Fat and protein counting in type 1 diabetes

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Abstract
The prevalence of obesity in type 1 diabetes is increasing and may be exacerbated by the use of an intensive insulin therapy regimen which improves glycaemia but is associated with weight increase. There are a plethora of diets and weight loss programmes to choose from, but balancing the insulin doses to achieve good glycaemic control is challenging. Mealtime insulin doses are traditionally calculated to match the amount of carbohydrate in the meal but evidence, particularly from continuous glucose monitoring, suggests that protein and fat can also have an effect on postprandial glycaemia.

This article looks at the effect of fat and protein on the glycaemic response of a meal, alternative algorithms to calculate the bolus doses, their timing and delivery, and considers their effectiveness in supporting weight loss in overweight or obese individuals with type 1 diabetes. Copyright © 2016 John Wiley & Sons.


Key words
type 1 diabetes; obesity; fat and protein; intensive insulin therapy

Introduction
There are 3.5 million people diagnosed with diabetes in the UK: 6.25% of the adult population. Ten percent of these have type 1 diabetes. In other words, there are over 300 000 adults and approximately 44 000 children under 19 years diagnosed with type 1 diabetes in the UK.1 The majority of these people are treated with intensive insulin therapy (IIT), either a multiple daily injection (MDI) regimen or continuous subcutaneous insulin infusion (CSII) therapy. Both therapies require the patient to use variable insulin dosing, usually calculated to match the carbohydrate component of the meal.

The DCCT/EDIC study showed that this approach improved overall glycaemic control compared to conventional insulin therapy in patients with type 1 diabetes and reduced the risk of non-fatal myocardial infarction, stroke or cardiovascular death by 57%.2 However, the IIT group also gained an average of 4.6kg more than the conventionally treated group with the average BMI increasing from 24 to 31 in those gaining the most weight.3 In contrast, there was no significant difference in weight gain in a seven-year follow up in the DAFNE study (2.4±6.0kg vs 2.8±6.6kg).4 This may be due to differences in glycaemic management. DAFNE teaches self-management skills in dose adjustment whereas the DCCT was more algorithm-led by the health care professional.

Obesity and type 1 diabetes
Type 1 diabetes is not normally associated with obesity yet, over recent years, like the rest of the population, it has increased. A cohort of patients diagnosed with type 1 diabetes in childhood in the Pittsburgh Epidemiology of Diabetes Complications Study, found that the prevalence of obesity had increased 7-fold from 3.4% to 22.7% and overweight had increased from 28.6% to 47% over 18 years.5 In England and Wales, 59.5% and 63.8% respectively of patients with type 1 diabetes are overweight or obese although these figures are gradually decreasing.6

Genetic and lifestyle factors, which lead to the development of type 2 diabetes in the general population, may also exist in patients with type 1 diabetes. Those who have a family history of type 2 diabetes tend to be more prone to being overweight and insulin resistant, leading to the concept of ‘double diabetes’. In addition, a family history of type 2 diabetes is associated with an increased risk of cardiovascular disease and albuminuria in people with type 1 diabetes. In the DCCT/EDIC study a high estimated glucose disposal rate (eGDR), a surrogate marker of insulin sensitivity, was associated with a lower risk of retinopathy and nephropathy.3 The DCCT/EDIC study also found that those gaining the most weight developed higher blood pressure, LDL, triglycerides and lower HDL which
would increase the risk of cardiovascular disease.

### Weight reduction

People with type 1 diabetes should follow the nutritional guidelines for the general population including maintenance of a healthy body weight with weight reduction counselling recommended for those who are overweight. In addition, they should receive education on carbohydrate counting and meal composition.7–9 While it is the total carbohydrate which has the greatest effect on glycaemic control, total energy intake is the main predictor of weight. There are many weight loss programmes available, some advocating low fat, others high protein, high fat, low carbohydrate or low glycaemic index. Dyson reviewed the most popular diets and concluded that no one diet is more effective than another in the long term.10 However, the different macronutrient composition of these diets will have different effects on blood glucose control which may require adjustments to insulin dosing to achieve glycaemic targets.

