Basal insulin requirement of youth with type 1 diabetes differs according to age

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ABSTRACT

We investigated the percentage of total basal insulin dose to total daily insulin dose (% TBD) among Japanese youth of different ages with type 1 diabetes. The study enrolled 69 patients with type 1 diabetes who were treated with multiple daily injections of insulin. The participants were divided into the following age groups: group A, 0 to <10 years ($n = 18$); group B, 10 to <20 years ($n = 31$) and group C, 20 to <25 years ($n = 20$). We found no difference in the sex ratio, body mass index, and glycated hemoglobin and 2-h postprandial C-peptide levels among the three groups. Participants assigned to group B had a significantly higher percentage of total daily insulin dose than those in group A and group C (49.7 ± 10.4% vs 38.5 ± 13.7% and 38.3 ± 8.2%, $P = 0.0005$). In conclusion, the basal insulin requirements of Japanese youth with type 1 diabetes might have an age effect that is associated with puberty.

INTRODUCTION

It has been reported that worldwide, basal–bolus insulin therapy (BBT) with multiple daily injections (MDI) is frequently used by youth with type 1 diabetes. The use of long-acting insulin analogs for basal insulin and rapid-acting insulin analogs for bolus insulin is currently the standard MDI routine[1]. The bolus insulin dosage is usually determined according to the amount of carbohydrate in the daily diet, as assessed by carbohydrate counting. However, the basal insulin requirement could be influenced by age, body mass index (BMI), glycemic control and residual β-cell function[2–6].

We compared the ratio of total basal insulin dose (TBD) to total daily insulin dose (TDD) among Japanese youth of different ages with type 1 diabetes, so as to ascertain the effect of age on basal insulin requirement.

MATERIALS AND METHODS

The study enrolled 69 Japanese youth with type 1 diabetes who were treated with BBT using MDI. The characteristics of the participants were as follows: 32 males and 37 female, aged 15.1 ± 5.8 years, 8.3 ± 5.1 years of duration of diabetes, and 0.7 ± 0.5 of standard deviation scores of BMI (SDSs-BMI)[7]. At

the time of the study, the mean values of glycated hemoglobin (HbA1c) and 2-h postprandial serum C-peptide (S-CPR) of the participants were 7.3 ± 0.9% and 0.1 ± 0.2 ng/mL, respectively. The participants were divided into the following three age groups for an analysis of the age effect on basal insulin requirement: group A, 0 to <10 years ($n = 18$); group B, 10 to <20 years, ($n = 31$); and group C, 20 to <25 years ($n = 20$). The characteristics of participants and their TBD to TDD percentage (%TBD) were compared between the three age groups.

Information about insulin dose of MDI was obtained from the medical records in each patient. TBD and TDD were estimated by calculating the mean values for TBD and TDD from the records over a 1-month period. Insulin glargine was given as basal insulin in a once- or twice-daily injection regimen, and either lispro, aspart or glulisine was given as bolus insulin before each meal in the MDI therapy. The mean number of bolus injections was 4.0 ± 1.0 daily. Patients were instructed to adjust basal insulin doses to attain self-monitored fasting plasma glucose (FPG) levels between 90–140 mg/dL[1], and to determine bolus insulin doses according to carbohydrate counting.

HbA1c was determined by a high-performance liquid chromatography method at centralized Diabetes Control and Complications Trial accredited laboratory, and expressed as a National Glycohemoglobin Standardization Program value[8] (normal: 4.6–6.1%).

Table 1 | Clinical characteristics of patients in groups A, B and C

	Group A	Group B	Group C
n	18	31	20
Male/female	13/5	11/20	6/14
SDS-BMI	0.7 ± 0.4 (−0.1 −1.2)	0.7 ± 0.5 (0.0 −1.69)	0.7 ± 0.5 (0.0 −1.3)
HbA1c (%)	7.5 ± 0.9 (5.2 −8.5)	7.3 ± 0.8 (5.9 −8.8)	7.1 ± 0.9 (5.3 −8.7)
CPR (ng/mL)*	0.2 ± 0.1 (0.2 > −0.6)	0.2 ± 0.2 (0.2 > −0.5)	0.2 ± 0.2 (0.2 > −0.3)

*2-h postprandial level. CPR, C-peptide; HbA1c, glycated hemoglobin; SDS-BMI, standard deviation score of body mass index.

The Kruskal–Wallis test was used to assess differences between the three groups. The results are expressed as mean ± standard deviation and $P < 0.05$ was considered statistically significant.

