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# Type 2 diabetes – which BGLs matter?

## The fasting, pre- and post-prandial glycaemia debate

**Background**
There is vigorous debate about the relative importance of targeting fasting blood glucose levels (BGLs) and postprandial BGLs.

**Objective**
This article assesses the contribution of pre- and post-prandial BGLs to overall glycaemia and provides a practical strategy for improving overall glycaemia in patients on insulin.

**Discussion**
In most patients who need to commence insulin therapy, the A1c is 8.0% or more. At these levels, fasting and other premeal BGLs contribute more to the A1c than does postprandial BGL. The higher the A1c, the more important the fasting and premeal BGLs. The 'keep insulin safe and simple' (KISS) approach is useful when starting insulin in type 2 diabetes.

**The Diabetes Control and Complications Trial for type 1 diabetes,[1] and the United Kingdom Prospective Diabetes Study for type 2 diabetes[2] clearly showed that reducing overall glycaemia, as reflected by the haemoglobinA1c (A1c), slows the development and/or progression of diabetic microvascular complications. However, there is vigorous debate about the relative importance of targeting fasting and postprandial blood glucose.**

### Glycaemia 24/7

The components of the 24 hour blood glucose profile can be divided into two major components:

- 'basal' glycaemia, including the 24 hour contribution from fasting blood glucose[1] as well as any day time incremental rise in the 'basal' blood glucose before the evening meal[2], and
- 'postprandial' glycaemia where the contribution depends on the peak of the increment and the duration of the increase above the basal preprandial blood glucose.[3]

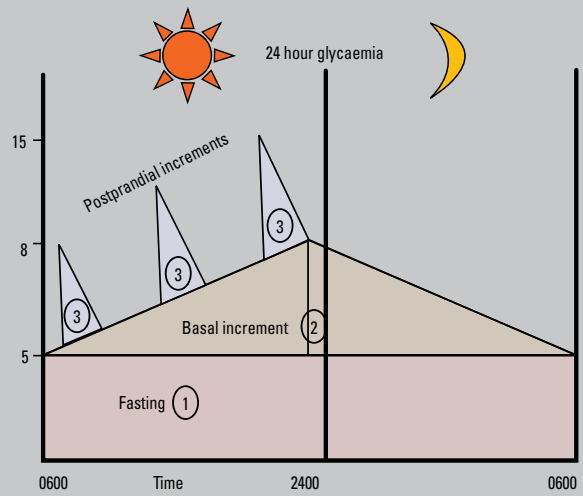
Simplifying the 24 hour blood glucose profile and assuming the postprandial profile is triangular in shape allows assessment of the relative contributions of the basal and postprandial components to overglycaemia (*Figure 1*).

The case for targeting postprandial blood glucose is that:

- glycaemic exposure in absolute terms is highest after meals so hypoglycaemic therapy should focus on controlling these glycaemic surges. This case is reinforced by clinical experience of postprandial values in the teens and 20s
- we have good interventions to tackle postprandial glucose levels; we understand how to reduce glycaemic load and/or add medications that slow carbohydrate digestion (acarbose), promote short lived pancreatic insulin release (glitinides) and/or add exogenous rapid or very rapid acting insulin analogues.

While it is claimed that postprandial glucose is a better predictor of cardiovascular disease than fasting glycaemia, at this time there is no hard endpoint data to support the concept that improving blood glucose levels (BGLs) postprandially will reduce glycaemic burden

Figure 1. 24 hour blood glucose profile




Fasting glycaemia contributes to 24 hour glycaemia (1)
A day time increment in basal glycaemia may occur (2)
Postprandial increments add to basal glycaemia (3)

24 hour glycaemia is expressed as the total glycaemic exposure (BGL [mmol/L x hours]) and is the total area under the curve

1. Fasting glycaemia: assuming fasting glycaemia is constant over 24 hours: contribution to glycaemic exposure = 24 x FBG
2. Basal day time increment: the triangle (2) above fasting BGL: contribution to glycaemic exposure = 1/2 x 24 x (peak basal – fasting BGL)
3. Postprandial increment = meal time increment above basal (assuming the same increment and duration after each meal): contribution to glycaemic exposure = 3 x (1/2 increment x duration of increment)

compared with lowering fasting BGLs.

