INSULIN REQUIREMENT OF SIMPLE AND COMPLEX CARBOHYDRATE FOODS IN TYPE 1 (INSULIN-DEPENDENT) CSII-TREATED DIABETIC SUBJECTS, OBTAINED BY BIOSTATOR. CORRELATION WITH GLYCAEMIC INDEX

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Diet is a cornerstone of therapy for patients with both Type 2 (non-insulin-dependent) and Type 1 (insulin-dependent) diabetes mellitus[18].

In an effort to optimize diet recommendations, several studies have been carried out in Type 2 diabetic patients to determine whether the ingestion of different carbohydrate rich food results in different plasma glucose responses[1, 4-6, 14, 16, 19, 20].

Fewer studies[3, 12, 13, 23] have tried to elucidate whether different insulin requirements follow the ingestion of carbohydrate from different sources in Type 1 diabetic patients. Furthermore, these previous studies only evaluated glucose responses after carbohydrate meals in conditions of fixed insulin infusion[12, 13] or after a standardized subcutaneous insulin bolus[3, 23].

To accurately assess whether different carbohydrate foods produce different insulin requirement in Type 1 diabetic patients one needs to connect the patients to a 'closed loop' device such as the artificial beta cell and to measure the amount of insulin needed to maintain the postprandial glucose curve close to normal physiology after the ingestion of different carbohydrate foods.

The aim of the present work was therefore to determine, with the use of an artificial beta cell, the net insulin requirement produced by the same amount of commonly used carbohydrate of different kinds in CSII-treated Type 1 diabetic patients.

Key-words: Carbohydrates; CSII; Diet; Glycaemic index; Insulin requirement; Type 1 diabetic subjects.

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SUBJECTS AND METHODS

Eight CSII-treated Type 1 diabetic males were recruited for the study after giving fully informed consent, according to the Helsinki declaration. All were C-peptide negative after intravenous glucagon stimulation (tab. 1) (intraassay variation <6%; detection limit: 0.07 ng/ml). None had detectable plasma levels of anti-insulin antibodies. Their clinical characteristics are reported in tab. 1.

They were invited to consume a weight maintaining diet containing 200-250 g of carbohydrate/day for a week before the study and were admitted to our hospital unit the evening before the study. At 19^{00} they were given a standard meal (10 kcal/kg body weight (b.w.), 50% carbohydrate, 35% lipids and 15% protein) and their usual predinner subcutaneous bolus of regular insulin. Throughout the night and throughout the duration of the study patients received their usual basal continuous subcutaneous infusion of regular insulin delivered by their insulin microinfuser (Ames bolus II) at the average rate of 14 ± 1.3 mU/kg/h.

The next morning at 08^{00}, patients whose blood sugar was below 6.7 mmol/l were connected to an artificial beta cell (Biostator, Miles Laboratories, USA) programmed with the following constants: KR = 40, BI = 80, QI = 30, RI = 0.2/kg b.w., FI = 300, BD = 65, QD = 25, RD = 23, FD = 250 and used in the 'closed loop' mode.

When blood glucose was brought to a level of 4.4 mmol/l by insulin delivered by the Biostator, patients were given foods containing 75 g of carbohydrate which was ingested within 10 min. Postprandial insulin requirement was then calculated as the amount of insulin delivered by the Biostator from the first rise in blood glucose until the time when blood glucose was back to baseline.

The experiment was repeated for each subject on 6 different days allowing at least one week between experiments. On each occasion a different food was administered containing either complex carbohydrate (bread, pasta - durum wheat -, potatoes) or simple carbohydrate (apples - without the skin -, oranges, sucrose - in 200 ml of water). The order of the foods was randomized. All the food used was part of the usual diet of the patients, with the exception of sucrose, which was studied due to the importance of sweeteners in the diabetic diet[21].

Carbohydrate content of foods (tab. 2) was calculated from published composition food tables[8]. All patients received regular insulin (Actrapid HM, Novo, Denmark) for subcutaneous and intravenous infusion. Before connecting the patients to the Biostator, plasma glucose was measured by a Beckman BG2 glucose analyzer (Beckman Instruments Inc., Fullerton, CA, USA) which was also used to calibrate the Biostator membrane every 30 min during the study.

Data were analyzed using ANOVA for repeated measures and Pearson correlation coefficient.

subjects	age (years)	BMI (kg/m^2)	HbA_{1c} (%)	duration of diabetes (years)	insulin requirement (U/d)	C-peptide after glucagon 1 mg (ng/ml)
1. C. A.	32	27.8	7.3	12	55	<0.07
2. D. I.	59	24.0	6.8	13	48	<0.07
3. D. O.	25	21.8	7.4	5	53	0.18
4. N. A.	42	28.1	8.2	16	51	<0.07
5. R. O.	58	25.9	7.7	12	49	<0.07
6. M. G.	35	21.3	7.5	10	47	0.16
7. D. A.	29	23.2	7.9	8	54	0.15
8. S. F.	32	22.4	7.2	9	52	0.12
mean	39.0	24.3	7.5	10.6	51.2	
SEM	4.5	0.9	0.2	1.2	1.3	

Tab. 1 - Clinical characteristics of the subjects. *(BMI = body mass index).*

meals	amount	CHO/100 g
sucrose	75 g	100
apple	675 g	11.1
orange	806 g	9.3
bread (white, wheat)	124 g	60.6
pasta (spaghetti, white)	97 g	77.4
potato (new, boiled)	426 g	17.6

Tab. 2 - Amount of each meal and carbohydrate content according to food tables[8].

