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Basal or bolus dose, which is the key factor in CSII?

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Abstract: Objective: To observe the value of HbA_1c level evaluating the total daily basal insulin dose by continuous subcutaneous insulin infusion (CSII) in 268 patients with type 2 diabetes mellitus. Methods: 5-point capillary blood glucose was monitored in pre- and post-CSII and the insulin dose which could stabilize blood glucose was defined as the total daily dose of insulin, including basal and bolus total dose. Correlation between HbA_1c level and total daily dose of insulin in patients with type 2 diabetes mellitus was analyzed. Correlation between HbA_1c level and 5-point capillary blood glucose was also analyzed. Results: Obvious correlation was observed between HbA_1c level and the basal total daily dose of insulin if HbA_1c was more than 9.3% (r=0.635, P<0.05). The average of 5-point capillary blood glucose was best correlated with HbA_1c and fasting blood glucose next best. Conclusion: HbA_1c level can forecast basal total daily dose of insulin in CSII.

Key words: Type 2 diabetes mellitus, HbA_1c, Basal total daily dose of insulin, CSII (continuous subcutaneous insulin infusion)
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INTRODUCTION

The aim of insulin therapy should give emphasis to control fasting blood glucose, if the patient has a higher level of HbA_1c. For this reason, 268 hospitalized type 2 diabetes mellitus patients treated with CSII were observed to see if HbA_1c level could forecast the basal total daily dose of insulin.

OBJECTS AND METHODS

Objects

Patients (n=268) with type 2 diabetes mellitus were hospitalized from May in 2003 to May in 2005. Their mean age was (65±10.5) years (45~80 years), male and female ratio 1:1.1, diabetes mellitus duration (4.5±1.4) years (2~15 years), BMI (body mass index) (26.6±2.3) kg/m^2, average stay in hospital only (12.3±3.5) d, average fasting blood glucose (8.6±3.8) mmol/L and average postprandial blood glucose (12.8±4.6) mmol/L pre-CSII and average fasting blood glucose (7.2±1.8) mmol/L and average postprandial blood glucose (8.6±2.3) mmol/L at the post-CSII. All the patients were diagnosed by the standard of WHO diagnostic criteria. Patients with serious complication such as infection, ketoacidosis, hyperosmolar nonketotic diabetic coma, heart failure, liver or renal disfunction were excluded. Patients who were greatly influenced by oral hypoglycimic drugs were also excluded.

Methods

HbA_1c and 5-point capillary blood glucose were measured two or three times pre-CSII when patients were hospitalized. The average blood glucose at each time point of each measurement and the general mean blood glucose of 5 points were calculated. Correlation analysis between HbA_1c and 5-point capillary blood glucose was performed by pearson correlation.

Both alimentary control and CSII, basal and bolus before three meals, were accepted by all 268 patients who had not taken any oral hypoglycimic drugs. The insulin dose was regulated by the 5-point capillary blood glucose (fasting, three postprandial, and at 3 a.m. point) monitored. The fasting and 3 a.m.

time point blood glucose levels were used to regulate the basal insulin dose, three postprandial blood glucoses regulated the bolus dose. The insulin dose which could stabilize blood glucose was defined as the total daily dose of insulin, basal and bolus. Correlation between HbA_1c level and insulin total dose in patients with type 2 diabetes mellitus was analyzed by CSII.

Statistical treatment

Statistical treatment was analyzed by SPSS 11.5 statistics soft ware.

RESULTS

Correlation between HbA_1c and 5-point capillary blood glucose pre-CSII

Table 1 shows the significant correlation between HbA_1c and fasting blood glucose, especially HbA_1c and average blood glucose of 5-point.

Table 1 Correlation between HbA_1c (%) and 5-point capillary blood glucose (mmol/L) pre-CSII

	Mean value	Standard deviation	Correlation (r)	P
HbA_1c	8.96	1.90	–	–
Fasting	8.74	2.77	0.583	<0.05
Postbreakfast	12.49	4.45	0.429	>0.05
Postlunch	12.87	3.72	0.412	>0.05
Postdinner	12.16	3.80	0.415	>0.05
Average postprandial	12.51	2.94	0.568	>0.05
3 a.m.	8.81	2.97	0.408	>0.05
Average of 5-point	11.02	2.49	0.631	<0.05

Correlation between HbA_1c and insulin basal total dose

Table 2 shows the significant correlation between HbA_1c and insulin basal total dose if HbA_1c >9.3%.

