Beta-cell function in Chinese youngsters with type 1 diabetes and assessment of surrogate markers of severe insulin deficiency

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Abstract

Objective:

Type 1 diabetes mellitus (T1DM) results from insulin deficiency. We assessed whether beta-cell function progressively decreases over time with greater diabetes duration using a gold-standard mixed-meal tolerance test (MMTT). As MMTT is invasive to perform requiring a hospital setting, we also assessed simpler and more practical surrogate parameters for routine clinical use.

Methods:

We studied 57 children and adolescents with T1DM in Hangzhou (China), who were aged 10.8 years (range 4.4 to 16.8 years), of whom 56% were females. Mean age at T1DM diagnosis was 8.3 years (range 2.3 to 15.3 years), with an average diabetes duration of 2.5 years (range 2 weeks to 8 years). A 120-minute MMTT was performed with plasma C-peptide measurements taken every 30 minutes. Urine C-peptide and creatinine levels were simultaneously measured at 0 and 120 minutes. Beta-cell function was assessed by the C-peptide area under the curve (AUC). Severe insulin deficiency was defined as a C-peptide peak from the MMTT <0.2 nmol/l. C-peptide peak in urine and the C-peptide to creatinine ratio were calculated.

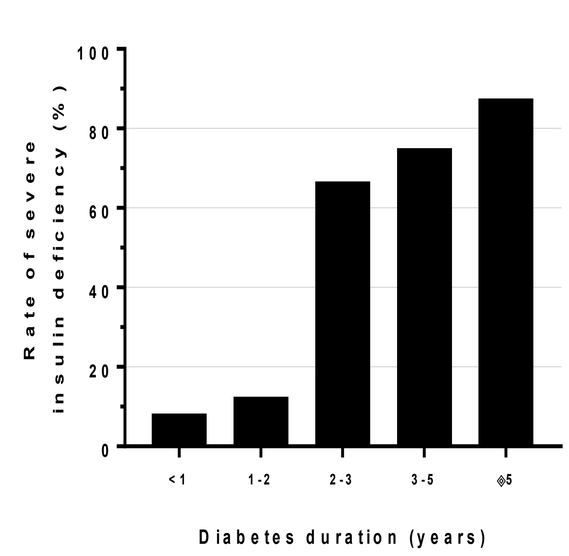

Figure 1. Rate of severe insulin deficiency among 57 children with type 1 diabetes in Hangzhou (China) in association with time elapsed since diabetes diagnosis.

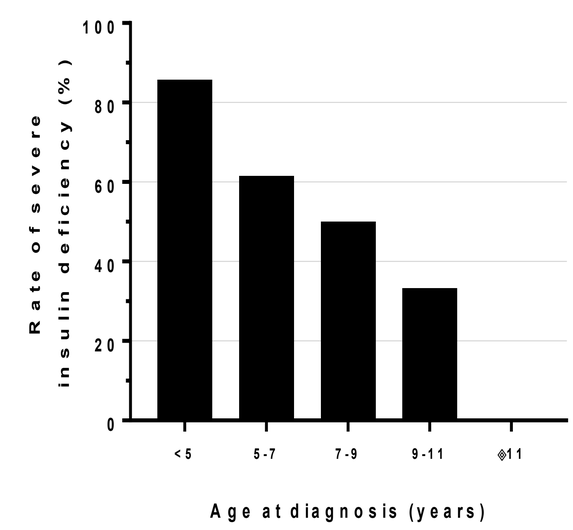

Figure 2. Rate of severe insulin deficiency among 57 children with type 1 diabetes in Hangzhou (China) in association with age at diabetes diagnosis.

