Carbohydrate Counting, Mixed Meals, and Food Glycemic-Index Management

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Achieving optimal glucose control in individuals with type 1 diabetes (T1DM) continues to pose a significant challenge. While continuous insulin infusion systems have shown promise as an alternative to conventional insulin therapy, there remains a crucial need for greater awareness regarding the necessary adaptations for various special circumstances. Nutritional choices play an essential role in the efficacy of diabetes management and overall health status for patients with T1DM. Factors such as effective carbohydrate counting, assessment of the macronutrient composition of meals, and comprehending the concept of the glycemic index of foods are paramount in making informed pre-meal adjustments when utilizing insulin pumps.

Keywords: type 1 diabetes mellitus ; insulin pumps ; nutrition ; carbohydrate counting ; mixed meals ; GI

1. Introduction

In light of the rising global incidence of type 1 diabetes mellitus (T1DM), with approximately 8.75 million individuals affected in 2022, optimizing therapeutic strategies has become imperative ^[1]. Continuous subcutaneous insulin infusion (CSII), or insulin pump therapy, has emerged as a valuable option for both adults and pediatric patients. CSII offers precise insulin delivery, mirroring natural secretion patterns that often yield better glycemic control than multiple daily injections (MDI) ^[2]. Notably, studies have demonstrated that CSII reduces glycemic variability, modestly reduces HbA1c levels without increasing the risk of hypoglycemia, offers flexibility, minimizes the number of injections, and improves quality of life in diabetes management ^{[3][4][5][6][7]}. Combining CSII with education and training on nutrition, exercise, and insulin adjustment maximizes its effectiveness in diabetes care, significantly improving glycemic control and reducing hypoglycemia in T1DM patients ^[8].

2. Carbohydrate Counting, Mixed Meals, and Food Glycemic Index Management

Carbohydrate counting is a crucial aspect of medical nutrition therapy for individuals with T1DM treated with insulin pumps. This meal-planning approach involves matching bolus insulin doses to the total carbohydrate content of every meal by quantifying it through various methods, such as 15 g exchanges, 10 g portions, or total grams of carbohydrate consumed ^[9]. Studies in both adults and adolescents using CSII with insulin to carbohydrate ratio (ICR) have reported improvements in glycemic control, dietary flexibility, and overall quality of life ^{[10][11][12]}. Bolus calculators integrated in insulin pumps play a significant role in facilitating the effective implementation of carbohydrate counting ^[13]. By automating the process of insulin dose calculation based on carbohydrate intake and correction for active insulin from previous boluses, bolus calculators can reduce the risk of insulin stacking and subsequent hypoglycemia, as well as reduce both overall and meal-related fluctuations in postprandial glucose levels, leading to an increase in post-meal glucose values within the target range ^[12]. Due to the challenges faced by some individuals who do not consistently adopt carbohydrate counting for estimating meal boluses, it is evident that more comprehensive and targeted education is needed to improve its implementation effectively ^[11]. Advancements in technology are expected to reduce the need for manual patient input into pump systems, possibly leading to a future when users can eat without meal announcement, carbohydrate counting, or blood glucose level entry ^[14].

There is growing interest in closely examining the combination of carbohydrate counting with insulin treatment in addition to other dietary factors proven to substantially impact blood glucose regulation, such as fat and protein content as well as the glycemic index (GI) of foods. As far as mixed meals management is concerned, various pediatric and adult studies have revealed that \geq 35 g of fat and \geq 40 g of protein consumed in combination with carbohydrate or \geq 75 g protein consumed alone result in significant delayed hyperglycemia occurring 3 to 6 h after the meal while reducing the early

postprandial rise observed at 1 to 2 h ^{[15][16][17]}. This is attributed to the impact of such meals on delaying gastric emptying, leading to sustained glucose responses after meals, which underscores the limitations of relying solely on carbohydrate-based formulas for insulin dosage calculations ^{[18][19]}. To address the complexities produced by fat and protein content in meals, a number of recommendations for insulin dose adjustment have been proposed.