Table 2 Correlation between HbA_1c (%) and insulin basal total dose (IU/d)

HbA_1c (range)	n	HbA_1c (mean±SD)	Basal total dose	Correlation (r)	P
<7.3	49	6.73±0.43	6.35±4.89	0.350	>0.05
7.3~9.3	110	8.39±0.55	11.27±5.47	0.400	>0.05
>9.3	109	11.28±1.49	16.41±7.57	0.635	<0.05

If HbA_1c>9.3% (n=109), obvious correlativity between HbA_1c and basal total dose was observed (r=0.635, P<0.05). Linear regression analysis produced a relationship formula of basal dose=3.233×HbA_1c–20.059, P<0.05, S_b (standard error of regression coefficient)=0.381, 95% confidence interval of β (total coefficient of regression) was 2.48~3.99 (Table 3).

Table 3 Relationship between HbA_1c (%) and basal prediction dose (IU/d) according to relationship formula

HbA_1c	Basal prediction dose
9.3	10
11.3	16.47
13.3	22.94
14.3	26.17

No correlation between HbA_1c and bolus total dose before three meals

Table 4 reveals no correlation between HbA_1c and bolus total dose before three meals no matter of HbA_1c level.

Table 4 Correlation between HbA_1c (%) and insulin bolus total dose (IU/d)

HbA_1c (range)	n	Bolus total dose before three meals	Correlation (r)	P
<7.3	49	27.96±9.04	0.117	0.425
7.3~9.3	110	28.61±7.69	0.059	0.538
>9.3	109	33.82±7.18	0.243	0.112

DISCUSSION

The use of CSII can result in improved quality of life, cost savings for treatment, and potential reduction in diabetes-related complications based on the decline in HbA_1c. This treatment method may be a novel alternative for patients with type 2 diabetes and insulin resistance who have not met goal glycemic control with standard intensive regimens or who require insulin doses exceeding current insulin pump delivery capacity (Knee *et al*., 2003). Otherwise, there were few studies on the use of CSII therapy in type 2 diabetes mellitus, even less on relationship between HbA_1c and basal or bolus dose in CSII. Basal or bolus dose, which is the key factor in CSII? Crawford *et al*.(2000) observed 19 patients (16

women and 3 men) with type 1 diabetes in pre-CSII and follow-up data. The total daily insulin-to-weight ratio also significantly decreased from 0.66 IU/kg to 0.53 IU/kg (P<0.05). Before insulin pump use, the regular/NPH insulin ratio was 0.5 IU; at follow-up, the pump bolus/basal insulin ratio was 1.0 IU (P=0.02). CSII therapy in patients with type 1 diabetes improves glycemic control and lowers the total daily basal insulin dose without affecting weight. In another study that attempted to identify the optimal basal insulin in the context of multidose therapy with insulin lispro, NPH insulin yielded lower blood glucose levels and a trend toward better glycosylated hemoglobin levels than did Ultralente insulin. For improvement of glycemic control during insulin lispro therapy, adjustments in the ratio of bolus to basal insulin and the number of basal insulin injections have been shown to be useful. For full benefit of short-acting insulin analogues, adjustments must be made in basal insulin replacement (Zinman, 2000). HbA_1c is regarded as a better index to evaluate the state of diabetes mellitus, which can reflect the average level of blood glucose during a period of time because of its stability compared with blood sugar monitoring, and HbA_1c itself is less influenced by other factors (Abbasi and Reaven, 2002). Now people are prone to think that the contribution of postprandial and fasting glucose increments to overall hyperglycemia differs significantly due to the different level of glycosylated hemoglobin. If HbA_1c<7.3%, postprandial blood glucose contributes mostly and the major appearance of the disease is the augmented postprandial blood glucose. If HbA_1c>10.2%, fasting blood glucose contributes mostly and the major appearance of the disease is the increased fasting blood glucose. The relative contribution of postprandial glucose decreases progressively from the lowest to the highest level of HbA_1c, whereas the relative contribution of fasting glucose increases gradually with increasing levels of HbA_1c (Monnier *et al*., 2003). So the aim of insulin therapy should give emphasis to control fasting blood glucose, if the patient has a higher level of HbA_1c.

We found that fasting blood glucose correlates with HbA_1c best compared with postprandial blood glucose. The reason might be that postprandial blood glucose was influenced by many factors such as meal intake and meal time (Bonora *et al*., 2001). Fasting blood glucose can be regarded as a pragmatic blood glucose monitoring point. In our study we found that the effectiveness of estimating the total basal insulin dose using HbA_1c was poor if HbA_1c<7.3%. We did not find the tendency of the total bolus insulin dose according with the rising HbA_1c from 7.3% to 9.3% or >9.3%. If >9.3%, HbA_1c did correlate with basal insulin dose obviously reflecting the total basal insulin dose due to the increased effect of fasting blood glucose. Obvious correlation between HbA_1c of different levels and the bolus insulin before meals was not observed, the reason might be that the rangeability of the total bolus insulin dose ahead of meal was comparatively large due to many influencing factors of postprandial blood glucose. So HbA_1c level can forecast the total basal insulin dose in CSII.

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