### Glycaemic control

For the majority of patients with type 1 diabetes, the target HbA1c is 48mmol/mol or less. This significantly reduces the risks of developing diabetes complications.11 Research and the use of continuous glucose monitoring (CGM) have demonstrated that other dietary components such as fat and protein as well as the glycaemic index/load of a meal can significantly affect postprandial glycaemia.12 Therefore alterations to current insulin dosing algorithms which only take carbohydrate into consideration may be needed to support those choosing weight loss diets with various macronutrient compositions.

### Carbohydrate counting and insulin dose adjustment

The majority of people with type 1 diabetes should be treated using an MDI insulin regimen or CSII,13 and be taught about carbohydrate counting and dose adjustment of insulin which allows flexibility in meal composition and timing and enables adjustments to be made to the insulin dose to take into account factors such as the pre-meal blood glucose and exercise or physical activity.8 Monitoring carbohydrate intake is a key strategy in achieving good glycaemic control8 but even when carbohydrate is carefully counted and the appropriate amount of insulin is given, achieving optimal glucose levels is challenging.14 The calculation of insulin doses may need to take fat and protein into consideration.

### Effect of protein on postprandial glucose in type 1 diabetes

Peters and Davidson found that the addition of approximately 50g of protein to a meal containing approximately 50g of carbohydrate increased the glucose response more than the addition of 24g of fat, mainly as a result of the late (150–300 mins) glycaemic response.15 Borie-Swinburne et al. found no difference following the addition of 21.5g of protein to a standard meal which also contained carbohydrate and 37g fat.16 Smart et al. found that 35g of protein added to a meal containing 30g of carbohydrate increased the blood glucose by an additional 2.6mmol/L after 5 hours.17 In the absence of carbohydrate, a small to moderate portion of protein (12.5–50g) did not increase the blood glucose whereas the addition of a large portion (75–100g) caused an increase in plasma glucose similar to that produced by 20g of carbohydrate.18 A systematic review concluded that:

- Protein does have an effect on postprandial glycaemia.
- This effect is delayed by approximately 1.5 hours.
- A smaller amount of protein will affect blood glucose when consumed with at least 30g of carbohydrate but, without carbohydrate, at least 75g is needed to produce an effect.12

Further support for the delaying effect of protein on glycaemia comes from a study in type 2 diabetes where the postprandial response was significantly reduced when the protein component of a meal (55g of protein) was consumed 15 minutes before the carbohydrate component (68g) compared to when protein was consumed after the carbohydrate.19

### Effect of the amount of fat on postprandial glucose in type 1

High fat meals such as pizza or fried chicken cause prolonged hyperglycaemia.20 Lodefalk et al. demonstrated that a high fat meal (38g fat) caused a delay in glycaemia over the first 2 hours and that this was associated with delayed gastric emptying, compared to a low fat (2g) meal.21 Peters and Davidson found a meal with a higher fat content (36g vs 13g) had a lower glucose response in the first 3 hours post-meal than the standard meal.13 One study using a closed-loop insulin delivery system found that a high fat meal (60g fat) required more insulin and increased the blood glucose more than a lower fat meal (10g fat) despite a similar protein (41g) and carbohydrate (96g) content.22 The insulin requirement to maintain glycaemia varied markedly between individuals from -17% to 108%. Smart et al. found that 35g fat added to 30g carbohydrate increased the postprandial glucose by 2.3mmol after 5 hours and the effect was additive when added to protein and carbohydrate, causing a rise of 5.4mmol after 5 hours.17 A systematic review concluded that:

- Fat reduces the postprandial glucose response 2–3 hours after eating and delays the peak glucose response due to delayed gastric emptying.
- Fat causes delayed hyperglycaemia 3–5 hours after eating.
- Additional insulin may be required for high fat meals which can increase blood glucose.
- There are marked interindividual differences in the effect of fat on postprandial blood glucose.
- Further research is needed to identify the amount of fat which affects glycaemia and whether the type of fat makes a difference.12

### Effect of the type of fat on postprandial glucose

One randomised controlled trial in patients on CSII found that monounsaturated fat (extra virgin olive oil) reduced the early postprandial glucose response produced by a meal containing high glycaemic index carbohydrate by 50% compared to saturated fat. No differences were seen with a low glycaemic index carbohydrate meal.23
Fat and protein counting in type 1 diabetes

