Diabetes DIGEST
The easy way to stay up to date with developments in diabetes

Editorial

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Editor

If it does what it says on the tin...

'I can't understand why people are frightened of new ideas. I'm frightened of the old ones.' – John Cage

For a variety of reasons, the management of the glucose component within type 2 diabetes seems to be intensifying. As a consequence an ever-increasing number of individuals are being started on insulin, having been identified as tablet 'failures'. The foundation for this belief arose from a subsequent epidemiological analysis of the UKPDS (Stratton et al, 2000). However, this has been questioned – particularly if one looks at the randomised aspect of the UKPDS, where changes in HbA_{1c} had no impact on the mortality associated with diabetes (Shaughnessy and Slawson, 2003). Tight control of blood glucose was associated with a decreased aggregate outcome of 21 complications but most of this was due to less change in creatinine levels and the need for retinal laser therapy without any differences in rates of visual loss or dialysis. Nevertheless, there are unquestionable benefits from insulin in terms of symptomatic improvement and relief from the side-effects of certain oral agents.

Unfortunately, it is not always easy being an insulin therapist as most people with type 2 diabetes are overweight or obese and the introduction of insulin is invariably associated with weight gain. As individuals become fatter, there is increased risk of premature mortality as well as an association with a number of other serious medical conditions (Conway and Rene, 2004). Thus, care should be taken in encouraging exercise and calorie restriction if insulin is being considered for an overweight individual with type 2 diabetes.

Over the next few years it is likely that agents with glucagon-like peptide 1 (GLP-1) actions will come to market for the treatment for type 2 diabetes. Pre-clinical studies suggest that this class of drug may have a number of potential benefits (Vilsboll and Holst, 2004):

- Insulinotropic actions – i.e. glucose-dependent insulin secretion combined with inhibition of glucagon release. These effects disappear as peripheral blood glucose levels fall to below 6 mmol/l, thereby avoiding the possibility of hypoglycaemia. Without a risk of hypoglycaemia, regular blood glucose monitoring may be unnecessary. The combination of stimulation of insulin release and inhibition of glucagon lowers blood glucose levels.
- Insulin biosynthesis and gene transcription stimulation leading to continuous insulin availability.
- Trophic effects promoting ß-cell proliferation, differentiation from progenitor cells and inhibition of apoptosis. Therefore, one of the fundamental deficits in type 2 diabetes, insulin deficiency, could be corrected by GLP-1 therapy.

In addition, studies in healthy volunteers and patients with diabetes indicate that GLP-1 treatment is associated with slowing of gastric emptying, suppression of appetite and thus possibly weight loss. On the flip side, the most common side-effect is transient nausea and that the drug has to be given by subcutaneous injection, although trials of oral agents that prevent the breakdown of GLP-1 are also underway (Edwards, 2004). There is also the intriguing possibility of combining GLP-1 with insulin sensitisers, tackling both of the underlying defects in this form of diabetes. If these drugs 'do what they say on the tin' then the management of type 2 diabetes is about to get a whole lot more interesting, but it does raise the question about whether this approach is best left with primary care.

Although insulin per se is not a panacea for the treatment of type 2 diabetes, it has stood the test of time and the problems are well-recognised. GLP-1 sounds like the best thing since sliced bread but, like all new therapies, needs to prove itself beyond the stage of simply coming to the market place. There are many unanswered questions and given the recent furore over Vioxx, there can never be any substitute for good and robust evidence. Let's hope the companies have the same view.

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