



Carbohydrate Tolerance Threshold for Unannounced Snacks in Children and Adolescents With Type 1 Diabetes Using an Advanced Hybrid Closed-Loop System

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OBJECTIVE

To find a carbohydrate (CHO) tolerance threshold for unannounced snacks to avoid the 2 h increase in glycemia (difference between pre- and postmeal blood glucose [Δ BG]) ≥ 50 mg/dL in advanced hybrid closed-loop (a-HCL) users.

RESEARCH DESIGN AND METHODS

Fourteen children and adolescents with type 1 diabetes (7 females; mean age [\pm SD] 14.5 ± 3.6 years), users of the Medtronic MiniMed 780G, participated in the study. For 12 days, they did not perform insulin bolus before breakfasts, with defined different quantities and types of CHO, with or without fats, performing blood glucose (BG) before and 2 h after the meal.

RESULTS

A cutoff of 19.8 g of total CHO was found to determine a Δ BG of 50 mg/dL. BG never exceeded 250 mg/dL. Mean time in range was $\geq 70\%$ in the 2 h following each snack.

CONCLUSIONS

Unannounced snacks of up to 20 g of CHO can avoid Δ BG ≥ 50 mg/dL in MiniMed 780G users, although unannounced meals of up to 30 g of CHO are safe.

The advanced hybrid closed-loop system HCL (a-HCL) systems differ from the standard by providing autocorrection insulin boluses to help correct high sensor glucose readings (1) with better glycemic outcomes (2,3), especially overnight, when postprandial glucose excursions are absent (4); however, they still require user interaction with meal boluses, inserting the grams of carbohydrates (CHO) to be consumed to fully control postprandial glucose excursions (1).

So far, it is unknown whether the algorithm used by a-HCL can tolerate, without significant hyperglycemia, a certain amount of CHO, as it may happen for unannounced snacks (e.g., small children at school).

The primary outcome of this study was to find a CHO tolerance threshold for unannounced snacks for which the a-HCL Medtronic MiniMed 780G can avoid

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2 h hyperglycemia, defined as a difference between pre- and postmeal blood glucose (Δ BG) ≥ 50 mg/dL (5).

RESEARCH DESIGN AND METHODS

Study Participants

This study was approved by the Institutional Review Board. Inclusion criteria were diagnosis of type 1 diabetes (6), between 7 and 21 years of age, use of the SmartGuard feature (Auto mode) of the Medtronic MiniMed 780G for at least 1 month, with a glycemic target of 100 mg/dL, and insulin action time of 2 h.

Study Procedures

Participants were asked to have an unannounced snack in the morning, to start with the best possible glycemic control (4), with no premeal bolus for 12 days. The participants used a scheme provided by the dietitian with an exact indication of type and quantity of food, with progressive amounts of CHO (~10, 20, or 30 g), complex or simple, with or without fats (crackers, juice, chocolate biscuits, and chocolate bars) (Supplementary Table 1). Participants were free to choose the order of snacks. Blood glucose (BG) had to be performed before (pre-BG) and 2 h after the meal (post-BG). Data were considered valid only if the SmartGuard feature was active, the premeal BG was <150 mg/dL, and the BG was measured 2 h after breakfast; if in the 2 h after breakfast there were no other meals and no physical activity was performed; and if no fever or other acute clinical illness were reported.

Statistical Analysis

Data are presented as mean (\pm SD) for continuous variables and absolute frequency and percentage for categorical variables. A multivariate repeated-measures model was applied to identify factors influencing glycemia level changes between pre- and postmeal. To obtain the optimal cutoff for total CHO identifying hyperglycemia, as described above, a repeated-measures receiver operating characteristic curve was constructed, and Youden index was then calculated. A P value <0.05 was considered statistically significant. All statistical analyses were performed with SAS software, Version 9.4 (SAS Institute Inc., Cary, NC). Additional

statistical details can be found in the Supplementary Material.

RESULTS

Fourteen individuals with type 1 diabetes (7 females; mean age 14.5 ± 3.6 years) were consecutively enrolled and completed all snacks. Characteristics of participants are described in Supplementary Table 2. A box plot with the Δ BG for each snack is shown in Fig. 1.

Regarding the multivariate repeated-measures model, Δ BG increased by 2.4 (95% CI 1.80; 3.04) with increasing 1 g of complex CHO ($P < 0.0001$), increased by 2.02 (95% CI 1.23; 2.80) with increasing 1 g of fats ($P < 0.0001$), increased by 0.8 (95% CI 0.23; 1.41) with increasing 1 g of simplex CHO ($P = 0.01$), and decreased by -0.54 (95% CI -0.82 ; -0.25) with increasing 1 mg/dL premeal glycemia ($P = 0.0003$). For the receiver operating characteristic analysis for repeated measures, a cutoff of 19.8 g of total CHO was found to determine a Δ BG of 50 mg/dL with a sensitivity of 0.94 and a specificity of 0.46 (area under the curve 0.96).

No post-BG levels ≥ 250 mg/dL were found with any kind of unannounced snack up to 30 g of CHO, and the mean time in range (TIR) was $\geq 70\%$ in the 2 h after the snacks.

Additional data on pre-BG, post-BG, Δ BG, insulin dose delivered, automatic correction, and sensor-specific measures of glycemic control for each day are reported in Supplementary Tables 3 and 4.