Most studies suggest that for high-fat and/or high-protein meals, the total insulin dose needs to be increased by 25–60%, followed by a combination bolus delivery over 2–3 h [10][16][20][21][22][23][24]. However, there is no state-of-the-art consensus regarding the precise duration and distribution of the insulin bolus. Studies have proposed various recommendations regarding the latter, ranging from 70:30% to 30:70% [10][16][20][21][22][23]. According to a recent study by Smith et al. focused on the effects of a high-fat, high-protein (HFHP) breakfast on postprandial glycemic excursions, significant late hypoglycemia was observed when higher adjustments in insulin dose were implemented (at 160% of the ICR) [16]. As a result, the authors recommend a more conservative approach in practice, although the observed inter-individual differences in insulin dose requirements for meals rich in fat and protein may pose difficulties in optimal glucose management [16][22]. They suggest initiating insulin dose increases with 10-20% of the ICR, distributed at a 60:40 ratio over a 3 h period. In cases of sustained hyperglycemia, the insulin dose may be escalated in gradual increments of 10% $\frac{160}{1}$. Consistent with this, Bell et al. proposed that for HFHP meals containing more than 40 g of fat and 25 g of protein, patients should consider augmenting their insulin dose by approximately 25 to 30% and administering 30 to 50% of the calculated dose initially, and the remaining insulin gradually over a period of 2 to 2.5 h [22]. Personalized guidance based on postprandial glucose monitoring for up to 6 h, facilitated by the integration of continuous glucose monitoring (CGM) with pump therapy, is imperative to optimize insulin dosing and achieve effective management of mixed meals in patients with T1DM treated with pumps $^{[10]}$.

The optimal management of pre-meal insulin delivery should incorporate carbohydrate quality, in conjunction with the aforementioned dietary determinants. Utilizing the GI can help stabilize post-meal blood glucose fluctuations ^[25]. Parillo et al. indicate that low-GI meals lead to a 20% lower glycemic response compared to high-GI meals ^[26], while a recent study demonstrates that higher glycemic load, primarily from sugars, predicts reduced post meal time in range (TIR) ^[27]. One could conclude that the key strategies include improving nutrition choices, carefully quantifying food, and fine-tuning insulin administration via pumps ^{[10][28]}.

In terms of the latter, administering pre-prandial insulin is deemed favorable compared to during or post-meal insulin administration for all types of meals $^{[29]}$. More specifically, when addressing lower GI foods, known to undergo a slower digestion and absorption process due to their content in fibers, protein, and/or fat, unless gastroparesis is evident, a suggested approach involves using a combination bolus $^{[30][31]}$. A clinical study focusing on insulin dosing techniques for improving postprandial glycemia after low-GI meals among pump users indicated that a dual-wave bolus, half given before the meal and half distributed over 2 h, led to a 47% reduction in postprandial glucose area under the curve in contrast to a standard bolus for low-GI meals $^{[31]}$.

A corresponding study involving well-controlled patients with T1DM suggested the use of combination bolus for lower GI selections over a square bolus, the latter being associated with undesirable early-phase hyperglycemia when compared with standard boluses ^[32]. However, for meals of moderate GI, an extended bolus may prove more effective if administered 20–30 min before the meal ^{[32][33]}. In cases of high-GI foods, early insulin delivery 15 min before eating could mitigate the postprandial glucose spikes that usually occur due to quick carbohydrate absorption. When these foods are combined with fats and/or proteins, a greater upfront insulin dosage through a combination bolus may be required ^{[17][30]}. Another proposed approach involves a super bolus defined as a 50% augmented initial insulin bolus followed by a reduction in basal rate for 2 h, aligning insulin action with glucose absorption after high-GI meals ^{[17][34]}. Nonetheless, since elevated postprandial glucose levels tend to persist after high-GI meals, irrespective of premeal bolus type, optimal nutrition choices play a vital role in conjunction with appropriate insulin pump settings ^[27].

