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The effect of carbohydrate counting on metabolic control in patients with type 1 diabetes mellitus

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SUMMARY

We aimed to investigate the effect of carbohydrate counting on metabolic and clinical parameters in patients with type 1 diabetes mellitus (DM) who were on flexible multiple daily insulin therapy. Nine volunteer adolescent patients using intensive insulin treatment (short acting insulin before meal plus two doses of long acting insulin (NPH) per day) were enrolled in the study. Clinical and metabolic parameters of these patients were retrospectively recorded from their files. The mean diabetes duration and age were 4.23±3.53 years and 15.45±1.47 years, respectively. Median HbA1C levels before and after carbohydrate counting were 9.26% and 8.26%, respectively. Total insulin dose, total cholesterol, HDL cholesterol and triglyceride levels were not different between before and after carbohydrate (CH) counting. However the LDL cholesterol levels decreased significantly with the treatment (p=0.036). The differences in the frequency of hypoglycemia and mean body mass index standard deviation scores were not significant before and after CH counting. The present study suggests that treatment with CH counting and two doses of intermediate-acting NPH plus short-acting insulin analogues may be an alternative treatment method for type 1 DM patients who are unable to use insulin pump due to financial problems also providing flexibility in meal-planning especially for adolescent type 1 DM patients.

Key words: *Carbohydrate counting, type 1 diabetes mellitus*

ÖZET

Tip 1 diyabetli hastalarda karbonhidrat sayımının metabolik kontrol üzerine etkisi

Bu çalışmada esnek çoklu insülin enjeksiyon tedavisi almakta olan tip 1 diyabetes mellituslu hastalarda karbonhidrat sayımının metabolik ve klinik parametreler üzerine olan etkisini araştırmayı amaçladık. Yoğun insülin tedavisi alan (öğün öncesi kısa etkili insülin ve günde iki doz uzun etkili insülin [NPH]) dokuz gönüllü adölesan hasta çalışmaya alındı. Hastaların klinik ve metabolik parametreleri hasta kayıtlarının geriye dönük olarak incelenmesi sonucu elde edildi. Ortalama diyabet süresi 4.23±3.53 yıl ve ortalama hasta yaşları 15.45±1.47 yıl olarak saptandı. Karbonhidrat sayım öncesi ve sonrası ortalama HbA1c değerleri sırasıyla %9.26 ve %8.26 olarak saptandı. Karbonhidrat sayım öncesi ve sonrası total insülin dozu, total kolesterol, HDL kolesterol ve trigliserid düzeylerinde istatistiksel olarak anlamlı farklılıklar saptanmadı. Ancak, tedaviyle beraber LDL kolesterol düzeylerinde anlamlı azalma saptandı (p=0.036). Karbonhidrat sayım öncesi ve sonrası hipoglisemi sıklığında ve vücut kitle indeksi standart sapma skorlarında istatistiksel olarak anlamlı farklılıklar saptanmadı. Bu çalışma, karbonhidrat sayımının iki doz uzun etkili NPH ve çok kısa etkili insülin tedavisi ile beraber özellikle adölesan tip 1 diyabetes mellituslu hastalarda öğünde esneklik de sağlayarak maddi nedenlerle insülin pompası kullanamayanlarda alternatif bir tedavi yöntemi olabileceğini göstermiştir.

Anahtar kelimeler: *Karbonhidrat sayımı, tip 1 diyabetes mellitus*

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Introduction

Carbohydrate (CH) counting is a meal-planning approach offering a number of influential advantages and not a new concept, which was initially used in the 1920's in diabetic patients' meal plan following the discovery of insulin (1,2). It is a single nutrient focused method providing a more specific method of matching food and mealtime insulin resulting in improved blood glucose control (2,3).

Insulin requirements are mainly determined by the CH content rather than the protein or fat content of a meal (3,4). Following a CH-rich meal, most of the absorbed CH enters bloodstream in the first 15 minutes and converted to glucose in approximately 2 hours (1,3). Therefore, postprandial blood glucose levels are directly related with the amount of CH consumed with meals (1,5,6).

Carbohydrate counting has recently gained popularity with the widespread use of insulin infusion pumps (6,9). In order to minimize the unpredictability of blood glucose levels for patients with stable insulin dosage, it is recommended not to exceed the predetermined daily CH amount (6). Consequently, this may cause disruption in metabolic control and problems with compliance to treatment in type 1 diabetic patients, who wish a compliant life style but are unable to use an insulin pump due to social security and financial problems. In the present study, we aimed to assess the effect of CH counting, which is easily learned, of no additional cost and provides flexibility while choosing food, on metabolic control in patients using multiple insulin injection therapy.