CONCLUSIONS

To our knowledge, this is the first study to report that an unannounced CHO snack of <20 g of CHO is well tolerated by the a-HCL Medtronic MiniMed 780G in a pediatric cohort, determining a maximum Δ BG of 50 mg/dL after 2 h, when premeal BG is <150 mg/dL. Moreover, we did not find any glycemic level ≥ 250 mg/dL, and the mean TIR over the 2 h after the snacks was $\geq 70\%$ with unannounced snacks up to 30 g of CHO.

Meal-related glycemic control has always been a challenge for the pediatric population with type 1 diabetes, especially adolescents who underestimate or miss insulin doses for ingested CHO (7–10).

There is hope that fully closed-loop systems will reduce user burden through a

completely automated insulin (or multi-hormone) delivery; however, the attempts made so far resulted in suboptimal glycemic control because of higher peaks in postprandial glucose or increased time spent in hypoglycemia (11–13). Meanwhile, understanding the potential of currently marketed systems can help improve glycemic control and quality of life for individuals with type 1 diabetes (14).

The only study reported so far with the a-HCL MiniMed 780G system on unannounced meals (up to 80 g of CHO) showed a TIR $<70\%$ (15). However, this study was conducted in adults, focused on longer-term (3 months) control, and did not discriminate the amount of CHO under the threshold of 80 g.

We demonstrate that eating <20 g of CHO without bolusing the a-HCL MiniMed 780G system can avoid increasing glycemia ≥ 50 mg/dL 2 h after the meal. We also found that the rise in BG at 2 h after the meal is mainly driven by complex CHO and fats. As a matter of fact, eating up to 30 g of simple CHO usually led to an increase in glycemia <50 mg/dL, while the limit for complex CHO or any CHO with fats is only 10 g.

The limitations of this study include the small number of subjects, the broad age range with possible interference of insulin resistance in pubertal subjects, the absence of variables such as physical activity or daily stressors that could interfere with glucose levels, and a starting glucose <150 mg/dL. Nevertheless, the strength is that the study was conducted at home, in a real-world setting, using a commercial device, providing generalizable and valuable findings.

In conclusion, although there is always the need to reinforce the importance of bolusing before meals, in selected circumstances, MiniMed 780G pediatric users can eat unannounced snacks up to 20 g of CHO (preferably complex CHO without fats or simple CHO with fats), preventing a glycemic excursion ≥ 50 mg/dL at 2 h, and up to 30 g of CHO avoiding glycemia ≥ 250 mg/dL and still with a mean TIR $\geq 70\%$. This information may be particularly helpful for children who are still not autonomous in providing insulin boluses through the pump when not assisted by an a-HCL skilled caregiver (e.g., school teachers and babysitters). To put things in

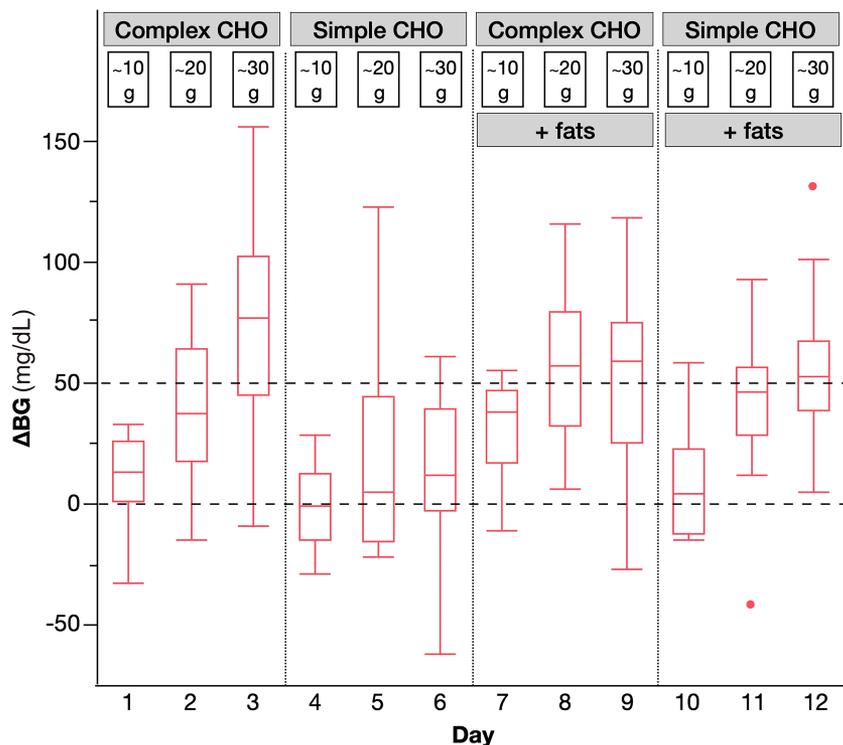


Figure 1—Box plot with differences between blood glucose (BG) before and 2 h after unannounced snacks ($\Delta\text{BG} = 2\text{-h postmeal BG} - \text{premeal BG}$).

a real-life setting, 20 g of CHO corresponds roughly to a sandwich with two bread slices, which can be ideal for a snack break at school. Further studies are needed in larger cohorts for bigger unannounced meals, with any starting glycaemia, and with other a-HCL systems.

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contributed to the discussion and reviewed the manuscript. All authors read and approved the final manuscript. G.T. is the guarantor of this work and, as such, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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