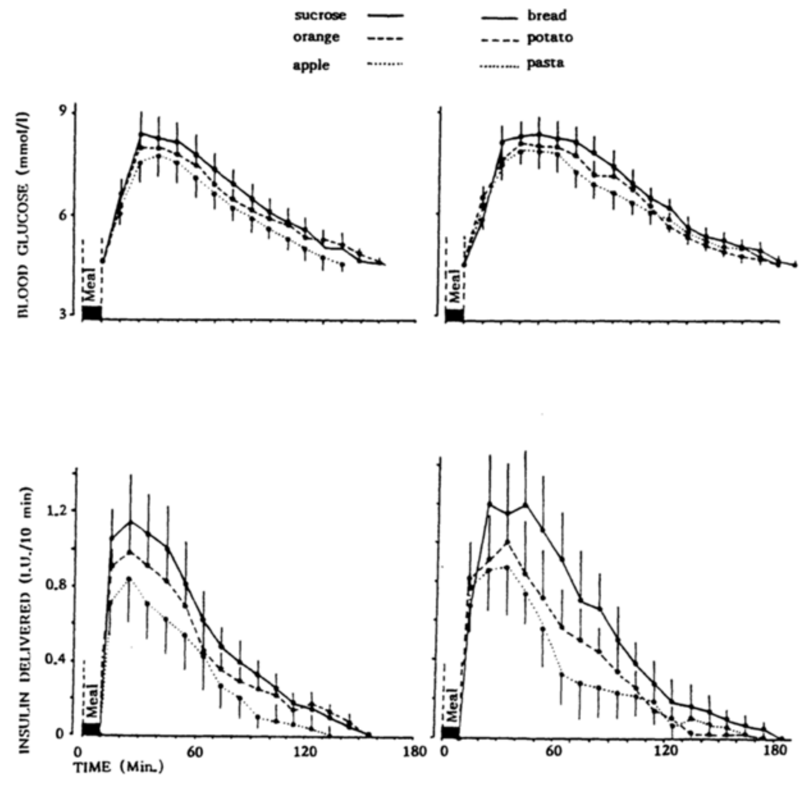

Fig. 1 - Mean plasma glucose values (± SEM) (upper panel) and mean insulin delivered by the artificial pancreas (± SEM) (lower panel) following the food ingestion in 8 insulin-dependent diabetic patients. Each food was given in amount containing 75 g of carbohydrate.

subjects	1	2	3	4	5	6	7	8	mean	SD	CV
bread	8.50	12.70	8.60	6.50	9.60	10.90	7.30	9.10	9.15	1.97	21.48
sucrose	7.50	4.00	11.40	7.00	9.00	8.20	5.70	9.80	7.83	2.33	29.83
potato	6.00	5.50	12.70	5.50	6.00	8.90	6.80	5.00	7.05	2.58	36.61
orange	2.50	7.40	8.00	4.00	9.70	4.50	4.70	8.90	6.21	2.62	42.10
pasta	7.50	6.00	7.00	5.30	4.00	4.20	6.80	7.20	6.00	1.37	22.77
apple	3.25	3.00	7.00	5.60	4.10	3.70	3.90	5.80	4.54	1.42	31.24
mean	5.88	6.43	9.12	5.65	7.07	6.73	5.87	7.63	6.80		30.67
SD	2.41	3.35	2.33	1.02	2.63	2.92	1.31	1.90			
CV	42.02	53.90	26.18	18.16	38.29	44.70	22.68	25.36	33.91		

Tab. 3 - Individual and mean values for the net insulin requirements following the food ingestion (75 g CHO). CV for subjects and for meals is also given.

RESULTS

Figure 1 shows the overall mean patterns for blood glucose values and insulin requirements following each of the 6 meals.

