The growing number of options for lipid lowering

In my editorial last November, I promised the second guide in our new *Prescribing Pearls* series would tackle the practical aspects of prescribing sulfonylureas. An old class of blood glucose-lowering drugs, perhaps, and unlikely to be top of our "go-to" list given that there are other medications with benefits beyond glucose-lowering; however, there are situations where glucose lowering is the priority, if only as a short-term measure, such as rescue therapy or to manage steroid-induced hyperglycaemia. Sulfonylureas are well-established agents, and most healthcare professionals will have experience prescribing them, albeit less frequently in recent years.

The rationale for creating the *Prescribing pearls* series was to remind ourselves of how some of these older drugs work, their dosing schedules, cautions and contraindications, potential adverse effects and, importantly, how to prescribe them safely. So often we use HbA_{1c} as the measure of glucose-lowering effectiveness, but in this scenario it has huge limitations and we need to be guided by capillary glucose monitoring. An HbA_{1c} result will not tell us about the rise and fall of glucose levels on a daily basis, so regular self-monitoring is required to guide dose adjustment and, of course, to identify hypoglycaemia. I hope you find it useful, and we shall be tackling DPP-4 inhibitors and pioglitazone next in the series.

Lipid lowering

As well as an increasing number of glucose-lowering therapies, we are faced with much more choice when it comes to lipid-lowering therapies, with recommendations to consider ezetimibe (as monotherapy or combined with a statin) and the launch of several new drugs, including bempedoic acid, icosapent ethyl, PCSK9 inhibitors (evolocumab and alirocumab) and inclisiran. It is becoming an increasingly complex landscape to navigate!

Previously, statins were the mainstay for lowering LDL-cholesterol and the prevention and treatment of atherosclerotic cardiovascular disease. The updated NICE (2022) NG28 guideline places greater emphasis on cardiovascular risk assessment and stratification, encouraging the use of newer blood glucose-lowering agents (specifically, SGLT2 inhibitors) much earlier in the treatment pathway for those at increased cardiovascular risk. Of course, these are the very same individuals for whom a statin should be considered/offered. For those who fit the criteria (i.e. the majority of those we see) and who are not currently taking a statin, perhaps there is an opportunity for us to revisit lipid lowering. In my experience, there is something of a love–hate relationship with statins. Only last week, I spoke to a patient who was convinced, 8 years post-stent, that taking a statin was the reason he was still alive. Not everyone is so positive, however, and persuading someone to start a statin for primary prevention can be challenging. These are drugs that seem to attract more newspaper attention – often conflicting – than any other.

NICE published its CG181 guidance on cardiovascular risk assessment and lipid modification back in 2014. This was accompanied by a patient decision aid intended to help people make informed decisions about taking a statin for primary prevention of cardiovascular disease. The tool is designed to present evidence-based estimates of the benefits and risks of the treatments in sufficient detail that people are better able to judge their value. Something similar might help increase the uptake of SGLT2 inhibitors for cardiovascular protection – perhaps we should develop one here at the journal? Let us know your thoughts!

But back to statins. Currently, NICE recommends offering statin therapy to people who have a 10-year risk of developing cardiovascular disease of 10% or greater according to the QRISK2 assessment tool. Since the publication of CG181, the QRISK2 tool has been superseded by QRISK3, which incorporates

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NICE (2022) *Type 2 diabetes in adults: management* [NG28]. Available at: www.nice.org.uk/guidance/ng28 (accessed 24.04.23)

some additional features, and which will capture a larger population at risk. NICE is in the process of updating CG181, and the consultation draft incorporates QRISK3, but the rumour was that the 10% threshold might be lowered. Looking at the draft, this does not appear to be the case; however, very few people with type 2 diabetes will score below 10% anyway. In younger people (those under 40 years of age), we should be using a lifetime score, as QRISK3 will underestimate (for more information, see *At a glance factsheet: Lipids, cardiovascular risk and treatment targets*).

There is no proposed change with respect to lipid targets, with the goal still being a 40% reduction in non-HDL-cholesterol (calculated as Total cholesterol minus HDL-cholesterol). And if that is not achieved, what next? I guess this is where we have a number of options. Helpfully, the NHS Accelerated Access Collaboration has published a summary of national guidance on lipid management for primary and secondary prevention of cardiovascular disease (NHS England, 2022a). While we wait for the CG181 update, this is a really useful two-page guide.

It has been estimated that around 9% of people are truly statin-intolerant (Bytyçi et al, 2022), and the Accelerated Access Collaboration has also created a statin intolerance pathway we can follow (NHS England, 2022b). If statin intolerance is confirmed, we can now consider ezetimibe 10 mg monotherapy (NICE, 2016; TA385) and subsequently, if this alone does not control non-HDL-cholesterol sufficiently, the combination of ezetimibe 10mg and bempedoic acid 180 mg is an option (NICE, 2021; TA694). These agents can also be added to a statin where cholesterol targets are not reached.

In this issue

Sticking to the topic of bempedoic acid, in this issue, Kevin Fernando provides a summary of the CLEAR Outcomes trial, designed to establish the effects of this agent on cardiovascular outcomes. Read it here – you will see you can always rely on Kevin for a memorable title!

In another summary, "I would walk 10 000 steps but should I walk 10 000 more?" (no prizes for guessing his favourite tune!), Kevin explores the impact of increasing daily step count on mortality, cancer and cardiovascular disease. The findings favour increased daily step counts, so, as the weather improves, this could help to motivate the people we see (and indeed ourselves) to walk 10 000 steps each day.

I think we all understand the benefits of physical activity on diabetes, but this can be very difficult for many – including those with painful neuropathy. In October 2022, we published our *At a glance factsheet* on diabetes-related sensory peripheral neuropathy (Newman, 2022), and we have followed up in this issue with a *Need to know* guide on the pharmacological treatment options available, which are often very difficult to manage. Read it here.

With so many new therapies, there is a danger that we focus all our attention and energy on medications and physical health, and perhaps forget the emotional challenges people with diabetes face every day. Living with diabetes can negatively impact upon a person's emotional wellbeing and quality of life, yet Diabetes UK (2019) has reported that three quarters of people with diabetes who felt they needed specialist mental health support could not access it. This is an area of diabetes care provision that is severely lacking, and I struggle to know where to signpost to for support. Pam Brown provides a great book recommendation on this topic: *Psychology in Diabetes Care and Practice*, written by Dr Val Wilson, who herself has lived with type 1 diabetes for 45 years. This is a really valuable read for us as healthcare professionals to better understand the perspectives of people with diabetes, but we may also wish to share it with our patients struggling with the emotional demands of diabetes.

Finally, gestational diabetes (GDM) affects around 5% of women during pregnancy and, while most women have a healthy pregnancy and a healthy baby, there can be complications. Identifying GDM early is key to optimising management and minimising the risks to mother and baby. In this issue's interactive case study, David Morris provides an overview of GDM and an opportunity to work through the two scenarios testing your knowledge on screening, identification and management of GDM, as well as the post-pregnancy follow-up that is recommended. Take the opportunity to test your knowledge with some interactive learning! ■