Insulin:carbohydrate ratio (ICR) 1:10g
Insulin sensitivity factor (ISF) 1:2mmol/L

<table>
<thead>
<tr>
<th>Meal carbohydrate</th>
<th>60g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin = 60÷ICR = 60÷10</td>
<td>6 units</td>
</tr>
<tr>
<td>Target glucose</td>
<td>6mmol/L</td>
</tr>
<tr>
<td>Pre-meal blood glucose</td>
<td>12mmol/L</td>
</tr>
<tr>
<td>Insulin = 12 minus 6mmol = 6</td>
<td>3 units</td>
</tr>
<tr>
<td>6÷ISF = 6÷2</td>
<td></td>
</tr>
<tr>
<td>Total dose = meal + correction</td>
<td>6+3=9 units</td>
</tr>
</tbody>
</table>

Box 1. Example of calculation using the insulin:carbohydrate ratio and insulin sensitivity factor

| Insulin:carbohydrate ratio (ICR) | 1:10g |
| Meal carbohydrate | 77g |
| Insulin = 77÷ICR = 77÷10 | 7.7 units |
| Calories from fat and protein (672 minus 288kcal) | 384kcal |
| 1 fat/protein unit (FPU) | 100kcal |
| Total FPU | 4 |
| Additional units of insulin | 4 units |
| Additional units are given as an extended bolus over 3–6 hours |

Box 2. Calculation of insulin bolus using the Warsaw formula for a small pizza (672kcal)

Effect of insulin bolus calculations for fat and protein

Insulin doses are usually calculated by dividing the amount of carbohydrate in the meal or snack by the patient’s insulin to carbohydrate ratio (ICR). This is added to any correction dose needed to bring the pre-meal glucose into the target range. This is calculated using the insulin sensitivity factor. An example is given in Box 1.

Studies and patients’ own experiences have shown that some meals which are higher in fat and/or protein may require additional insulin, above that which is needed for the carbohydrate component. This has led to new algorithms being developed:

• The Warsaw Pump Therapy School (WPTS) or ‘Warsaw’ formula.
• Food Insulin Index (FII).

The Warsaw formula uses the usual ICR to calculate the insulin dose for carbohydrate which is given as a normal dose before the meal. Additional insulin is calculated using a fat/protein unit (FPU) where 1 unit of insulin is given for every 100kcal in the meal from fat and protein. The additional insulin is given as an extended bolus over 3–6 hours, depending on the number of FPUs, using CSII. Following a high fat, high carbohydrate meal, postprandial hyperglycaemia was reduced using this algorithm but there was more hypoglycaemia in the early postprandial period. This was attributed to sub-optimal basal insulin. An example is given in Box 2. Another study used 50% of the usual ICR to calculate the insulin for protein and fat, with the additional insulin given over an extended period.

The FII consists of a database of around 220 food items based on the glycaemic response to 1000kJ (239kcal) portions of food in non-diabetic individuals. The insulin dose calculated for a meal using this method was twice the amount calculated for carbohydrate alone and resulted in a lower rise in blood glucose after 2 hours without a significant increase in hypoglycaemia. Use of this method is limited by the size of the database and the specificity of the foods tested.

Further trials are required to assess how practical this is in the real-world situation.

Discussion

The main factor limiting good glycaemic control is hypoglycaemia. Patients often cite this as a barrier to achieving weight loss. There are numerous diets recommended for weight loss, the majority of which are not supported by published evidence. Of those that have been published, no one diet has a better outcome in the long term. Patients may choose a programme which includes more protein or fat than their usual diet and this can affect blood glucose control. Meals which are high in protein and/or fat can have an effect on postprandial glycaemia. However, there are no definitions of ‘high fat’ and ‘high protein’, with studies using varying amounts making it difficult to draw clear comparisons. Meals containing more than 20g of fat could be considered high fat but, with such variable responses between individuals, any increase in insulin dose needs to be personalised. The amount of protein needed to cause an effect on postprandial glycaemia is affected by whether or not it is consumed with carbohydrate. Much larger portions are needed, equivalent to a 250g steak or 10 eggs, if consumed alone whereas 30g of protein, equivalent to 100g of meat or fish, increase blood glucose when eaten with at least 30g of carbohydrate, for example two slices of bread. This may be important for those people who choose to follow a high protein/low carbohydrate diet for weight loss, but may also be helpful in preventing nocturnal hypoglycaemia.