The case for targeting fasting glycaemia is that:

- although less conspicuous, the contribution to overall glycaemia of fasting glucose is significant
- the fasting blood glucose sets the trend for BGLs across the day, and that higher fasting or 'base line' BGLs will lead to elevated BGLs across the day, and
- relatively simple interventions (eg. once daily basal insulin), exist to treat fasting hyperglycaemia.

The gold standard measure of overall glycaemia is the A1c. The higher the A1c, the more important is the contribution to the A1c level of fasting and premeal rather than postprandial hyperglycaemia. This is demonstrated in the scenarios in *Figure 2*.

In scenario A the fasting blood glucose is normal (4 mmol/L), but even when there is no day time basal glucose increase and the postprandial increase is large (8 mmol/L), preprandial glycaemia is the major contributor to overall glycaemic exposure (67–80%). If there is a day time basal increment and/or if the fasting glucose is higher (scenario B, C and D) the contribution of preprandial glycaemia is even larger (75–91%).

Several things are clear:

- the contribution from fasting glycaemia to total 24 hour glycaemia is the largest
- further increments in day time basal glycaemia are potentially significant contributors
- postprandial contributions, even when there is a large increment above basal (8 mmol/L) are only the predominant abnormality if both fasting and day time basal increments in blood glucose are near normal.

Therefore in these schematic scenarios, which are very common clinically in terms of the BGL profile across the day, the basal glucose and related insulin requirements are most important in achieving glycaemia targets. While targeting the postprandial BGLs will further help in achieving A1c targets, targeting postprandial BGLs is a secondary aim. The main aim is to address the basal BGL and insulin requirements based on this.

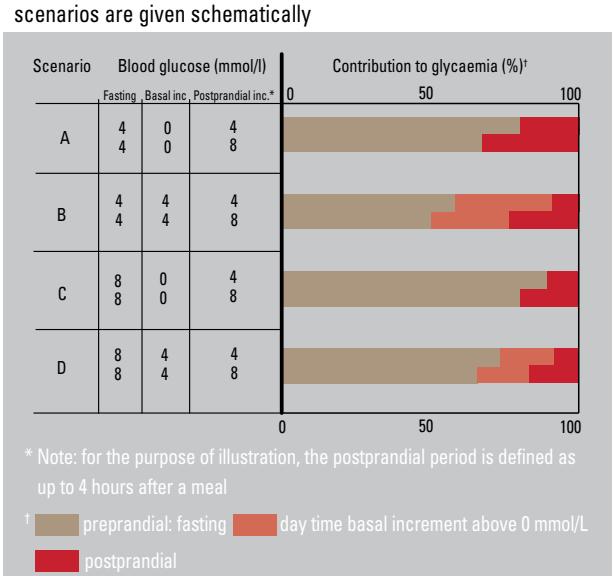
## Keeping insulin safe and simple (KISS)

In most patients who need to commence insulin therapy, the A1c is 8.0% or more and at these levels, the fasting and other premeal BGLs contribute more to the A1c than does the postprandial BGL. The following jingle provides an *aide memoir* for the insulin KISS for type 2 diabetes[3] (*Figure 3*):

First fix the fasting...
Then tackle tea...
Find the hidden hypers...
And check the A1c.

Management is based on continuing most or all previous oral hypoglycaemic therapy and adding bed time basal insulin[4] to control the fasting glucose. Both isophane insulins and insulin glargine work well in this setting. An alternative is to add a fixed

Figure 2. Relative contributions in absolute terms of pre- and post-prandial blood glucose to blood glucose after a meal. Typical clinical scenarios are given schematically




* Note: for the purpose of illustration, the postprandial period is defined as up to 4 hours after a meal