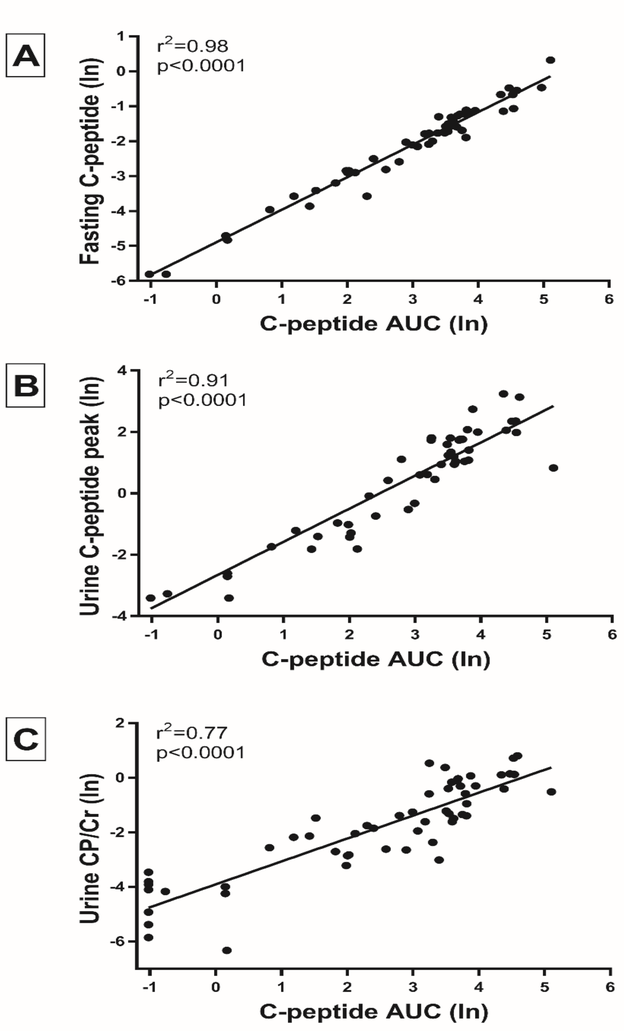

Figure 3. Linear associations between C-peptide area under the curve (AUC) from a mixed-meal tolerance test with other plasma and urine parameters. A) fasting C-peptide levels; B) Urine C-peptide peak levels from two samples at 0 and 120 minuntes; and C) Urine C-peptide to creatinine ratio (CP/Cr) at 120 minutes. All data have been log-transformed.

Results:

Every one-year increase in diabetes duration was associated with a 37% decrease in C-peptide AUC (p<0.001). The rate of severe insulin deficiency steadily increased over time, being particularly marked after two years when the rate of severe insulin deficiency increased from 13% to 67%. In addition, every one-year decrease in age at T1DM diagnosis was associated with a 20% decrease in C-peptide AUC (p=0.005). There was a consequent decline in the rate of severe insulin deficiency with increasing age at diabetes diagnosis, with a 86% prevalence among children under 5 years of age compared to virtually no cases among children aged 11 years or older.

All diagnostic measures from the MMTT or urine test examined were highly correlated. In particular, fasting C-peptide levels were almost perfectly corrected with both C-peptide peak and AUC, with urine C-peptide peak also highly correlated with the two MMTT parameters.

Twenty-five patients had severe insulin deficiency. The C-peptide peaks at any time point had 100% sensitivity and thus were able to detect all cases of severe insulin deficiency. However, the peak at 0-120 min was the only one with 100% specificity, with no false positives. Fasting C-peptide was somewhat accurate to detect cases of severe insulin deficiency, missing just one case (sensitivity 96%) and with no false positives (100% specificity). Urine C-peptide/creatinine at 120 minutes had 100% sensitivity, but poor specificity at 63% with 11 false positives (out of 30 negatives). Urine C-peptide peak had nearly perfect sensitivity at 96%, and its specificity was considerable better than that of the ratio at 87%.

Conclusions:

There seems to be a steady decrease in beta-cell function with increasing duration of diabetes. In addition, children diagnosed at a younger age tend to have a much more marked loss in beta-cell function. Importantly, we showed that surrogate makers can be used in a routine clinical setting to detect severe insulin deficiency in Chinese children and adolescents, particularly fasting C-peptide levels and a 120-minute urine C-peptide peak.

Acknowledge

Fundings: JY is supported from Zhejiang Provincial Key Science and Technology Project (No.2014C03045-2), National Key Research and Development Programme of China (No.2016YFC1305301), Natural and Science Foundation of Zhejiang Province (LY14H070003), National Health and Family Planning Commission Scientific Research-Zhejiang major medical and health science fund "Study on Early Identification and Standardized Treatment of Children Metabolic Syndrome". JGBD is supported by a travel fellowship from the New Zealand-China Non-Communicable Diseases Research Collaboration Centre.