Glycaemic effect of colestyramine therapy

A 77-year-old woman with type 2 diabetes of 15 years' duration was referred to a secondary care diabetes clinic due to a rapid deterioration in her glycaemic control.

The patient had been diagnosed with idiopathic bile acid malabsorbtion four months previously as part of investigations for chronic anaemia. She was therefore prescribed colestyramine 4g twice daily. Initially, her pharmacist dispensed Questran, and the patient's glycaemic control was noted to deteriorate, with her HbA1c rising to 8.7% (72mmol/mol) from a stable pre-treatment value of around 7.2% (55mmol/mol); (Figure 1). Her home blood glucose monitoring (HBGM) diary concurred with this finding. She was advised to change to sugar free Questran Light instead. Six weeks prior to her first diabetes clinic appointment, Questran Light was sourced, and this had been dispensed from that time. When she was reviewed in clinic, six weeks after the change in formulation her HbA1c was 5.5% (37mmol/mol), and her blood glucose had reverted to well controlled levels.

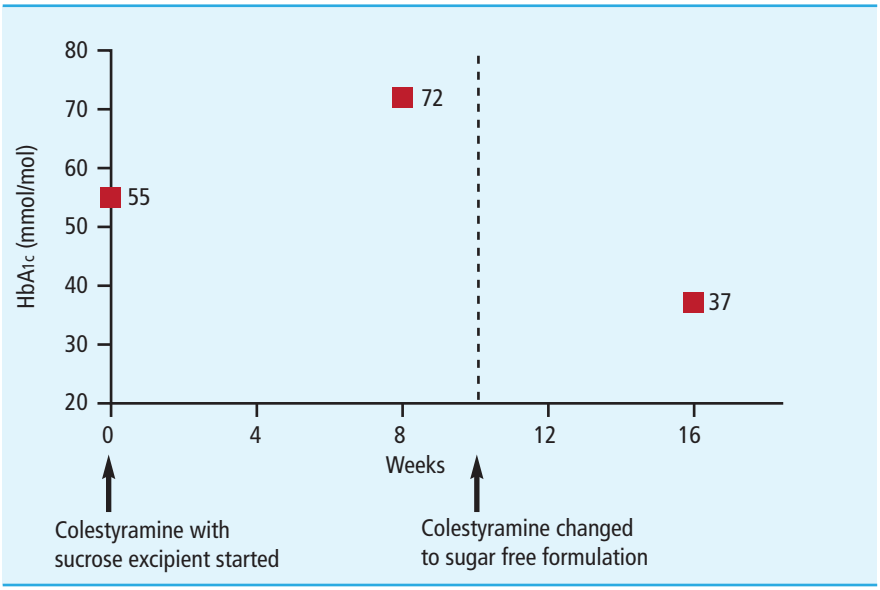

Figure 1. The effect of a colestyramine preparation containing sucrose on HbA1c measurements, as well as the reduction in HbA1c observed after the change to a 'sugar free' formulation

Discussion

Questran contains 4g anhydrous colestyramine as its active ingredient. The SPC (section 4.4) states that 'Questran contains 3.79g sucrose' and the PIL contains a warning to 'take special care if you are diabetic as Questran contains sucrose'. Our patient was therefore ingesting the equivalent of two teaspoons of sugar per day in this medication, with an immediate and notable effect on her HBGM results.

It is recognised that anaemia can affect HbA1c results;[1] however, her HBGM diary also reflected the hyperglycaemia associated with Questran therapy, and its resolution with Questran Light. The patient confirmed that she was following medical advice about avoiding coadministration of colestyramine with her other oral medications. Due to its effects on bile acid reabsorption, colestyramine can have an interaction with drugs that are metabolised via the enterohepatic circulation; however, this patient's diabetes medication prescription remained unchanged throughout this period, so the effects on her glycaemic control are not attributable to this. Nor can they be attributed to the effects of bile acid sequestrants on glycaemic control as there is a body of evidence describing *improved* glycaemic control associated with these medicines.[2] This may explain the later improvement in the patient's HbA1c on the sugar free drug regimen.

An individual's biological coefficient of variation of HbA1c (the random, minor fluctuations in a person's HbA1c level as well as the slight variations due to season etc) is estimated to be around 3.4%.[3,4] Our evaluation of the laboratory analysers, on which all of this patient's samples were measured, has previously shown them to have an intra assay coefficient of variation of 1.4% with excellent concordance between machines. Together, these data can give an estimated total coefficient of variation of 3.7%. This figure may then be used to calculate that any increase in this patient's HbA1c of >0.7% is statistically significant ($p<0.05$) and cannot be explained by biological or analytical variations.[5] These figures may be approximations, but there is no doubt about the significance of the effect of Questran on her diabetes control.

Although Questran contains moderate amounts of sucrose, regular administration caused a significant deterioration in our patient's glycaemic control and we would urge all those caring for patients with diabetes to be aware of the clinical effects of excipients in medications. Sucrose is commonly used in this manner, and some medications such as linctus and lozenges for coughs, many vitamin D3 preparations, over the counter antacids and oral solutions of many drugs contain significant amounts, as well as less commonly used drugs such as amphotericin B. Diabetologists should therefore endeavour to prescribe sugar free alternatives where these are available.

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Declaration of interests

There are no conflicts of interest declared.

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References are available online at www.practicaldiabetes.com.

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