Material and Methods

Nine volunteer adolescent patients with type 1 diabetes mellitus (DM), who have been followed up for at least one year in the Department of Pediatric Endocrinology and Adolescence, used multiple insulin injection therapy (premeal short acting insulin+intermediate acting

insulin twice a day neutral protamine hagedorn [NPH]), and wanted a flexible multiple daily insulin (FMDI) therapy were recruited into the study. Lispro insulin (Humalog Pen®, Lilly) or Aspart insulin (Novorapid®, Novo Nordisk Pharmaceuticals, Princeton, NJ, USA) were used as short-acting insulin and NPH (Insulatard® or Humulin–N®) was used as intermediate-acting insulin. The mean diabetes duration and age of the study patients was 4.23±3.53 and 15.45±1.47 years, respectively, and neither of them was in the honeymoon period.

Before CH counting, each patient and family were given recommendations and education regarding nutrition, meal planning, and the use of CH counting with FMDI regimen in a mean duration of three months. Food labels, exchange lists, food models, and restaurant reference guides were used as educational tools. Each patient was evaluated by a nutritionist at quarterly clinic visits. A 24-hour dietary recall with assessment of CH counting skills was performed at each clinic visit. All patients were taught insulin treatment algorithm for blood glucose levels above and below the target ranges. The same members of the intramural diabetes team of our department, including a physician, diabetic educational nurse, and dietitian instructed and followed the study patients, who were asked to monitor blood glucose levels for a minimum of four times a day and to report their blood glucose at regular intervals. During the CH counting, the target ranges of blood glucose levels were designated as follows: preprandial 80-150 mg/dL, postprandial 120-180 mg/dL and bedtime >110 mg/dL. Patients and their families were requested to demonstrate their understanding about the concepts of CH counting and their ability regarding the use of insulin to CH ratios. During the transition to CH counting, the CH/insulin ratios and insulin sensitivity indexes of each patient were calculated as 500/total insulin and 1800/total insulin, respectively. Each patient and family were instructed to adjust unit per CH ratio and correction dose based on 2-hour postprandial blood glucose. Basal and premeal bolus doses were modified if fasting and postprandial blood glucose levels were above target ranges, respectively.

For each patient, metabolic and clinical data were collected for one year prior to FMDI initiation and for the first year of FMDI therapy. Among the clinical and metabolic variables of the patients, who were regularly examined with 3-month intervals, height, weight, HbA1C, insulin dose, lipid profile, preprandial and postprandial blood glucose levels, basal-bolus insulin ratios, presence of ketoacidosis were recorded prospectively at regular intervals throughout the 12 months before and after institution of FMDI therapy. Data of home blood glucose meters were downloaded, and the frequency of checks in the 14 days before each visit was evaluated along with the number of hypoglycemic events (defined by a blood glucose level below 65 mg/dL). HbA1c levels were measured with Cobra Integra 400 plus (Roche Diagnostics®, Switzerland). Normal HbA1c levels were accepted as 4.5-5.7 g/dL.

Anthropometric data [body mass index (BMI)] were converted to standard deviation scores (SDS) by using data from the National Health and Nutrition Examination Survey (7). Insulin dosages were expressed as the total daily dose (TDD) in units per kilogram of body mass.

Patients who were taught to count carbohydrates but did not contact with the treatment team for at least six months were excluded. Among nonparametric tests, Wilcoxon test was used to compare the clinical and metabolic variables before and after CH counting. The reported values were expressed as median (minimum-maximum). A p value of <0.05 was considered statistically significant.

Results

With respect to before CH counting state, the mean HbA1c levels of the patients showed a decrease of 1%, which did not differ statistically (Table I). No statistically significant differences were detected between the before and after CH counting values of total insulin doses (IU/kg/day), HDL cholesterol, total cholesterol, and triglycerides (p=0.086, p=0.183, p=0.173, p=0.813, respectively) (Table I). The decrease in LDL cholesterol with CH counting was statistically significant (p=0.036) (Table I). No statistically significant differences were detected between the before and after CH counting assessments regarding the hypoglycemia frequency and BMI SDS (p=0.575, p=0.109, respectively) (Table I). None of the patients developed severe hypoglycemia or diabetic ketoacidosis during the CH counting. At the end of one year, a decrease more than 1% in HbA1c levels was observed in four patients (44%). Three patients' HbA1c levels (33.3%) declined below 8%. No statistically significant differences were found regarding bolus-basal insulin ratios although the ratio increased with CH counting (p=0.051). In terms of metabolic control, post-CH counting levels of morning fasting blood glucose were statistically significantly lower than the pre-CH counting state (p=0.028) (Table II). No statistically significant differences were observed regarding the one year after CH counting levels of other blood glucose measurements throughout the day although they were lower than the year before's (p>0.05) (Table II).

