Late to the Party: Importance of Dietary Fat and Protein in the Intensive Management of Type 1 Diabetes. A Case Report

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Insulin dosing in type 1 diabetes (T1D) has been focused primarily on carbohydrate intake, but recent evidence highlights the importance of dietary fat and protein in glycemic excursions. Several methods have been developed to incorporate dietary fat and protein into insulin dose calculations, including fat-protein units (FPUs) that estimate insulin requirements based on ingested fat and protein, as well as extended combination insulin boluses. However, insulin dosing based on meal fat and protein content is challenging to incorporate into clinical practice.

We present the case of a 40-year-old man with T1D using continuous subcutaneous insulin infusions and continuous glucose monitoring. He followed a diet that restricted carbohydrate intake, with compensatory increases in dietary protein and fat. He had poor glycemic control with frequent postprandial hyperglycemia. He began incorporating FPUs into his insulin dosing calculations and used extended dual wave boluses to administer prandial insulin. Over the next 6 months he experienced a significant improvement in glycemic control.

Fat and protein have both been shown to cause delayed postprandial hyperglycemia, leading to poor glycemic control with carbohydrate-focused insulin dosing in our patient on a high-fat, high-protein diet. It is difficult to incorporate dietary fat and protein into insulin dosing in the clinical setting. However, our patient experienced an improvement in glycemic control with the application of FPUs and dual wave boluses in prandial insulin dosing, showing that methods such as these can be used successfully in T1D management.

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Carbohydrate-based approaches to insulin dose calculation have long been the backbone of prandial insulin therapy for patients with type 1 diabetes (T1D). However, multiple recent studies and growing clinical experience in the era of continuous glucose monitoring (CGM) increasingly highlight the inadequacy of this approach to limiting meal-induced hyperglycemia [1]. Dietary fats and protein are now well recognized as complex "late-comers" to the T1D nutrition environment, as both patients and clinicians become increasingly aware that overall meal composition, rather than carbohydrate content alone, is important in meeting glycemic targets [1, 2]. This awareness is particularly pertinent given the rise of popular diets that prioritize low carbohydrate intake, with a subsequent increase in other macronutrients, resulting in high-fat or high-protein diets.

Abbreviations: CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; FPU, fat-protein unit; T1D, type 1 diabetes.

However, adjusting insulin boluses according to meal fat and protein content is complex and rarely incorporated into daily practice. Several approaches are available to guide insulin dose decisions for ingested fat and protein in people with T1D using continuous subcutaneous insulin infusions (CSIIs). Most incorporate a combination bolus method of insulin dosing, in which a percentage of the insulin needed for the fat and protein in a meal is delivered as an extended bolus over several hours [2]. However, if little or no carbohydrates are consumed it is difficult to determine the additional insulin needed to account for fat or protein intake. One approach to address this problem has been suggested by the Warsaw Pump Therapy School, which recognizes that the macronutrient composition of a meal has variable effects on the rate of intestinal carbohydrate absorption and subsequent postprandial glycemic excursions [3]. This approach suggests that bolus doses via CSII for meal carbohydrate are delivered as a normal bolus, and fat or protein boluses should be administered as an extended square wave bolus. It also uses the fat-protein unit (FPU) as a method of estimating the insulin requirements for fat or protein intake. An FPU is defined as 100 kilocalories ingested from fat or protein, and it is thought to roughly approximate an insulin requirement equivalent to that of 10 g of ingested carbohydrate [3]. Given the delayed carbohydrate absorption rate after meals with higher fat and protein content, a square wave bolus is used based on the number of FPUs consumed, allowing insulin delivery over a longer interval. The duration of the square wave bolus is typically programmed to 3 hours for 1 FPU, 4 hours for 2 FPUs, 5 hours for 3 FPUs, and 8 hours for >3 FPUs.

Other methods, such as the Food Insulin Index, which is the relative measure of insulin demand for food derived from the insulin response observed in healthy people, account for all dietary components of a meal. They may be superior to carbohydrate counting when calculating insulin doses for high carbohydrate meals [4]. However, an important limitation of all approaches remains: Not all high-fat or high-protein meals result in predictable postmeal glucose excursions in individual patients [1, 2, 5]. In addition, almost all rely on the individual patient's capacity to calculate insulin requirements based on currently available nutrition labels.

We present a case of a patient with T1D using sensor-augmented CSII on a lowcarbohydrate, high-fat, high-protein diet who had improvement in glycemic control after incorporation of FPU-based insulin dosing and combination insulin boluses.

1. Case Report

A 40-year-old man with T1D for 39 years complicated by mild nonproliferative retinopathy presented to our diabetes clinic. He had used CSII for 17 years, augmented by CGM for several years. He was following a popular diet restricting carbohydrate intake, with compensatory increases in protein and fat content. He was consuming <50 g of carbohydrate daily. Most of his consumed calories consisted of fat or protein during his largest meal at dinner. His hemoglobin A1c was 8.0% (64 mmol/mol). Review of his 14-day CGM data revealed an average sensor glucose of 144 mg/dL (6.7 mmol/L), with a standard deviation of 48 mg/dL (2.7 mmol/L). Also, 77% of readings were within target range (70 to 180 mg/dL), 21% above target (\geq 180 mg/dL), and 2% below target (\leq 70 mg/dL), without severe hypoglycemia (\leq 55 mg/dL). He had frequent episodes of delayed postdinner hyperglycemia, resulting in fasting hyperglycemia the next morning. Previous attempts to increase his insulin bolus dose or extend his bolus for a few hours after dinner had resulted in early postdinner hypoglycemia, without correction of his overnight hyperglycemia.

