Putting newer therapies into practice

Gwen Hall

Gwen Hall is a DSN in Primary Care, Haslemere, Surrey.

With the much higher than expected rise in the numbers of people with diabetes, DSNs look set to have a job for life. Not only are numbers of people with diabetes increasing rapidly, but so are the treatment regimens available and the complexity of the condition as people live longer, and healthier, with diabetes. More than ever, we need nurses with experience, knowledge and skill in diabetes to provide leadership in keeping up with medical advances. In the past, the armoury we had to treat diabetes was fairly simple. Metformin and, when necessary, a sulphonylurea. Insulin was a last resort.

How times change. Diabetes nurses used to be insulin adjusters. Now we have a holistic view of people with diabetes and their needs. We know that type 2 diabetes is progressive, and we are now in the position that many people are outliving the effectiveness of some of these traditional therapies. Since nothing on the horizon suggests that obesity (and therefore type 2 diabetes) is likely to dwindle, we need more options to treat diabetes.

In May 2008, NICE published its updated guidance for the management of type 2 diabetes (National Collaborating Centre for Chronic Conditions [NCCCC], 2008). Recommendations on glucose control focused on the traditional oral agents, updated advice on thiazolidinediones and included one of the two available long-acting insulin analogues. It takes time to develop NICE guidance, so it is unsurprising that at the time of publication many newer agents were already available or in the pipeline and healthcare professionals, and many people with diabetes, were clamouring for advice on how best these might be used. Several different algorithms emerged, and consensus among specialists in diabetes was widely published (Nathan et al, 2006). However, non-specialists and Primary Care Organisation (PCO) members needed direction from NICE. PCOs wanted cost-effectiveness information to enable them to agree protocols and treatment pathways with healthcare professionals.

So, just 1 year later, NICE has provided another update (NICE, 2009), this time including the newer agents (although several have been around for quite some time). These newer agents include dipeptidyl peptidase-4 (DPP-4) inhibitors, thiazolidinediones (commonly referred to as glitazones), the glucagon-like peptide-1 (GLP-1) receptor agonist – exenatide – and long-acting insulin analogues. The guideline indicates where in the care pathway these newer agents should be used. A short, simplified guide to each follows here; for completeness, the older agents are listed first. Readers should refer to the guidance for advice on how each should be used (NICE, 2009).

Biguanides

Metformin is now the only biguanide used in the UK. This agents inhibits hepatic glucose production and improves glucose uptake. It does not stimulate insulin production and, when used as monotherapy, is very unlikely to produce hypoglycaemia. It also benefits cardiovascular disease (UK Prospective Diabetes Study Group, 1998). Gastrointestinal side-effects can be ameliorated through the use of the prolonged release formulation.

Sulphonylureas

This class of agents stimulate the pancreatic beta-cells to secrete insulin. They rely on the individual having effective beta-cells, they have a fairly rapid response (over a few days), but can cause weight gain and hypoglycaemia. There are a number of occupations where sulphonylurea treatment is best avoided, such as working with heavy machinery, at heights or driving. NICE seems to have adopted the American spelling of "sulfonylureas". No, I don't know why either!

Thiazolidinediones

Pioglitazone and rosiglitazone: these agents have an effect on insulin resistance, and are only likely to be associated with hypoglycaemic episodes if used with a sulphonylurea or insulin. They can take 3–6 months to demonstrate improvements in HbA_{1c}. They should not be used in people with heart failure, or in those with a high risk of fracture. NICE recommends their use as second- or third-line therapy along with metformin, a sulphonylurea or both. They can cause oedema and weight gain.

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DPP-4 inhibitors

Sitaglitpin, vildagliptin and others in the pipeline. DPP-4 is an enzyme that breaks down the hormone GLP-1, which, in turn, stimulates release of insulin (but only after food intake), slows gastric emptying and promotes satiety, along with glucose-dependent insulinotropic polypeptide.

The theory is that if you inhibit DPP-4, you can improve the function of GLP-1. This effect tends to make DPP-4s weight neutral and, except when in combination with sulphonylureas, they are very unlikely to cause hypoglycaemia.

They are generally well tolerated but should be used with caution in people with renal disease. NICE recommends their use as second line, with certain caveats when in combination with metformin or a sulphonylurea. Sitagliptin is licensed for triple therapy with those agents. The DPP-4 inhibitors should not be used in combination with GLP-1 receptor agonists.

GLP-1 receptor agonists

Exenatide, with others in the pipeline. Exenatide is resistant to the DPP-4 inhibition effect, and has been developed to have a longer duration of action than natural GLP-1. It therefore lowers glucose, promotes satiety and can be associated with weight loss. It is given by subcutaneous injection twice a day. Nausea is a fairly frequent side-effect, but can be limited through adhering to the correct principles of use – which I do not have the space to discuss here. It should not be used in combination with DPP-4 inhibitors or in severe renal or gastrointestinal disease.

Long-acting insulin analogues

NICE advises the use of long-acting insulin analogues if:

- The person with diabetes needs help from a carer or healthcare professional to administer the injection *and* if the analogues allow the total number of daily injections to be reduced.
- The person's current insulin is causing recurrent symptomatic hypoglycaemia.
- He or she cannot use the devices available for the older formulations of insulin.
- The person would otherwise need twice-daily neutral protamine Hagedorn (NPH) insulin in combination with oral agents.

In practice, insulin detemir and insulin glargine are used routinely rather than NPH insulin in many areas. Interestingly, NICE recommends considering initiating insulin if HbA_{1c} is ≥7.5% (≥58 mmol/mol) on maximally tolerated oral therapy. Combine this with Quality and Outcomes Framework (QOF) targets of 7% (53 mmol/mol), 8% (64 mmol/mol) and 9% (75 mmol/mol), and I fear we will see more hypoglycaemic episodes and more hypoglycaemia-related concerns.

Conclusion

This new guidance is opportune. I know I am not alone in experiencing higher referral rates since the QOF HbA_{1c} indicators were lowered. Most of the routine care of people with type 2 diabetes happens in the community, in general practice. This is where these agents are likely to be prescribed. Primary care teams are looking for leadership and guidance from consultants who may not often see people whose control is just beginning to slip at the level set by NICE for escalation of therapy at an HbA_{1c} level of 6.5% (48 mmol/mol) or above. Therapies are now available that can be tailored, with the person's agreement, to suit individual needs. Decisions can be taken to limit episodes of hypoglycaemia, reduce weight, be combined with other drugs to reduce the total pill count or be available in slow-release forms.

Particularly pleasing in this new guidance is the emphasis on the full participation of the person with diabetes in making decisions about their treatment. They have a right to know the potential side-effects and benefits of proposed changes, and to make an informed choice. This fits neatly into plans to introduce information prescriptions (www.informationprescription.info) for all people with a long-term condition.

Practice nurses pressed to initiate insulin can take heart from NICE's recommendation that it must be carried out only through a structured programme using active insulin dose titration, telephone support and by "an appropriately trained and experienced healthcare professional". I'm sure people with diabetes would appreciate that reassurance too. NICE advocates regimens with proven cost-effectiveness, but which are not commonly used nowadays. However, clinical judgement is encouraged as part of a care plan, with agreed goals and targets made through discussions with the person with diabetes.

Sadly, in my travels around the country recently I find that care plans are more fiction than fact, although advocated by many. We need motivation and resources to implement ones that are effective and truly engage people in their own, increasingly complex, needs. Nursing management of diabetes was never simple. Inwardly digest this document and put your clinical experience into practice. ■

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