Table I. Clinical characteristics of the patients before and one year after carbohydrate counting

Variables	Before carbohydrate counting*	After carbohydrate counting*	p value**
Body mass index standard deviation scores	1.05 (-0.96-1.65)	1.16 (-0.23-1.46)	0.066
Hemoglobin A1c (%)	9.26 (7.02-12.31)	8.26 (7.31-9.30)	0.110
Triglyceride (mg/dL)	81 (46-199)	94 (69-177)	0.813
Cholesterol (mg/dL)	172.5 (139-280)	171 (129.5-183)	0.173
HDL (mg/dL)	57 (47-69.5)	62 (48.5-120)	0.183
LDL (mg/dL)	92.75 (59-192)	71.7 (47-105)	0.036
Hypoglycemic episodes/patient/year	51 (24-151.92)	66 (27.96-144)	0.575
Total insulin dose (IU/kg/day)	1.07 (0.6-1.46)	1.04 (0.7-1.49)	0.086
Bolus dose (IU/kg/day)	0.65 (0.27-0.99)	0.55 (0.35-0.72)	0.214
Basal dose (IU/kg/day)	0.40 (0.30-0.57)	0.54 (0.35-0.78)	0.015
Bolus/basal insulin ratio	1.46 (0.69-2.31)	1.11 (0.62-1.53)	0.051

*: median (minimum-maximum), **: Wilxocon test

Table II. The effect of carbohydrate counting on metabolic control

Glucose (mg/dL)	Before carbohydrate counting*	After carbohydrate counting*	p value**
Prebreakfast	204.15 (152.25-219.5)	246.6 (157-347)	0.028
Postbreakfast	219.5 (150-292)	167 (109-197.75)	0.465
Prelunch	171 (108-213)	145.17 (95-235)	0.237
Postlunch	134.99 (64-181)	145.17 (95.5-235)	0.917
Predinner	194.75 (118-320.41)	156.62 (124-215.64)	0.021
Postdinner	148 (121.68-267.16)	179.12 (110-259.33)	0.715
Bedtime	198.31 (119.83-272.88)	163.5 (143.75-204.69)	0.051
Midnight (3:00 am)	214 (118-238)	185.65 (8144.95-244)	0.735
Mean	214 (118-238)	170 (104-202.54)	0.021

*: median (minimum-maximum), **: Wilxocon test

Discussion

Nutritional education programs play an important role in the management of metabolic control in diabetes mellitus (3,6,8). It has been shown that metabolic control is better when nutritional therapy methods are applied successfully (6,8,9). The primary goals of nutritional treatment are to maintain healthy growth, achieve near normal blood glucose levels, reduce the risk of severe hypoglycemia, improve quality of life, and avoid vascular complications (6,10,11). Recently, important advances have taken place in the management and treatment of type 1 DM. Among these, the most important one is the increasing use of CH counting method together with various intensive insulin treatment regimens (4,12,13). It was shown in numerous studies that the use of CH counting, particularly in conjunction with insulin pump provided better metabolic control (12-14).

Adolescence is a period, in which metabolic control is more hardly achieved with respect to young children and adulthood. The increased metabolic disturbance during puberty is attributed not only to insulin resistance, growth hormone secretion and sex steroids, but also to psychological and behavioral changes, which may result in considerable non-adherence to regimens during this period. In the present study, an improvement in metabolic control was accomplished with a shift to the flexible insulin regimen and CH counting despite these hormonal changes encountered in adolescence. Therefore, we think that the flexible insulin regimen with CH counting is an important treatment method regarding providing flexibility in meal-planning in the particular period of frequent behavioral alterations and eating disorders.

In the medical literature, most of the studies regarding CH counting were performed on patients using

premeal regular insulin+NPH, premeal lispro+bedtime glargine, premeal lispro+ultralente insulin and insulin pump (12-15). On the other hand, we did not encounter such a study evaluating the outcome of CH counting method on patients using two doses of NPH insulin and short-acting insulin analogues (lispro or aspart), and that is why our study is important.

