

HOW TO GET THE RIGHT MEAL TIME INSULIN DOSE WITH TYPE 1 DIABETES



CARBOHYDRATE ONLY

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ABBREVIATIONS

AA = Amino Acid
ADP = Adenosine Di Phosphate
ATP = Adenosine Tri Phosphate
AUC = Area Under the Curve
BCAA = Branches Chain Amino Acids
Ca = Calcium
CGM = Continuous Glucose Monitoring
FFA = Free Fatty Acid
FPU - Fat and Protein Units
GDH = Glutamate Dehydrogenase
GI = Glycaemic Index
GL = Glycaemic Load
GLP-1 = Glucagon-like peptide-1
GIP = Gastric Inhibitory Polypeptide
GPCR = G-Protein Coupled Receptor
I:G = Insulin to Glucagon ratio
ICR = Insulin to carbohydrate ratio
MDI = Multiple Daily Injections
MUFA = Monounsaturated Fatty Acids
KATP = ATP-regulated potassium channel
mTOR = mammalian target of rapamycin
SFA = Saturated Fatty Acid
TCA = Tri-Carboxyl-Acid cycle

WHAT DOES THE PANCREAS DO WHEN CARBOHYDRATE ONLY IS CONSUMED?

INSULIN

Put simply, the B-Cells secrete extra insulin into the portal vein to move the glucose from digested carbohydrate into the liver for storage as glycogen. Glucose not stored as liver glycogen enters the circulation, and insulin moves the glucose from the blood into body's cells for energy production and storage as glycogen. All the signals that control insulin secretion have been discussed previously, but the most important ones when carbohydrate only is consumed are:

- A. Intestinal Y cells release GLP-1 which is a strong positive regulator of B-Cell insulin secretion, accounting for up to 50% of insulin secretion (10).
- B. Increased glucose uptake by the B-Cells increases the energy state which causes insulin secretion.

GLUCAGON

Put simply, the A-Cells reduce secretion of Glucagon when carbohydrate only is consumed. The I:G increases ensuring the body moves into energy storage mode. All the signals that control glucagon secretion have been discussed previously, but the most important ones when carbohydrate only is consumed are:

- C. Intestinal release GLP-1 is correlated with the suppression of A-Cell Glucagon secretion(10). However, the suppression of Glucagon is mainly a secondary action of GLP-1 increasing insulin from the B-Cell. It is insulin that mainly inhibits Glucagon release (15).
- D. It is a common belief that the increasing glucose level from digested carbohydrate directly reduces A-Cell Glucagon secretion, by negative regulation. However, research using people with Type 1 Diabetes who consume a carbohydrate meal with no insulin does not support this (5). In this study the increase glucose levels to 10 - 20mmol/l (180 - 360mg/dl) actually increased Glucagon release (5).Just like with GLP-1, it is the increased insulin secretion from the B-Cell in response to the rising glucose that negatively regulates the A-Cell. Therefore, it is the secondary action of glucose increasing insulin via the B-Cell, not glucose directly(6, 16).

The above two points are essential to consider for a person with type 1 diabetes.

Why?

The automatic negative regulation of the A-Cell that is not provided by B-Cell secretion of insulin. They have to deliver insulin in the correct amount to not only move glucose and AA into cells, but also to elicit the inhibition of Glucagon secretion.

Consider this situation;

Not enough, or no insulin is delivered for a carbohydrate only meal, such as fruit or sweets. There is a double effect;

- Not enough insulin to move glucose from the blood into the cells, therefore the blood glucose level rises.
- Not enough insulin to negatively regulate A-Cells to stop glucagon production. Glucagon slightly increases, liver glycogenolysis increases, blood glucose increases further.

SUMMARY

Very simply, when carbohydrate alone is consumed at 50g, the I:G ratio increases putting the body into storage mode. This is regulated by an increase in GLP-1 and glucose stimulating insulin secretion, and the consequent direct negative regulation of Glucagon release. The job of the person with Type 1 Diabetes is to match the amount of insulin the B-Cells would release for carbohydrate only. Too little leading to hyperglycaemia, too much leading to hypoglycaemia.

From this point forward, I want you to consider the insulin response to 50g of carbohydrate alone as 100% over 5-6 hours. Also consider the Glucagon response as a reduction on 20% over 5-6 hours.

