# Management of type 1 diabetes

## Glucagon-like peptide-1 receptor agonist use in type 1 diabetes

**Daniel Flanagan**
*Consultant Physician, Derriford Hospital, Plymouth*

It seems that diabetes clinicians have a particular problem with prescribing medications beyond their licensed indications. As new regulatory trials are completed, the licensed indication for medicines change and, unless you are working within the field day-to-day, it can be extremely difficult to have confidence that your chosen drug combinations do fall within the licences. For example, within a class of drugs, some medications will be licensed in combination with a second drug, whereas others within the class may not, and, in some cases, medications are only licensed if a drug combination is started in a specific order.

Prescribing beyond the licensed indication is a recognised and acceptable part of clinical practice. However, it should be made clear to the patient when this is happening, which is part of the responsibility of being a specialist.

Licences are based on regulatory trials, which are expensive, cumbersome and slow, and clinical medicine often moves rapidly beyond the recommendations of these trials. The Association of British Clinical Diabetologists' audits of exenatide (Ryder et al, 2010) and liraglutide use (Ryder et al, 2013) have clearly demonstrated this. The findings showed that a significant proportion of medicine prescriptions were outside of the licensed indications and beyond NICE guidance. It is likely that, since then, the amount of prescribing beyond the licence has grown.

The glucagon-like peptide-1 (GLP-1) receptor agonists (the class that exenatide and liraglutide belong to) have benefits beyond glucose lowering. The beneficial effects on weight loss are an important feature of these agents, and this is likely to be a feature that the pharmaceutical companies will want to make use of not just in people with diabetes. For people with type 2 diabetes, the desire for weight loss is an important reason to start these treatments. People with type 1 diabetes are not spared the problem of weight gain and subsequent insulin resistance, so it is logical that this class of drug may also be of benefit here.

The small study by Sarkar and colleagues (summarised alongside) explores the effects of adding exenatide to insulin therapy in 14 participants with type 1 diabetes. This report is a substudy of their initial work (Rother et al, 2009) investigating whether exenatide combined with immunotherapy could improve beta-cell function in people with established type 1 diabetes (it did not). Interestingly, half of the participants in this study of type 1 diabetes were overweight or obese.

Over the course of this short study by Sarkar et al, the addition of exenatide to insulin therapy resulted in an improvement in postprandial glucose but caused no change in $HbA_{1c}$. The participants displayed an improvement in weight and insulin sensitivity, which suggests benefits that may be more important than a direct glucose-lowering effect. This is a small study but probably a sign of things to come. ■

Rother KI, Spain LM, Wesley RA et al (2009) Effects of exenatide alone and in combination with daclizumab on beta-cell function in long-standing type 1 diabetes. *Diabetes Care* **32**: 2251–7
Ryder RE, Thong KY, Cull ML et al (2010) The Association of British Clinical Diabetologists (ABCD) nationwide exenatide audit. *Pract Diab Int* **27**: 352–7
Ryder RE, Thong KY, Blann AD et al (2013) Liraglutide pancreatitis: The ABCD nationwide liraglutide audit. *Br J Diabetes Vasc Dis* **13**: 253–9

**Diabetes Care**

## Exenatide treatment for adults with long-standing T1D

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| Readability | ✓✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! Factor | ✓✓✓✓ |

1 Exenatide is an injected glucagon-like peptide-1 receptor agonist mainly used for the treatment of T2D.

2 It has been shown to reduce postprandial hyperglycaemia among adolescents with T1D. In this analysis, the authors investigated exenatide's effects on glucose homeostasis in adults with long-standing T1D alongside insulin therapy.

3 Fourteen participants with a T1D duration of 20.5±11.8 years and a mean age of 37.3±10.7 years took part in a crossover study of 6 months on exenatide (10 µg four times a day) and 6 months off exenatide.

4 After 6 months, the exenatide group had a weight loss of 4.2 kg compared with the off-exenatide group ($P$=0.0003).

5 Participants also required significantly less administered insulin while on exenatide ($P$=0.007), which was a result of reduced bolus insulin. Basal insulin requirements stayed the same.

6 Exenatide therapy reduced postprandial blood glucose but was associated with higher fasting glucose concentrations without net changes in $HbA_{1c}$. It also increased insulin sensitivity beyond the effects expected as a result of weight reduction.

7 Exenatide is a promising adjunctive agent to insulin therapy for people with T1D because of its beneficial effects on postprandial blood glucose, weight loss and insulin sensitivity.

