g Hyperglycaemia

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came from?ó Very frequently I am asked this or a similar question by patients who are frustrated that their blood glucose is high in the morning having gone to bed with a satisfactory reading.

To better understand the causes of fasting hyperglycaemia and to provide a simple explanation to our patients, examine figures 1 and 2.

The centre panel represents glucose in the circulation often called blood glucose. Glucose enters this blood pool either from the gastrointestinal tract or from the liver. The liver is the major source of glucose in the fasting state and a significant contributor between meals, or following a meal with low carbohydrate content. See figure 1.

Glucose is removed from the circulation by what can be considered two separate pathways: one activated by insulin, the other not requiring insulin. The brain and some other tissues do not need insulin to use glucose. Adipose tissue and muscle have increased glucose uptake in the presence of insulin. See figure 2.

Normally there is a tight balance between the amount of glucose entering the circulation and that leaving. The concentration of glucose in the circulation is tightly controlled. Insulin is a major factor in achieving this balance or control. Several hours after a meal, blood glucose is maintained by the gradual release of glucose from the liver. This provides a supply of glucose for the relatively constant needs of the insulin independent tissues such as the brain. In patients with diabetes when there is not enough insulin or insulin does not work well enough (insulin resistance) to control the amount of glucose made in the liver, the inhibitory effect of insulin on glucose release by the liver is lost. Thus, in some patients with diabetes, the liver produces an excess of glucose overnight. The excess release is not matched by increased uptake into the insulin sensitive tissues, as there is not enough insulin present. The net result is a fasting glucose that is higher than the pre-bedtime reading. There are individual variations in these responses possibly reflecting diversity in the (as yet undiscovered) causes of type 2 diabetes. The mismatch, with increased liver production and no increase in peripheral uptake, results in hyperglycaemia even in the absence of food. The blood glucose levels may fall during the day as physical activity increases. Physical activity can increase peripheral utilization particularly in muscle. Hence, the increase in physical activity resulting in increased peripheral utilization better matches the increased liver production.

The type of fasting hyperglycaemia reported in the introduction can be difficult to treat. A walk after dinner before bed may help or surprisingly, in some people, a snack before bed helps. Many patients note that alcohol with the evening meal reduces the fasting glucose. This is due to the inhibitory effect of alcohol on glucose production by the liver. As with all the beneficial effects of alcohol it is potentially dangerous to encourage alcohol use different from the usual practices of the person involved. If fasting hyperglycaemia persists, medication is required. My step-wise approach is an initial trail of Metformin with the evening meal. If that fails to normalize the fasting glucose, as often happens, I next trial glibenclamide initially 2.5mg or even 1.25mg with the evening meal, or before bed in selected patients. Once the safety of this approach has been confirmed by the absence of hyperglycaemia, the dose of glibenclamide can be titrated as required to normalise the fasting glucose. If this fails I introduce nocturnal long-acting insulin.

Figure 1

In the fasting state, blood glucose which is required for normal brain function, is maintained by the controlled release of glucose from the liver.

Figure 2

Following a meal insulin is released. Insulin inhibits liver glucose production and stimulates glucose uptake into fat and/or muscle. Absorbed glucose from the gut is utilized as required or it is stored.

Figure Legends

- means inhibits + means stimulates