From the desktop

GLP-1 agonists – a blessing in disguise

Ralph Audehm

Let me say from the outset that I like to have an evidence-based approach to management. So when the glucagon-like peptide-1 (GLP-1) receptor agonists came onto the Australian stage, I was slow to embrace them. Now, a short 18 months later, they are firmly embedded in my armamentarium despite the lack of long-term evidence. The lure of a good HbA_{1c} reduction and, specifically, weight loss has swayed me to become an early adopter and an advocate.

There are three GLP-1 agonists registered with the TGA for use in Australia. One, exenatide, is funded through the PBS. I have used exenatide and liraglutide in over 30 patients now and have been impressed with its tolerability and effectiveness. I was not prepared for the substantial amount of weight that many of my patients lost (and the related improvements in knee and back pain, reduced breathlessness and increased mobility), and neither were they. To say they were overjoyed is an understatement.

No drug is ever perfect, however. I have had three people stop exenatide due to nausea (the most common side effect, responsible for up to 10% of people having to stop), one due to constipation and two due to pancreatitis. Pancreatitis was a vexed storm for the GLP-1 agonists and dipeptidyl peptidase-4 inhibitors. It eventually settled to being known as an uncommon complication in a population that is prone to getting it (Suarez et al, 2014). Both my patients presented with typical symptoms of central abdominal pain, although not very severe, and elevated lipase.

GLP-1 agonists should not be used in people with an estimated glomerular filtration rate of <30 mL/min/1.73 m^2 or in anyone with a history of pancreatitis. I am also cautious of using them in people with inflammatory bowel disease and have not tried them in that population.

The mechanism of action of the GLP-1 agonists indicates that, when used as monotherapy or as dual therapy with metformin, they should not cause hypoglycaemic reactions; however, if coupled with a sulphonylurea or insulin, hypos can occur. I will often consider reducing the sulphonylurea dose by half or reducing insulin by up to one third according to glucose readings. I always ask my patients to test more often when starting a GLP-1 agonist and check that they know how to treat a hypo.

The current authority listing for exenatide is for use in people with an HbA_{1c} >53 mmol/mol (>7.0%), and it can be used as dual therapy with metformin or a sulphonylurea (if either one is contraindicated or not tolerated); as triple therapy with metformin and a sulphonylurea; or in combination with insulin (PBS, 2015).

Exenatide comes in two strengths – 5 µg and 10 µg. It is injected using the same technique and needles as insulin. I start with 5 µg twice daily and I always try to increase to 10 µg twice daily after 1 month. Each pen has enough for 30 days. The injection needs to be given before breakfast and before the evening meal (at a maximum of 60 minutes before eating and with the injections separated by at least 6 hours).

Finally, don't forget to sign the National Diabetes Services Scheme form to indicate that the person is now on injectable therapy so they can access free needles. ■

PBS (2015) *Exenatide*. Department of Health, Canberra, ACT. Available at: http://www.pbs.gov.au/medicine/item/3424f (accessed 24.11.15)

Suarez EA, Koro CE, Christian JB et al (2014) Incretin-mimetic therapies and pancreatic disease: a review of observational data. *Curr Med Res Opin* **30**: 2471–81

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About this series

The aim of the "From the desktop" series is to provide practical expert opinion and comment from the clinic. In this issue, Ralph Audehm advocates for the use of glucagon-like peptide-1 receptor agonists despite the current lack of long-term evidence.

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