^{2,3}	44.5	44.5
Protein (%)	16.7	18.8^{1,3}	16.6	16.5
Fat (%)	40.5	41.8	39.5	39.7

Table 2: Macronutrient content at Baseline and 3 months. Wilcoxon test for dependent samples was used to determine within group difference. Mann Whitney u test for independent samples was used to determine between group differences. [1]Comparison of within group differences from baseline, level of significance p<0.05. [2]Comparison of within group differences from baseline, level of significance p<0.06. [3]Change from baseline between-group difference p<0.05. [4]Change from baseline between-group difference p<0.06.

The data were examined for the possibility of an association between the change in the dietary components and their association to the amelioration of each of the parameters of MS separately. The decrease in carbohydrate intake was significantly correlated to the decrease in BMI z-score (p=0.049) and the decrease in the GI of the diet was correlated to the decrease in DBP (p=0.011). The decreases in GL, energy, grams of protein, fat and fiber were not found to be correlated to the changes in MS parameters (p>0.05).

Discussion

Energy restriction has been the cornerstone for treatment of obesity in children [9-12,14] and there is recent interest into whether a specific macronutrient composition of the diet could provide an additional benefit [15-18], not only for the treatment of obesity, but also of MS [17,19]. Considering that the Mediterranean diet is based on olive oil[31], it is of interest to examine whether an alternative to a low fat diet may be a realistic and effective approach. The attrition rate of our intervention group was high (96%) with no comments of discomfort in following the diet.

The dietary intervention presented, based on a hypocaloric, low

	Control group Initial visit N=(22) Median	Control group After 3 months N=(22) Median	p value*	Intervention group Initial visit (N=24) Median	Intervention group After 3 months (N=24) Median	p value*	p value **
BMI (kg/m²)	26.4	26.8	*0.100*	28.7	26.5	*<0.001*	*<0.001*
BMI z-score	3	2.9	0.693	2.6	2.3	*<0.001*	*<0.001*
SBP (mmHg)	110.0	110.0	0.500	115	110	*0.005*	0.625
DBP (mmHg)	67.5	67.5	0.500	75	70	0.326	0.331
WC (cm)	86	86.3	0.070	93.4	89.6	*0.001*	*<0.001*
Glucose (mg/dl)	84.0	82.0	0.702	92.5	93.5	0.968	0.631
TC (mg/dL)	168.0	188.0	0.301	166	154	*0.034*	*0.047*
LDL (mg/dL)	101.0	103.0	0.380	108	95	*0.013*	*0.016*
HDL (mg/dL)	50.0	49.0	0.243	43	42	0.892	0.216
TG (mg/dL)	67.0	82.0	0.226	82	86	0.935	0.332

Table 3: Anthropometric and plasma measurements before and after 3 months of intervention or no intervention. *p values represent significant within group differences after 3 months (significance level $p<0.05$) .**p values for between group comparison of the differences after 3 months. BMI: Body Mass Index, SBP: Systolic Blood Pressure DBP: Diastolic Blood Pressure, WC: Waist Circumference, TC: Total Cholesterol, LDL: Low-Density Lipoprotein, HDL: High Density Lipoprotein, TG: Tri-Triglycerides

glycemic index diet, achieved significant reduction in BMI, BMI z-score, waist circumference, total cholesterol and LDL compared to controls, results comparable to those by Mirza et al. [17] where both the low fat diet and the low GL achieved a significant reduction in BMI z-score and waist circumference in 113 obese Hispanic children. It should be noted that the results were maintained, as shown in their study, at 2 years follow-up. The 16.7% decrease in the prevalence of MS within the intervention group of our study is also similar to the one reported in the intervention study by Mirza et al. [17], where the low GL diet decreased the presence of MS by 18% at 3 months compared to a decrease of 2.5% achieved by a low fat diet [17].