Individual net insulin requirements following the different meals are shown in tab. 3. The highest insulin requirement was observed after the ingestion of bread (1.22 IU/10 g CHO) and the lowest after the ingestion of apples (0.60 IU/10 g CHO). A statistically significant difference was found by ANOVA among insulin requirements for the foods ($p<0.05$). Single comparisons be-

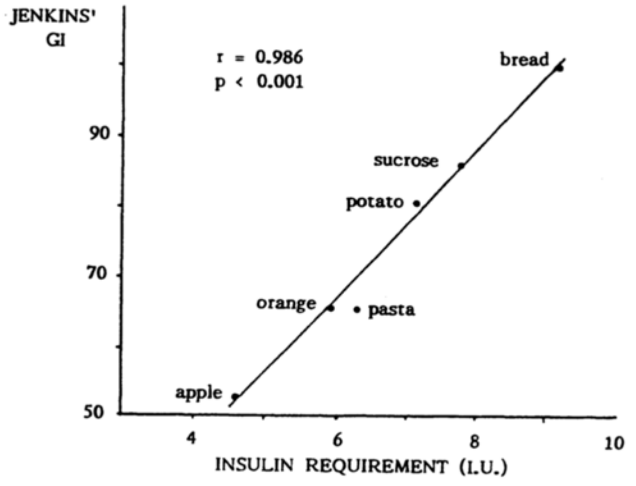

Fig. 2 - Correlation between Jenkins' glycaemic index[15] and insulin requirement.

tween insulin requirement for bread and other foods showed a statistically significant difference only between bread and apple ($p<0.05$).

A very high inter subject variability in insulin requirement after ingestion of the same food was observed (mean coefficient of variation 30.67%, range 21.5-42.1%).

No difference was found among foods regarding *1.* the time interval between beginning of meal intake and blood glucose increments, *2.* the duration of blood glucose curve above basal values and *3.* the peaks of blood glucose values.

We then wanted to compare the mean amount of insulin required after ingestion of different foods with the glycaemic index of the same food as calculated by JENKINS et al.[15] in nondiabetic subjects. A close, statistically significant positive correlation was found between the 2 variables ($r = 0.986$, $p<0.01$) (fig. 2).

DISCUSSION

Several authors[2, 9-11, 22] have suggested that the dose of regular insulin to be administered as a preprandial bolus in diabetic patients on intensive insulin therapy should be calibrated according to the carbohydrate content of the meal.

Support for this has been provided by SLAMA et al.[22] and, more recently, by HALFON et al.[10], who showed a close correlation between carbohydrate content of the meal and insulin requirement as assessed by artificial pancreas.

CHANTELAU et al.[2] obtained a quantification of this correlation and showed that the preprandial insulin bolus should be in the order of 1.1 IU of insulin/ 10 g of carbohydrate; similar results were obtained by HAMET et al.[11].

However it has been reported that different glycaemic responses follow the ingestion of the same amount of carbohydrate as different foods[15], and CHANTELAU et al.[3] found that in CSII-treated diabetic patients not only the total amount of carbohydrate ingested but also the type of carbohydrate (i.e. the glycaemic index) was important for the exact determination of the preprandial insulin bolus.

In this paper we addressed this last issue with a more controlled experimental design, determining by an artificial beta cell the net amount of insulin (detracted from basal) required to maintain the postprandial glucose profile within physiologic limits after the ingestion of the same amount of carbohydrate administered as different foods. Since the study was performed while patients continued to receive their usual basal continuous subcutaneous infusion delivered by their insulin microinfuser, the insulin requirement is due only to the carbohydrate ingested.

The overall mean insulin required after the ingestion of 75 g of carbohydrate was 6.8 ± 0.65 IU, or 0.91 IU/10 g of carbohydrate; a value slightly lower than those observed by CHANTELAU et al.[2] and by HAMET et al.[11]. Since we used an intravenous insulin infusion, this slight difference could be due to some subcutaneous insulin degradation[17] occurring in the previous studies, or simply it might depend on the type of algorithm used.

It must be pointed out that we measured insulin requirement after the ingestion of single food stuffs which are seldom, if ever, consumed alone in a common diet.

In conclusion, the high intraindividual variability of insulin requirement obtained in rigorous experimental conditions with single foods, does not advice the use of glycaemic index in assessing the prandial insulin dose during optimized insulin therapy.

SUMMARY

The aim of this work was to observe whether different types of carbohydrates might require different insulin doses. Five type 1 CSII-treated diabetic subjects (age 39 ± 4 years), C-peptide negative and in optimal metabolic control (HbA_{1c} 7.5 ± 0.2) were selected for the study. They were connected to the Biostator 6 times with an interval of 4-10 days between sessions and fed a meal containing 75 g of carbohydrates of different types: bread, pasta, potatoes, apples, oranges and sucrose. The following net (above basal) insulin requirement for the 30 meals were found (IU - mean + SD): bread 9.15 ± 1.97; pasta 6.00 ± 1.37; potatoes 7.05 ± 2.58; apples 4.54 ± 1.42; oranges 6.21 ± 2.62; sucrose 7.83 ± 2.33. A statistically significant difference was found by ANOVA among insulin requirements for foods ($p<0.05$). Single comparisons between bread and the other foods showed a statistically significant difference only between bread and apple ($p<0.05$). Mean coefficient of variation was 33.9% for the subjects and 30.7% for the meals. A significant correlation was found between Jenkins' glycaemic index and insulin requirement ($r = 0.897$; $p<0.001$). In conclusion, the high intraindividual variability of insulin requirement does not advice the use of the glycaemic index during optimized insulin therapy.

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