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

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CARBOHYDRATE, PROTEIN AND FAT

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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, FAT AND PROTEIN ARE CONSUMED?

INSULIN

Put simply, the B-Cells secrete a lot more extra insulin for anabolism, glucose storage, and FFA storage. All mediated by the regulators discussed previously. The most important factors being the positive regulation by GLP-1, and the extremely high energy state of the B-Cell.

GLUCAGON

Put simply, the A-Cells secrete slightly more Glucagon to promote FAA oxidation and gluconeogenisis later on. All mediated by the regulators discussed previously. Positive regulation by GIP, and negative regulation by insulin.

If the person with type 1 diabetes does not deliver the extra insulin required there will be serious hyperglycaemia that is prolonged.

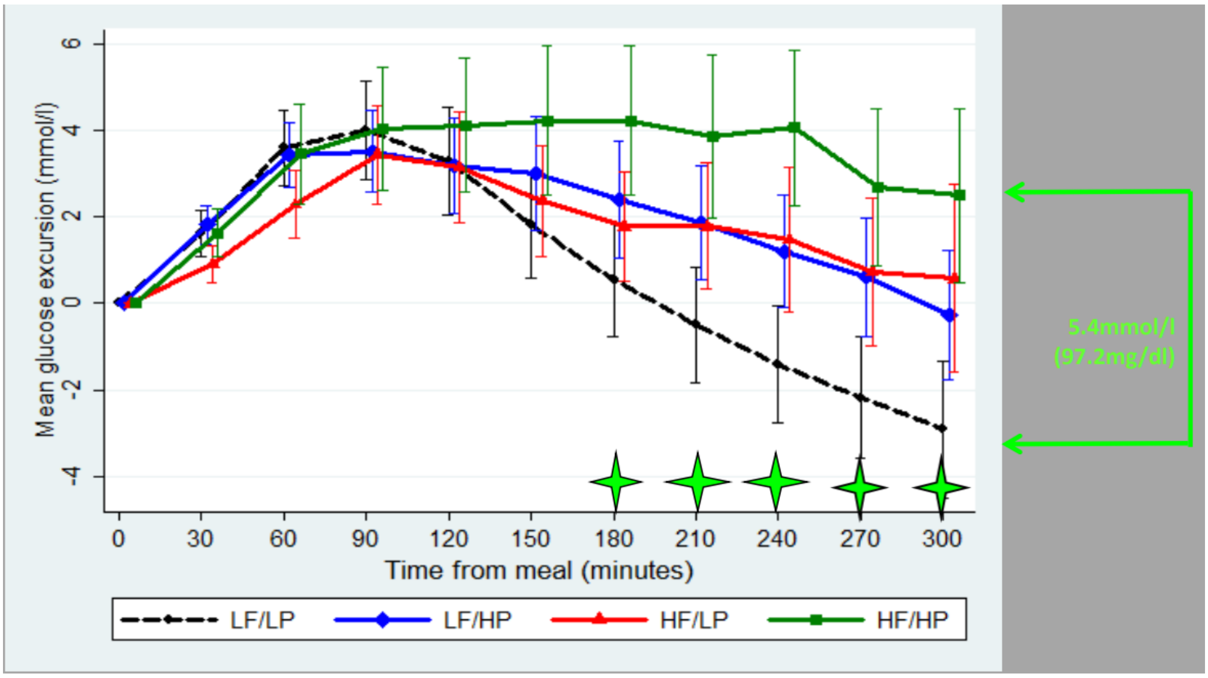
RESEARCH

We have already discussed the value of Smart and colleagues (28) meal study, which looked at the effect of adding protein and fat to carbs (28). However, this study did the tri-factor, it also studies when both fat and protein is added to carbs. Let's take a detailed look at this study.

This study first looked at what happens when you give the insulin dose suggested by the ICR for a moderate carbohydrate low fat low protein meal. Then using that same insulin dose, what happens to the glucose level when the other macronutrients are increased in a stepwise manner. I have put the macronutrient profile of all the different pancakes used in the study:

- Low Fat Low Protein (LF/LP) meal:
    - 30g carbohydrate, 4g fat, 5g protein, 176kcal
- Low Fat High Protein (LF/HP)
    - 30g carbohydrate, 4g fat, 40g protein, 316kcal
- High Fat Low Protein (HF/LP)
    - 30g carbohydrate, 35g fat, 5g protein, 446kcal
- High Fat/High Protein (HF/HP)
    - 30g carbohydrate, 35g fat, 40g protein, 595kcal

The graph below shows what happened to the thirty-three adolescents blood glucose profiles after consuming each of the four meals.