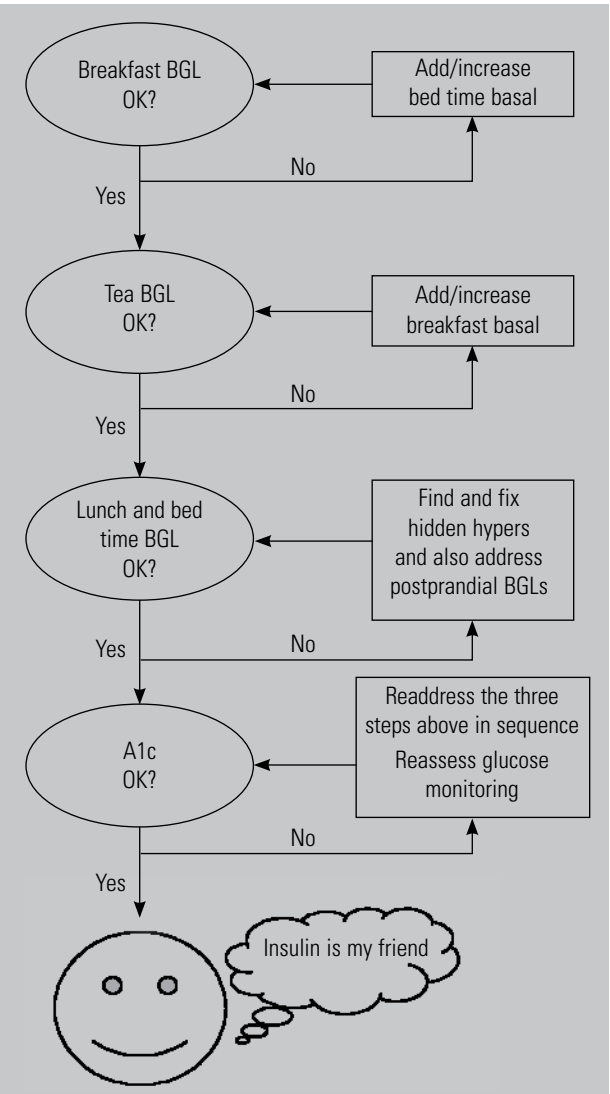
† preprandial: fasting day time basal increment above 0 mmol/L
postprandial

dose premixed insulin with the evening meal (eg. Humalog Mix 25 or Novomix30), but in this case also the emphasis needs to be first and foremost on titrating the insulin dose to get the fasting BGLs safely to its target.

Once the fasting BGLs have been managed, the next step is to check for any increase in basal glycaemia during the day (before the evening meal) and, if necessary, control this increase with a second dose of basal insulin at breakfast. Again, this may be isophane insulin alone or a fixed dose premixed insulin of rapid and longer acting insulin, with the emphasis on correcting the premeal BGLs.

Generally, once these two premeal basal glucose values are controlled, overall glycaemia is close to or near target. Occasionally, high blood glucose values ('hypers') can 'hide' in the middle of the day or late evening. Checking before lunch and before bed as well as 2 hours after main meals will identify these and suggest additional nutrition therapies and/or short acting insulin or hypoglycaemic medication (acarbose). If there are major increments in postmeal BGLs, these may be more significant, especially when one large meal dominates the day for the patient. In these cases, lowering the glycaemic load, acarbose and rapid acting insulin, especially the rapid acting analogues, may be utilised.

Figure 3. The insulin KISS




## Checking overall glycaemia – the A1c

If the basal BGLs and insulin doses have been adequately addressed as have the 'hidden hypers' and yet the A1c is not to target, then further emphasis should be given to the postprandial BGLs to 'fine tune' glycaemia.

## Summary of important points

- First address the fasting glucose as this is usually the largest contributor to overall glycaemia and the A1c. This is usually best achieved by a bed time basal insulin dose ('fix the fasting').
- Then address any increment in preprandial glycaemia especially the pre-evening meal as this can be a large contributor to overall glycaemia ('tackle the tea').
- Even if fasting and evening basal glucose are under control, check for elevated pre- or post-prandial values during the day, late evening or overnight ('find the hidden hypers').
- Make sure that the available blood glucose records are giving a complete picture of overall glycaemic control ('check the A1c').

Conflict of interest: none declared.

### References

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