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The relationship between carbohydrate and the mealtime insulin dose in type 1 diabetes

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ABSTRACT

A primary focus of the nutritional management of type 1 diabetes has been on matching prandial insulin therapy with carbohydrate amount consumed. Different methods exist to quantify carbohydrate including counting in one gram increments, 10 g portions or 15 g exchanges. Clinicians have assumed that counting in one gram increments is necessary to precisely dose insulin and optimize postprandial control. Carbohydrate estimations in portions or exchanges have been thought of as inadequate because they may result in less precise matching of insulin dose to carbohydrate amount. However, studies examining the impact of errors in carbohydrate quantification on postprandial glycemia challenge this commonly held view. In addition it has been found that a single mealtime bolus of insulin can cover a range of carbohydrate intake without deterioration in postprandial control. Furthermore, limitations exist in the accuracy of the nutrition information panel on a food label. This article reviews the relationship between carbohydrate quantity and insulin dose, highlighting limitations in the evidence for a linear association. These insights have significant implications for patient education and mealtime insulin dose calculations.

1. Introduction

Type 1 diabetes management guidelines around the world recommend quantifying carbohydrate for determining prandial insulin doses as one of the key elements of type 1 diabetes management (American Diabetes Association, 2015; Smart, Annan, Bruno, Higgins, & Acerini, 2014). It is based on the premise that, of all the macronutrients, carbohydrate has the most significant impact on raising postprandial blood glucose levels (Wolever & Bolognesi, 1996) and assumes a linear correlation between the amount of carbohydrate consumed and the mealtime insulin dose (Rabasa-Lhoret, Garon, Langelier, Poisson, & Chiasson, 1999). Since postprandial glycemia is a major determinant of HbA1c (Rudiger, 2004), it is believed that careful attention to carbohydrate quantity and distribution can improve glycemic control (Gillespie, Kulkarni, & Daly, 1998).

Studies in children and adults have reported glycemic and lifestyle benefits when carbohydrate counting is used as an intervention for people with diabetes (Laurenzi et al., 2011; Lowe, Linjawi, Mensch, James, & Attia, 2008; Scavone et al., 2010). These benefits include improved glycemic control as measured by lower HbA1c levels (DAFNE Study Group, 2002; Lowe et al., 2008; Trento et al., 2011); improved diabetes-specific quality of life (DAFNE Study Group, 2002; Lowe et al., 2008); and improved coping ability in daily life (Lowe et al., 2008; Trento et al., 2011).

Recent work into developing closed-loop insulin dosing algorithms have raised questions around the validity of assuming a linear relationship between carbohydrate and insulin and the degree of accuracy needed to estimate carbohydrate in order to achieve glycemic control. Indeed, there remains limited evidence as to what improvements in glycemic control can be anticipated with carbohydrate counting and the best methods for quantifying carbohydrate in intensive insulin therapy. These questions have important implications for the management of type 1 diabetes in clinical practice.

This paper will therefore review:

1) What impact does carbohydrate have on both acute postprandial blood glucose levels and long-term glycemic control (HbA1c)? 2) How accurately do people with type 1 diabetes *need* to count carbohydrate? 3) How accurately *can* people with type 1 diabetes count carbohydrate?

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2. What impact does carbohydrate have on glycemia?

2.1. Acute postprandial glycemia

2.1.1. Carbohydrate amount

Carbohydrate amount has been recognized as the most important determinant of postprandial rise (American Diabetes Association, 2004). Dietary carbohydrate is digested into glucose and other monosaccharides, which then enter the bloodstream. It has been postulated that about 90% of carbohydrate is converted to glucose within 1–2 h after eating (Halfon, Belkhadir, & Slama, 1989) and blood glucose levels typically peak within 60–90 min following a carbohydrate based meal in people with type 1 diabetes (Smart, King, McElduff, & Collins, 2012). However, the size of a meal and its nutritional composition influence the postprandial glucose excursion. Slama et al. (1981) and Halfon et al. (1989) showed that with mixed meals there was an increase in the postprandial glucose peak as carbohydrate content increased between 20 g and 80 g carbohydrate. Carbohydrate quantities over 80 g did not result in an increased peak but prolonged the glycemic excursion. Smart et al. (2013) showed that when protein and/or fat were added to a constant amount of carbohydrate, the height of the glycemic peak was similar but the late postprandial glucose excursion was increased.

It is probable that gastric emptying plays a significant role in the shape of the postprandial glycemic curve. The passage of food from the stomach to the duodenum has a significant impact on carbohydrate digestion and absorption. Gastric emptying occurs at a constant rate, which is determined by the energy content of the food. Food passes through the pyloric sphincter at a constant energy rate per minute (kcal/min) (Carbonnel, Lémann, Rambaud, Mundler, & Jian, 1994). This may explain why the glycemic peak does not increase after 80 g carbohydrate but rather results in a prolonged glycemic excursion and why high fat meals delay the glycemic rise.