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WHAT HAVE YOU NOTICED?

This study really helps bring together what we have been building towards. **What does the ICR actually cover?**

If you use your ICR and give insulin according the carbohydrate in the meal, what happens when:

- That meal is LFLP: You will go hypo! In this study the glucose level was on average 2.9mmol/l (52mg/dl) lower after five hours compared to baseline. This speaks to the fact that when you work out your ICR it is based on your usual mixed meals, not just the carbohydrate content! You can see by 300 minutes both LFHP and HFLP are back to baseline level, -0.3mmol/l (-5mg/dl) and +0.6mmol/l (11mg/dl) respectively. This just goes to show your ICR accounts for the insulin response needed for a mixed meal, not just carbohydrate.

- After 180 minutes the HPLF meal glucose level is significantly higher than the LFLP meal, whereas the HFLP was not. This is just a reiteration of an earlier discussion, that the increase in insulin for protein needs to be delivered before the meal. This will stop the rise at 180minutes.

- After 210 minutes the HFLP becomes significantly higher than the LFLP, and stays higher up to 300 minutes. Therefore the increase in insulin for fat needs to be delivered later on, and delivered as a spilt injection or extended wave on a pump.

- When HPHF was consumed there was a cumulative effect of adding both protein and fat to LFLP. At 180minutes HFHP was 3.7mmol/l higher than LFLP, and by 300 minutes that increased to 5.4mmol/l higher. The differences at 180minutes and 300minutes were almost a perfect addition of the individual effect of LFHP and HFLP. Basically showing that both fat and protein need accounting for when insulin dosing, and they are cumulative.

Let's bring this closer to home. Bell and colleagues in 2016 (40) used a closed loop insulin dosing method to find out how much insulin was needed when comparing a pizza base (50g carbs, 4g fat, 9g protein, 273kcla) with a cheese pizza (50g carbs, 44g fat, 36g protein, 764kcal) over six hours. Nine men and one woman with Type 1 Diabetes undertook the pizza challenge.

How much extra insulin do you think was needed?

A whopping 65% extra insulin on average. Not only that, due to the high fat content, the insulin needed to be spread out, 30% upfront and 70% over 2.5 hours via an extended wave on a pump.

Did all ten type 1 pizza addicts need 65% extra?

One person only needed 24% extra, whilst one person needed a massive124% extra. This is not surprising when you consider the evidence we discussed earlier showing people with insulin resistance have exaggerated insulin requirements for high protein and fat (11, 57).

SUMMARY

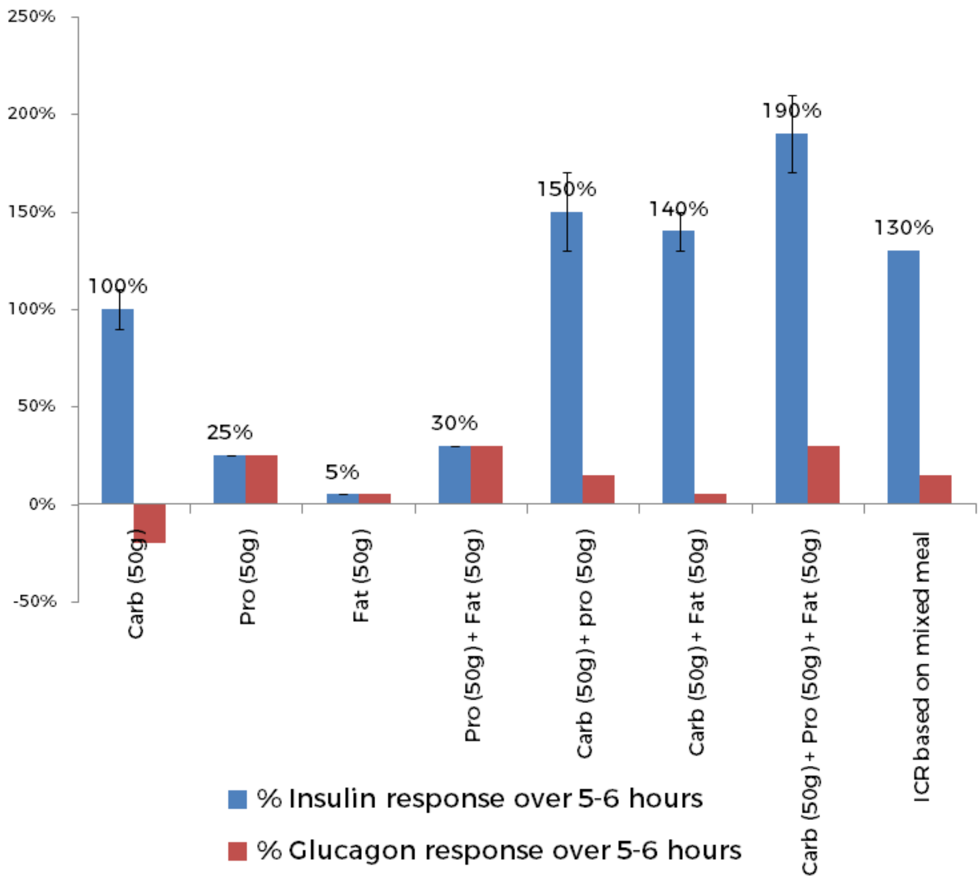
Very simply, when carbohydrate, fat and protein are consumed all at 50g, the extra Insulin required compared to carbohydrate alone is equal to adding the extra needed for both carbohydrate plus protein, and carbohydrate plus fat. The main factor is the synergy of glucose, AA, FFA in the B-Cell leading to a very high energy sate and insulin secretion. Glucagon only slightly increases, therefore the I:G is increased significantly. The increase in insulin is both immediate due to AA, and delayed due to FFA. This allows AA to be used for anabolism, glucose to be stored as glycogen, and FFA to be stored fat.