Given his high fat and protein intake, he was started on the Warsaw Pump Therapy School method of insulin dosing based on FPU [3]. To assist with calculating FPUs from fat and protein sources, he was given the booklet *Choose Your Foods: Exchange Lists for Diabetes* and encouraged to use the mobile application Calorie King, which lists the macronutrient composition for a wide variety of foods [6, 7]. For every 1 FPU he consumed, he would enter 10 g of carbohydrates into his pump bolus calculator. Based on his insulin/carbohydrate ratio of 1 unit of insulin for every 6 g of carbohydrates, he received an additional 1.7 units of insulin for every FPU. He was instructed to use the bolus calculator in his pump for all insulin

administration and to extend insulin boluses for high-fat, high-protein meals. This method resulted in a two-part prandial insulin regimen: 15 minutes before meals, he delivered his usual insulin bolus to cover carbohydrate intake at a 1:6 insulin/carbohydrate ratio, which was delivered as a "normal" bolus. The insulin dose to cover his FPU intake was then administered as an extended "dual wave" bolus, with 30% administered right before the meal and 70% administered evenly over the next 4 hours.

Within 6 months, his glucose control improved substantially. His average daily carbohydrate intake, which includes both actual carbohydrates and carbohydrate equivalents calculated from FPU, increased from 50 g daily to >100 g daily, effectively doubling his total prandial insulin requirement. His delayed overnight hyperglycemia improved significantly. However, he noted an increase in the frequency of postprandial hypoglycemia, primarily toward the end of the dual wave bolus. Therefore, his FPU carbohydrate equivalency was decreased from 10 to 5 g, and his hypoglycemic episodes largely resolved. His average sensor glucose decreased by 20 mg/dL (1.11 mmol/L), in concert with a significant reduction in his glycemic variability as determined by glucose standard deviation. In addition, the percentage of time with blood glucose readings within target improved from 77% to 91%, and time above target was reduced from 21% to 6% without an increase in hypoglycemia. His average fasting glucose decreased to 115 mg/dL (6.38 mmol/L) from 135 mg/dL (7.5 mmol/L), and bedtime average glucose dropped to 146 mg/dL (8.11 mmol/L) from 173 mg/dL (9.61 mmol/L), with an improvement in hemoglobin A1c to 6.9% (52 mmol/mol).

2. Discussion

Dietary fat and protein are important macronutrients that are often overlooked in the standard carbohydrate-focused method used for prandial insulin dosing in T1D. Both cause delayed postprandial hyperglycemia and transient insulin resistance that may necessitate larger prandial insulin doses than anticipated [1]. High-fat meals delay gastric emptying, and circulating free fatty acids impair insulin sensitivity and promote hepatic gluconeogenesis [8, 9]. Dietary proteins increase glucagon concentrations and gluconeogenesis from amino acids [8, 10].

Our patient was consuming a low-carbohydrate diet with a compensatory increase in fat and protein intake. Unfortunately, his glycemic targets were not being met, largely because of persistent postprandial hyperglycemia that was not addressed through the standard carbohydrate-oriented insulin dosing approach.

Despite evolving evidence supporting the effect of dietary protein and fat on glycemic targets, uniform recommendations are difficult to apply to the clinical setting. There is significant interindividual variation in insulin requirements in response to dietary fat [1, 5]. Not all patients with T1D report this "meal phenotype," presumably because the type of fat (monounsaturated vs polyunsaturated), total fat content (which is difficult to estimate), timing of meals in relation to diurnal insulin sensitivity variation, and overall macronutrient composition, including the glycemic index of meals, all need to be considered. Insulin dosing based on the carbohydrate content of meals is already an advanced concept for many people with T1D, and adding additional complexity can be challenging, even with the availability of advanced tools such as sensor-augmented CSII. However, the experience of our patient confirms that incorporating FPU and combination bolus delivery with sensor-augmented CSII can be successful in helping motivated patients who are willing to embrace "fat counting" to attain glycemic targets. Similar to previous studies reporting increased episodes of hypoglycemia associated with FPU insulin dosing [11], our patient experienced increased hypoglycemia frequency at the end of his extended insulin bolus, but this frequency decreased after the carbohydrate equivalency of his FPU was decreased. This result indicates that FPU and similar strategies that incorporate dietary fat and protein in prandial insulin decisions should be adjusted based on individual response.

The American Diabetes Association recommends that patients with T1D and type 2 diabetes who are proficient at carbohydrate counting should also be educated on the effects of fat and protein on glycemic excursions [12]. However, routine application of fat and protein counting in the intensive management of T1D remains nebulous and complicated, even for highly motivated patients and expert clinicians. A recently published review article discusses further options for accounting for fat and protein in the management of T1D [13], but clinical practice patterns remain highly variable and lack uniformity. This case highlights the need for further studies and dedicated nutritional counseling that incorporates these concepts into standard diabetes education.

3. Conclusion

FPU and extended combination insulin boluses can improve postprandial hyperglycemia in T1D adults eating high-fat, high-protein, and low-carbohydrate diets.

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