The most significant complication of CH counting, which is frequently in conjunction with intensive insulin therapy regimen, is the increase in weight and frequency of hypoglycemia (12,13,16,17). It is reported that the risk of severe hypoglycemia and obesity is increased by three-fold and two-fold, respectively, with intensive insulin therapy during adolescence (17). Nonetheless, in other studies, it has been detected that intensive insulin therapy regimen does not increase the risk for hypoglycemia in patients with type 1 DM (12,18). Especially in some studies, it is also stated that insulin pump application in type 1 DM patients does not increase the frequency of hypoglycemia and does not cause weight gain (12,18-21). But very few of these studies were randomized and all used regular insulin (20,21). Alemzadeh et al. found 52.3% decrease in the rate of hypoglycemia with morning-evening doses of basal ultralente insulin (12). Alemzadeh et al., in a study with CH counting patients comparing two different basal insulins, have detected that there is a statistically significant decrease in the risk for hypoglycemia in the insulin glargine group when compared to ultralente (morning and evening) group (13). In both of the above-mentioned studies, no statistically significant differences were observed between the groups regarding tendency to increase in BMI (12,13). In the study by Weintrop et al, statistically significant difference was not detected concerning increase in frequency of hypoglycemia in patients with type 1 DM, multiple daily injection therapy (regular insulin+NPH) using and CH counting group, when compared with the state prior to CH counting (14). Also in our study, we did not find a statistically significant increase in BMI SDS and hypoglycemia frequency when CH counting was combined with intensive insulin therapy regimen. In several studies, it is reported that NPH insulin increases the risk of hypoglycemia in diabetic patients (22,23). On the other hand, most of the trials reporting a decrease in hypoglycemia are studies with insulin glargine, which shows no peak. The reasons why no increased risk for hypoglycemia is observed in our study, even though the patients have been using NPH insulin, might be considered as the low number of patients and the same basal insulin used before and during the study.

In a number of studies, it has been shown that total insulin requirement is diminished with the transition from multiple insulin injection therapy to insulin pump (13,14,24). In a study by Weintrop et al., total insulin requirement of patients using insulin pump was found to be significantly lower than that of those using multiple insulin injection therapy (14). In the same study, no statistically significant difference was detected when patients using multiple insulin injection therapy were compared between before and after CH counting states regarding total insulin requirement (14). Also in our study, no statistically significant difference was detected regarding an increase in total insulin requirement although CH counting was implemented. In a study comparing multiple insulin injection therapy and insulin pump, Alemzadeh et al. detected that bolus-basal insulin ratio increased with CH counting (13). In another study by Alemzedah et al. assessing the benefit of FMDI therapy in type 1 diabetic adolescents and children, bolus-basal insulin ratio was detected lower in pubertal group when compared with prepubertal group (12). In our study, when before and after CH counting bolus-basal ratios were compared, bolus-basal ratio was found to be insignificantly reduced after CH counting. During the CH counting, basal rate of the patients, rather than the bolus doses, was found to be increased. Based on these data, it might be considered that basal insulin requirement further increases in pubertal stage, in which an increase in counter hormone effect takes place. In this study, it is considered that the increased basal insulin requirement might be explained with puberty, which all of the patients were experiencing meanwhile.

Although a quality of life questionnaire was not filled up by the patients in our study, we learned that all of them were satisfied with CH counting and none wanted to use the previous treatment method. Carbohydrate counting plays a significant role in maintaining metabolic control for patients with type 1 DM as well as introducing a flexible life style and increasing quality of life. In the study of Alemzadeh et al., in which flexible multiple insulin therapy with morning and night doses of ultralente insulin was carried out, a statistically significant reduction (1.3%, from 9.3% to 8.0%) was observed in mean HbA1c levels with CH counting (12). In the same study, they also stated that in 57% of the patients, HbA1c levels decreased by 1% with the therapy, which was considered significant regarding the potential future microvascular complications (12). It is stated in DCCT report that a 1% decrease in HbA1c levels diminishes the potential diabetic complications by 21% to 49% (25,26). Although statistical analyses did not show significant differences between

the groups, we considered the decrease in HbA1c level in our study important because of the above-mentioned findings.

In conclusion, the present study, despite the low number of cases, suggests that treatment with CH counting and two doses of intermediate-acting NPH plus short-acting insulin analogues may be an alternative treatment method for type 1 DM patients who are unable to use insulin pump due to financial problems also providing flexibility in meal-planning especially for adolescent type 1 DM patients.

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