The job of the person with Type 1 Diabetes is to match the amount of insulin the pancreas would release for this tri-factor. The main risk is not enough insulin leading to early and persistent hyperglycaemia. The risk of hypoglycaemia is very low when a meal as large as this is consumed.

How much insulin to deliver for carbohydrate, protein and fat on a gram basis?

This research suggests when adding protein and fat to carbohydrate, the increase in insulin requirement is cumulative. Therefore following our graphical model, we need to add the extra 50% and 40% together, to get a 190% requirement in comparison to carbohydrate alone. We also need to add a 30% error bar to include the type of protein and fat. With a meal high in Leucine (Dairy) and SFA (Butter, cheese, cream) having a higher requirement.

For a



carbohydrate, protein, fat meals the best fit equation for insulin load is:

Insulin load = ((protein (g) x 0.5) + (fat (g)x 0.4))+ g carbohydrate)

The Type 1 Diabetes research discussed suggests the increase insulin requirement for protein and carbs is mostly in the first three hours, and the additional requirement for fat would be later (28). Therefore, a split dose or extended wave would be needed for a high carb, fat and protein meal.

WHY DO MOST PEOPLE WITH TYPE 1 DIABETES NOT DO THIS?

Most people with Type 1 diabetes who carb count only do not see this effect, Why:

- As discussed ICR accounts for 130% of the effect of glucose, therefore there will be no issue as long as the protein and fat content of the meals is moderate.

- Why 130% for the ICR?

- Smart and colleagues (28) showed the ICR worked perfectly for a 30g carbohydrate meal with high fat low protein (35g, 5g) and low fat high protein (5g, 40g). But the ICR gave too much insulin for the 30g carb low fat low protein (5g,5g) meal. Finally the ICR did not give enough insulin for the 30g carb high fat high protein (35g, 40g) meal. It would therefore seem sensible that ICR accounts for about 130% of the effect on carbohydrate alone. This is obviously an approximation but helps put the insulin dosing strategies into context.

However, when they venture outside the normal fat and protein in meals they have an issue:

- Very high glucose levels after Pizza, Cheesy pasta, large meals with fancy desserts, BBQ.

- Hypoglycaemia when carbohydrate only meals are consumed and matched with insulin using the ICR. Meals such as fruit only.

If the person with type 1 diabetes wanted to use this very labour intensive approach of counting all macronutrient grams, they would have to consider a few things.

- First: Count every gram of carb, fat and protein, and apply the below formula to get the insulin load. But they must remember to relax their carb ratio by about 60%. For example, a 1u:10g would change to a 1u:16g. Also you would probable want to change the term to a meal ratio rather than carb ratio.

    - Insulin load = ((protein (g) x 0.5) + (fat (g) x 0.4))+ g carbohydrate

- Second, when the fat amount gets high (>40g) to split the insulin 50/50 by a second injection in an hour's time on MDI, or an extended wave for 2.5 hours if pump.

Now we have a good understanding of what the pancreas would do, let's see if the currently available insulin dosing strategies are fit for purpose.

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