To minimize postprandial glucose peaks and potentially enhance overall glycemic control, education should focus on substituting low-glycemic load for high-glycemic load foods ^[28]. Encouraging the consumption of whole, less-refined foods, like legumes, whole grains, fruits, and vegetables, while discouraging the intake of processed foods, such as sugary beverages, fast foods, and refined grains, is important ^[29]. Notably, the quality of dietary fat also influences the glucose response to high-GI meals. In a randomized crossover study involving T1DM patients on insulin pumps, high-GI meals rich in monounsaturated fats elicited lower glucose levels compared to saturated fats ^[35]. Interestingly, consistent research data demonstrate that consuming protein or fat approximately 15 min prior to a carbohydrate-rich meal results in reduced glucose response compared to consuming all macronutrients simultaneously ^{[36][37]}. The above data are analytically depicted in **Table 1**.

Table 1. Nutritional recommendations for patients with T1DM on pump therapy.

Study (Year)	Population	Meals	Recommendation
Gingras et al. (2018) ^[24] Wolpert et al. (2013) ^[23] Bell et al.	Individuals with T1DM in CLS Individuals with T1DM in CLS Individuals with T1DM in OLS		Increase TID by 25–60% for high-fat (>40 g) and/or high-protein (>25 g) meals. Initiate with a 10–20% ICR increase, gradually raise by 10% if hyperglycemia persists.
(2016) [22] Smith et al. (2021) ^[16] Lopez et al. (2017) ^[20] Al Balwi et al. (2022) ^[21]	Children and adolescents with T1DM on CSII Children and adolescents with T1DM on CSII Individuals with T1DM	HFHP	For HFHP meals, favor a combination bolus, delivering 30–70% of TID before meals and the remainder over 2–3 h based on individual requirements. High-GI foods alongside a HFHP meal might suggest the need for an elevated upfront dose.
ISPAD (2022) [<u>13</u>]	Children and adolescents with T1DM	Mixed meals	Utilize CGMs for achieving personalized management of mixed meals effectively.
O'Connell et al. (2008) ^[<u>31</u>]	Young individuals (8– 18 y.o.) with T1DM on CSII	Low-GI meals	Consider the use of a combination bolus (50:50 over 2 h).
Lopez et al. (2014) ^[32]	Children and adults with T1DM on CSII	Moderate-GI meals	Consider implementing an extended/wave bolus initiated 20–30 min prior to eating.
Lupoli et al. (2019) ^[30]	Individuals with T1DM		Consider administering insulin 15 min prior to eating.
Bell et. al. (2015) ^{[<u>17]</u>}	Individuals with T1DM	High-GI meals	An alternative strategy for high-GI meals includes a Super Bolus (=50% increase in the initial insulin bolus, followed by reduction in basal rate for the subsequent 2 h).
Bozzetto et al. (2019) ^[35]	Individuals with T1DM		Consider including a source of MUFAs alongside a high-GI meal for lowering the glycemic response.
ADA (2014) ^[29]	Individuals with T1DM	CHO rich meals	Aim to swap high-glycemic options with lower glycemic alternatives. In particular, promote the consumption of whole, less refined foods (i.e., legumes, whole grains, fruits, vegetables). Discourage the intake of processed products (i.e., sugary drinks, fast food, refined grains).
Faber et al. (2018) ^{[<u>37]</u>}	Young patients (7–17 y.o.) with T1DM		Consider intake of protein and/or fat 15 min prior to a CHO-rich meal for lowering the glycemic response.

Abbreviations: ADA = American Diabetes Association, CC = Carbohydrate Counting, CGM = Continuous Glucose Monitoring, CHO = Carbohydrate, CLS = Closed-Loop Systems, CSII = Continuous Subcutaneous Insulin Infusion, EASD = European Association for the Study of Diabetes, GI = Glycemic Index, HFHP = High Fat High Protein, MDI = Multiple Daily Injections, MUFAs = Monounsaturated Fatty Acids, TID = Total Insulin Dose, T1DM = Type 1 Diabetes Mellitus.

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