The success in the reduction of the parameters of MS in our study, is found to be linked to the decrease in carbohydrate intake (between group decrease of 48 g/day) and the decrease in the GI of the diet (by 4.2 units), significantly influencing BMI z-score and DBP respectively. This can be explained by the proposed greater satiating effect of lower GI foods such as fruits, vegetables, legumes, whole grains, milk and the observed reduction in high glycemic starch containing foods such as white bread, phyllo-pastry pies, croissants, pita breads, sweets and juices that have been suggested to contribute to overeating and obesity [6,15,32]. Analysis was not performed specifically for changes in food groups that would also be of interest. The observed effects of this diet on DBP are in agreement with findings from a randomized cross-over clinical trial in which a decrease in DPB was observed when adolescent girls with MS followed the Dietary Approaches to stop Hypertension (DASH) diet for 6 weeks, emphasizing on low GI foods such as fruits, vegetables, low fat dairy products, whole grains and legumes [18]. A possible mechanism leading to these beneficial effects may be the increase in potassium intake through the increase in fruits, vegetables, legumes and milk consumption, all good sources of potassium which has been linked to a decrease in BP [33].

Our intervention resulted in a significant decrease in mean energy intake by 300 kcal/day, reaching an energy intake of 1439 kcal/d, also proven to be effective in other nutrient balanced- energy-restricted diets [9,10,14]. Interestingly this decrease was not found to be significantly associated with the decrease in the parameters of MS. This could be possibly explained by the fact that all ages were grouped together for the analysis and thus the mean 300 kcal decrease may be enough to provide an effect for our younger population of 7-10 years of age, where there is more parental involvement [14] but not for adolescents who have higher energy requirements and were given meal plans of minus 500 kcal/d. Adherence to the diet proved better in the younger ages than in the older ones.

Regarding the macronutrient content of the diet, a within and between group decrease in grams of intake was observed at 3 months. However, when expressed as a %, an increase in % energy from protein was observed i.e. from 16.7% energy initially to 18.8%. This increase is in accordance with the results from the DioGenes study which concluded that a High-protein/low GI combination was more protective against childhood obesity compared to a Low-protein/High GI alternative [34,35]. The reported % energy from fat also increased, to 41.8% which is higher than the 35-40% planned, but representing still a decrease in total fat gram intake within the context of the Mediterranean diet. In addition, a great decrease in % energy from carbohydrate was observed i.e. 39.6% energy from carbohydrate at 3 months vs. 40-45% planned. However this diet cannot be described as low carbohydrate as it provides a mean of 147 g carbohydrate/day i.e. much more than 60 g carbohydrate/day [18] characterizing low-carb diets. Generally, the use of low carbohydrate diets for the treatment of obesity in children has not been proven to be more effective for weight loss compared to standard care [36].

Our data support the evidence that the combination of moderate carbohydrate reduction in combination to a low GI diet along with the provision of adequate amounts of protein and healthy fat, in the context of a hypocaloric diet, seems a promising approach [15,16,19] for the treatment of obesity and MS in children and adolescents. Strengths of the study include the success in following a GI/GL diet in children and adolescents, the high attrition rate, and using a 3-day dietary food record to assess intake. Limitations of the study include the small sample size, not differentiating the analysis according to Tanner stage where more significant results may become apparent and limitations applying to studies that use GI-GL i.e. the use of tabulated GI values from the International GI Tables for the calculation of the GI-GL of the diet [30,37], where foods from different countries are included that may not be of the same quality as the ones consumed, the estimation of some mixed meals is being based on the calculation from the individual foods and GI and GL is only one component of the diet and should not be used as a single tool.

On the other hand, this type of diet has been suggested to be more satiating [32,36] than the low fat alternative, has been shown in adults with higher insulin at 30 minutes after an OGTT to be more effective in decreasfing weight [37]and has produced weight and fat loss in children and adolescents with good attrition rates [15-17], thus proving to be practical to follow by different populations.

Conclusion

In conclusion, obese children and adolescents are exposed early on to a high risk for developing type 2 diabetes and cardiovascular disease. In this study we have demonstrated that a hypocaloric-low GI/GL diet, providing adequate protein and moderate amounts of healthy fat, resulted in a significant decrease in BMI, BMI z-score, waist circumference, LDL and total cholesterol compared to controls and a 17% decrease in the prevalence of MS after 3 months of intervention. The decrease in carbohydrate intake was significantly associated to the decrease in BMI z-score and the decrease in GI was positively, and independently of BMI, associated to a decrease in DBP. Thus, following a Mediterranean type hypocaloric- low GI/GL diet seems a promising intervention, incorporating traditional foods. Further large-scale studies are needed to confirm the efficacy of this diet on the long-term.

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