RESULTS

Clinical Characteristics of Patients in Groups A, B and C

As shown in Table 1, male-to-female ratios were 13:5, 11:20 and 6:14, and the SDSs-BMI were 0.7 ± 0.4, 0.7 ± 0.5, and 0.7 ± 0.5 in groups A, B and C, respectively. The mean values of HbA1c were 7.5 ± 0.9, 7.3 ± 0.8, 7.1 ± 0.9%, and for 2-h postprandial S-CPR were 0.2 ± 0.1, 0.2 ± 0.2, and 0.1 ± 0.1 ng/mL in groups A, B and C, respectively. There was no statistical difference in these indices among the three groups.

Comparison of TDD, TBD and %TBD Amongst Patients in Groups A, B and C

As shown in Table 2, the mean values for TDD and TBD in all the participants were 0.91 ± 0.19 and 0.40 ± 0.17 U/kg/day, respectively. For participants in groups A, B and C, the TDD values were 0.89 ± 0.16, 0.98 ± 0.20, and 0.80 ± 0.14 U/kg/day, and the TBD values were 0.35 ± 0.15, 0.49 ± 0.17, and 0.31 ± 0.10 U/kg/day, respectively. Participants in group B had a significantly higher TDD and TBD than those in groups A and C ($P = 0.0015$ and $P = 0.0001$ for TDD and TBD, respectively).

The mean %TBD for all the participants was 43.4 ± 12.1%. The mean %TBD was 38.5 ± 13.7%, 49.7 ± 10.4% and 38.3 ± 8.2% for groups A, B, and C, respectively. Participants in group B also showed significantly higher %TBD than those in groups A and C ($P = 0.0005$).

DISCUSSION

Several studies with Caucasians have reported the average % TBD to be approximately 40–70% in youth with type 1 diabetes treated with MDI or continuous subcutaneous insulin infusion (CSII)[2,5,6,9–11]. In contrast, previous studies in Japan found the %TBD to be less than 40%[3,4,12]. Kuroda et al.[12] reported that in adult patients treated with CSII, the %TBD is just 27.7 ± 6.9%, and Hashimoto et al.[5] found the %TBD in pediatric patients treated with MDI or CSII to be 35 ± 10%. These authors attributed the difference in %TBD between Caucasian and Japanese subjects to meal content. Traditional Japanese meals are known to have a higher carbohydrate energy ratio (CER) and a lower fat energy ratio (FER) than meals in Western countries. According to statistics from the United Nations, the FER in Japanese meals was 28%, but it exceeded 35% in meals from Western countries. However, a recent report by the National Health and Nutrition Examination Survey of the Japanese government showed that, in Japan, FER of meals is gradually increasing, whereas CER is decreasing, particularly in those consumed by teenagers. We hypothesized that dietary habits of adolescent participants were mostly Westernized with higher FER, which might be one of the reasons why patients assigned to group B had a higher %TBD as compared with those reported in previous Japanese studies.

Puberty is known to be associated with an increase in insulin resistance by 30%[13,14]. Adolescent patients tend to show elevated levels of FPG, and their basal insulin doses were adjusted to attain the recommended FPG level of 70–140 mg/dL. Because of this, adolescent participants in the present study might have had higher TBD, TDD and %TBD compared with the younger children in group A and the adults in group C.

Various other factors were reported to affect %TBD. Pankowska et al.[2] found a negative correlation between S-CPR and %TBD in Polish youth with type 1 diabetes, and Arai et al.[3] reported that patients with higher BMI had a higher % TBD. Poor glycemic control with an elevated level of FPG could also increase %TBD[5,6]. However, in the present study, we could not find significant differences in these indices among the three groups, and we did not find any correlation between these indices and %TBD (data not shown). Bauchmann et al.[5,6] reported that TBD significantly increased at the pubertal period among patients with type 1 diabetes using CSII, which agrees with the result in our patients treated with MDI.

Table 2 | Comparison of TDD, TBD and %TDD among patients in groups A, B and C

	Group A	Group B	Group C	P*
TDD (U/kg/day)	0.89 ± 0.16 (0.6 −1.1)	0.98 ± 0.20 (0.7–1.4)	0.80 ± 0.14 (0.7–1.3)	0.0015
TBD (U/kg/day)	0.35 ± 0.15 (0.2 −0.5)	0.49 ± 0.17 (0.2–0.8)	0.31 ± 0.10 (0.2–0.7)	0.0001
%TBD (%)	38.5 ± 13.7 (21 −58)	49.7 ± 10.4 (27–67)	38.3 ± 8.2 (23–57)	0.0005

*P: group B vs group B and C.

In conclusion, we showed that the basal insulin requirement of Japanese youth with type 1 diabetes treated with MDI has an age effect that could be associated with puberty. The way in which basal insulin is used could be an important technique to achieve adequate glycemic control, particularly among adolescents with type 1 diabetes[15,16]. Basal insulin dose for type 1 diabetes treated with MDI should be modified according to patient age. However, the present study was limited to a small number of participants, therefore it is necessary to confirm the results in a large number of patients treated with MDI.

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