A number of early studies were conducted to examine the relationship between the amount and type of carbohydrate and insulin delivery by an artificial pancreas (Halfon et al., 1989; Mirouze, Selam, Pham, & Cavadore, 1977; Service et al., 1983; Slama et al., 1981). All of these studies reported a significant correlation between carbohydrate and insulin, however there was disagreement on whether the relationship was linear or not. Slama et al. (1981) concluded the relationship was *not* linear for 20, 40 and 60 g of carbohydrate in a mixed meal or as dextrose. Conversely, Halfon et al. (1989) concluded that there *was* a linear relationship for mixed test meals containing 60, 80, and 140 g carbohydrate, whilst Service et al. (1983) reported that the relationship was "approximately linear". Rabasa-Lhoret et al. (1999) studied a linear relationship (ratio of 1 U of insulin:10 g of carbohydrate) and found that the 1 h postprandial average BGL was a constant 2.4 mmol/L higher than the preprandial BGL over a wide range of carbohydrate intakes (21–188 g) in free-living adults with type 1 diabetes and thus concluded that the relationship was linear. In all of these studies, insulin requirements for small amounts of carbohydrate (<20 g) were not studied.

Recent research using mathematical modeling is consistent with previous studies and also raises questions about the validity of the linear insulin:carbohydrate ratio (ICR) (Goodwin, Medioli, Carrasco, King, & Fu, 2015). The concept of the ICR suggests that a certain amount of carbohydrate requires an exact amount of insulin. However, it has been shown that a single insulin amount will cover a range of carbohydrate quantities. Smart, Ross, Edge, Collins, et al. (2009) demonstrated that an insulin dose calculated for 60 g of carbohydrate would cover meals containing 50 to 70 g of carbohydrate (Fig. 1). This implies that a carbohydrate-containing meal would be covered by ±16.7% of the insulin dose calculated from a titrated ICR. The ability of insulin to cope with a range of carbohydrate quantities may explain why authors have found that the linear ICR is able to achieve acceptable results within a limited range of carbohydrate quantities.

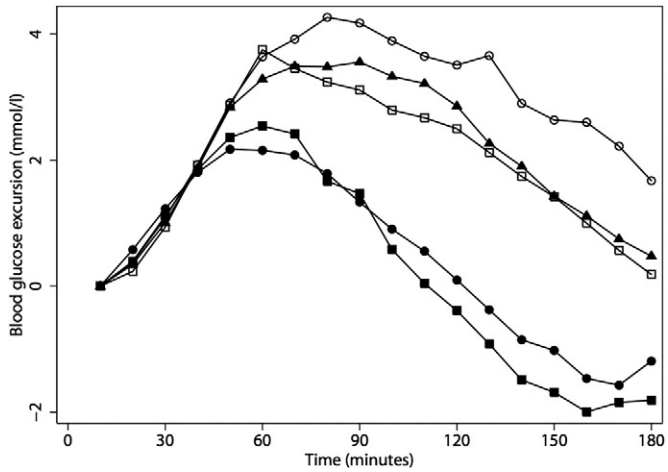

Fig. 1. Mean postprandial glucose levels for meals of 50 g, 60 g and 70 g of carbohydrate for 14 children on multiple daily injection therapy (MDI) and 17 children on insulin pump therapy (CSII). There was no difference between the insulin therapy groups at any time point for comparable carbohydrate loads (Repeated-measures ANOVA $P < 0.05$). The error bars represent 95% CIs.

Additionally, clinical evidence suggests that the usual linear ICR only estimates the insulin requirements when the amount and quality of the food are relatively close to the meals used to titrate the ICR. When the meal size varies significantly or the macronutrient composition is altered significantly then the outcome may be hyper- or hypo-glycemia

2.1.2. Carbohydrate type

In current clinical practice, total carbohydrate is used to calculate prandial insulin requirements; however carbohydrate type may also impact mealtime insulin needs or distribution.

Glycemic index (GI) ranks carbohydrate-containing foods based on their ability to raise blood glucose levels over 2 h in healthy subjects (Brand-Miller, Stockman, Atkinson, Petocz, & Denyer, 2009). High GI carbohydrates raise blood glucose levels rapidly, causing an early "spike" in blood glucose levels, followed by a rapid decline whereas low GI carbohydrates are digested and absorbed more slowly and therefore blood glucose levels rise and lower more gradually. The GI of individual foods has been found to strongly correlate with the incremental and actual glucose peak and the maximum amplitude of glucose excursion, providing a good summary of postprandial glycemia (Brand-Miller et al., 2009).

In individuals with type 1 diabetes using intensive insulin therapy, GI has been shown to have an impact on postprandial glycemic control (Bell et al., 2015). Mohammed and Wolever (2004) demonstrated that the GI of a food predicted the postprandial glycemic response of subjects using Lispro on intensive insulin therapy. Similarly, Parillo et al. (2011) demonstrated that the blood glucose area under the curve was 20% lower after a low GI meal than a high GI meal containing the same amount of carbohydrate ($p = 0.006$). Ryan et al. (2008) also found that the postprandial glucose excursion was significantly lower for a low GI meal compared with a high GI meal when preprandial short-acting insulin was administered for subjects on flexible multiple daily injections (MDI). From our clinical experience, carbohydrate is the predominant determinant of glycemia and therefore insulin requirements; however GI becomes increasingly important in large, high carbohydrate meals. The focus should remain on replacing high GI carbohydrates with low GI alternatives to improve diet quality and reduce the early glucose excursion.

Given the differences in the glucose response profile, the insulin dose may need to be adjusted for the carbohydrate type. There are