Sarkar G, Alattar M, Brown RJ et al (2014) Exenatide treatment for 6 months improves insulin sensitivity in adults with type 1 diabetes. *Diabetes Care* **37**: 666–70

## Diabetic Medicine

# Hypoglycaemia and impaired awareness associated with diabetes duration

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! Factor | ✓✓✓ |

1 The aim of this cross-sectional study was to investigate the association between diabetes duration and (1) hypoglycaemia symptom profiles and (2) the presence of impaired awareness of hypoglycaemia (IAH).

2 Questionnaires were sent to 636 adults with T1D attending an outpatient clinic in Norway; 445 completed questionnaires (70%) were returned. In total, 440 responses could be used for the analysis. Responders had a median age of 41 years and a median diabetes duration of 21 years.

3 Longer diabetes duration was associated with a lower intensity of autonomic symptoms (*P* for trend <0.001), but not associated with neuroglycopenic symptoms of hypoglycaemia.

4 IAH was identified in 17% (95% confidence interval, 14–21%) of the cohort, and increased with diabetes duration, from 3% for duration 2–9 years to 28% for duration ≥30 years (*P* for trend <0.001).

5 IAH was more common in those who had experienced multiple episodes of severe hypoglycaemia in the preceding year.

6 There was no significant trend found between IAH and gender or higher $HbA_{1c}$.

7 Longer diabetes duration was associated with a lower intensity of autonomic symptoms and a reduced awareness of hypoglycaemia.

Olsen SE, Asvold BO, Frier BM et al (2014) Hypoglycaemia symptoms and impaired awareness of hypoglycaemia in adults with type 1 diabetes: the association with diabetes duration. *Diabet Med* **31**: 1210–7

## Diabetic Medicine

# Pregnancy losses in women with diabetes

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! Factor | ✓✓✓ |

1 Data on pregnancies ending between 1993 and 2006 in women with T1D and T2D from the UK were used to measure the rate of pregnancy losses compared to the general population.

2 Spontaneous, induced (for medical or non-medical reasons) and unknown reasons for pregnancy loss were included in the data collection.

3 Women with gestational diabetes and T2D who were treated with diet alone were excluded.

4 The proportions of pregnancy losses were similar for women with T1D (19.6%) and T2D (21.1%), and both were higher than the proportion of losses in the general population (13.2%).

5 Pre-conception care for women with T2D is as necessary as care for women with T1D, given the similarity in outcomes.

McGrogan A, Snowball J, de Vries CS (2014) Pregnancy losses in women with type 1 or type 2 diabetes in the UK. *Diabet Med* **31**: 357–65

## Diabetes Care

# Cheiroarthropathy prevalence in T1D

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| Readability | ✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! Factor | ✓✓ |

1 Cheiroarthropathy is the periarticular thickening of skin on the hands causing limited joint mobility. It is known to be associated with diabetes, so the authors hoped to describe the prevalence of cheiroarthropathy in the DCCT/EDIC (Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications) cohort. In total, 1217 participants were included in this analysis.

2 Cheiroarthropathy was present in 66% of participants, with no significant difference between the control and intervention groups of the DCCT.

3 Its presence was associated with age, gender, diabetes duration, $HbA_{1c}$, neuropathy and retinopathy (*P*<0.005 for each).

4 Cheiroarthropathy is common among people with long-standing T1D, and should be included as part of patient examinations.

Larkin ME, Barnie A, Braffett BH et al (2014) Musculoskeletal complications in type 1 diabetes. *Diabetes Care* **37**: 1863–9

## Diabetes Care

# Closed-loop insulin delivery in youths

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓ |
| WOW! Factor | ✓✓✓✓✓ |

1 The feasibility, safety and efficacy of overnight closed-loop insulin delivery at home in youths with T1D was investigated.

2 Sixteen youths took part in an open-label, randomised, crossover study to compare sensor-augmented pump therapy with and without the addition of overnight closed-loop technology.

3 The two test periods were 3 weeks in duration, and the primary end-point was the time during which adjusted sensor glucose levels were between 3.9 and 8.0 mmol/L at nighttime.

4 Closed-loop delivery increased time spent with glucose in the target range by a median of 15% (*P*<0.001). Mean overnight glucose was reduced by a mean of 14 mg/dL (0.8 mmol/L; *P*<0.001).

5 Unsupervised home use of overnight closed-loop technology in youths with T1D is safe and feasible. Glucose control was improved, and there were fewer episodes of noctural hypoglycaemia.

Hovorka R, Elleri D, Thabit H et al (2014) Overnight closed-loop insulin delivery in young people with type 1 diabetes. *Diabetes Care* **37**: 1204–11

***"Unsupervised home use of overnight closed-loop technology in adolescents with type 1 diabetes is safe and feasible, with glucose control improving during the day and night and fewer episodes of noctural hypoglycaemia."***