High fat meals require more insulin than low fat meals with similar carbohydrate and protein content. They cause late postprandial glycaemia but may cause early hypoglycaemia. Substituting foods with lower fat alternatives would therefore require less insulin, reduce the need to ‘eat to prevent a hypo’ in the early postprandial period, and reduce the need for additional insulin to correct a high glucose in the late postprandial period. These are all factors which would support weight loss.
Timing of bolus dose
Elevated postprandial glucose increases the risk of cardiovascular disease, atherosclerosis and mortality.\textsuperscript{25} Giving the bolus dose of insulin 15–20 minutes before eating improves postprandial glycaemia. Patients on CSII may benefit from using dual waves; the percentage split and the duration of the bolus will depend on the macronutrient composition of the meal as well as the glycaemic index. If high fat or high protein meals are consumed and extra insulin is required, caution is needed to minimise the risk of early hypoglycaemia. For patients on MDI therapy an additional bolus could be given 1 hour after the meal to match the delayed absorption of the food.\textsuperscript{12} Equally, encouraging patients to consume lower fat, lower protein meals could improve postprandial glycaemia and, if these meals are also lower in calories, help promote weight loss.

Dietary intervention
All patients with type 1 diabetes, including those who wish to lose weight, should be reviewed by a registered dietitian who has the skills to work with them to develop an individualised eating plan which emphasises a variety of nutrient-dense food choices in appropriate portion sizes to support their overall weight and health goals.\textsuperscript{8} Additional guidance is needed to achieve these goals while avoiding hyperglycaemia and hypoglycaemia. This can be achieved by regular review of food and glucose records. An outline of nutritional interventions to improve postprandial glycaemia is given in Figure 1.

Conclusion
Matching insulin doses to carbohydrate consumed is challenging and, despite accurate estimation of the carbohydrate content of meals and snacks, the calculations do not always work. This paper has discussed the additional effect on blood glucose of meals containing large amounts of fat and/or protein and has included suggestions for insulin adjustment to reduce postprandial hyperglycaemia. But to date, the optimal insulin dosing adjustments are unknown and there are no validated alternative insulin dosing algorithms which are easy to use. Reviewing patients’
Approximately 60% of people with type 1 diabetes are overweight or obese. Mealtime insulin doses have traditionally been calculated according to the carbohydrate component of the meal, but the use of continuous glucose monitoring has shown that other macronutrients such as fat and protein, as well as the glycaemic index of the meal, affect postprandial glucose levels. Alterations to current insulin dosing algorithms may be needed to support those choosing weight loss diets with various macronutrient compositions. Diet and lifestyle need to be addressed in those gaining excess weight in addition to insulin bolus adjustments.

To treat obesity, multicomponent interventions are recommended which include behaviour change strategies to address eating behaviour, the quality of the diet, energy intake and physical activity. In clinical practice, rather than focusing exclusively on fine tuning insulin doses, it may be preferable to address meal choices and meal-time routines to achieve better blood glucose control and lose weight. Reviewing patients’ food records, blood glucose diaries and/or CGM may indicate if adjustments in the calculation or timing of bolus insulin doses could be beneficial.

There are no conflicts of interest declared.

Key points
- Approximately 60% of people with type 1 diabetes are overweight or obese.
- Mealtime insulin doses have traditionally been calculated according to the carbohydrate component of the meal, but the use of continuous glucose monitoring has shown that other macronutrients such as fat and protein, as well as the glycaemic index of the meal, affect postprandial glucose levels.
- Alterations to current insulin dosing algorithms may be needed to support those choosing weight loss diets with various macronutrient compositions.
- Diet and lifestyle need to be addressed in those gaining excess weight in addition to insulin bolus adjustments.

References