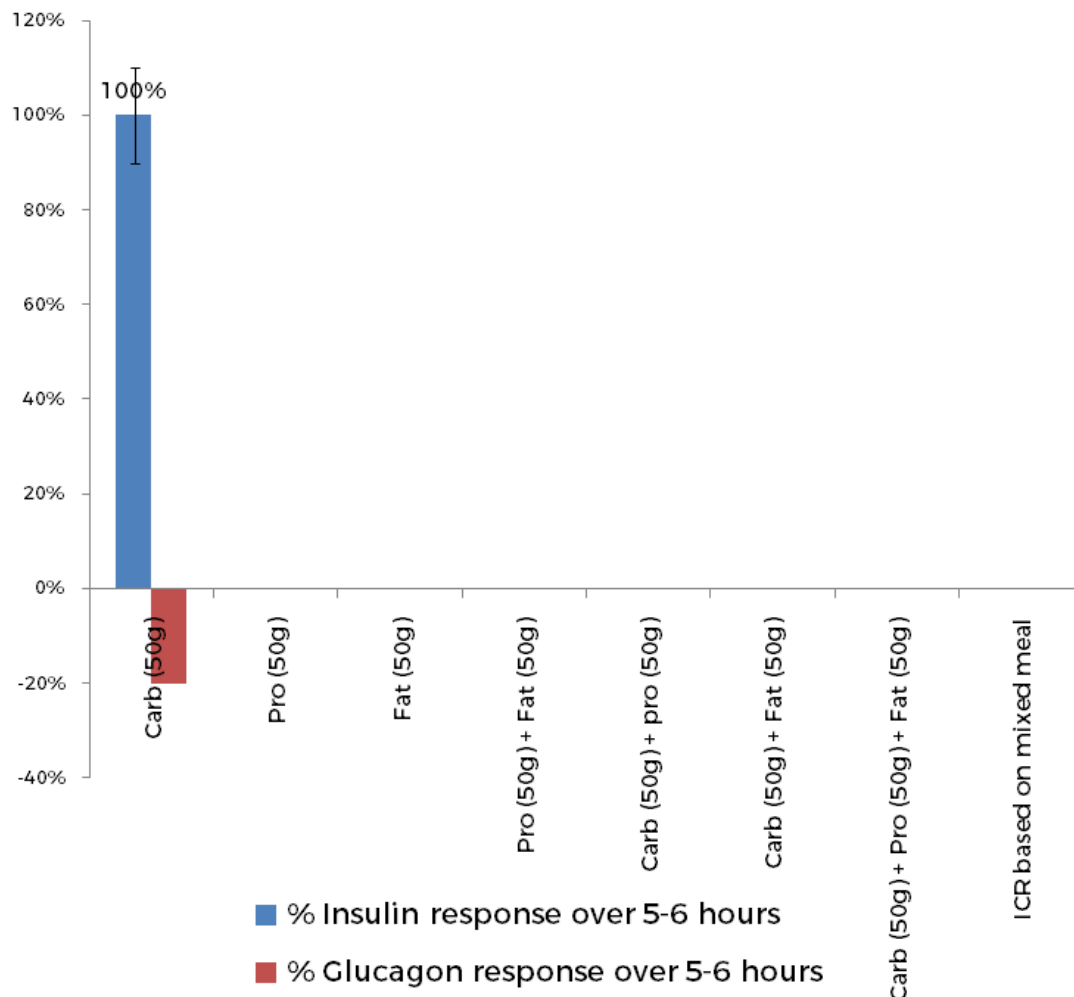
Why?

I want you to be able put the insulin and glucagon response for protein, fat, and their combinations with carbohydrate into context, relative to carbohydrate alone.

One important note is that not all carbohydrate elicits the same insulin response. Studies using people with Type 1 Diabetes investigated what happens if you deliver the same insulin dose for a low GI meal and high GI meal, whilst keeping the carbohydrate, fat and protein content exactly the same. They found the insulin dose worked perfectly for the high GI meal, but there was significantly more hypoglycaemia for the low GI meal over five hours (74,75).

The below graph will be built upon to model the insulin response required for the macronutrients singularly, and in combination. This will help put the insulin and glucagon response into perspective, and identify the challenge a person with type 1 diabetes has to match it. This graph is not a perfectly scaled, therefore it is not 100% factually correct, but it will prove valuable.

It uses a dose of 50g of the macronutrients to compare and contrast the insulin response over 5-6 hours. The 50g dose was chosen because most studies have used that amount as the standard measure, and this often reflects real life consumption. The time period of 5-6 hours was chosen because that is the post-meal monitoring duration of most studies. Once we have worked through all the macronutrients and their combinations, the graph will help determine which insulin dosing strategies will be most useful for certain diet or meal types.



The graph starts showing 50g of carbohydrate elicits a 100% insulin response over 5-6 hours, to serve as the reference. The graph also has error bars of 10% to show the effect of GI. If the 50g carbohydrate is high GI it may elicit a 110% response, if low GI only 90%. This highlights the first challenge of the person with type 1 diabetes when determining an insulin dose. The graph also shows Glucagon decreases by 20%.

To calculate the amount of insulin required for 50g carbohydrate, you would need to count every gram.

Insulin load = carbohydrate (g)

