Long-term glycemic instability increases risk of microvascular damage in T1DM

Whether fluctuations in blood-glucose levels influence the incidence of microvascular complications in patients with type 1 diabetes (T1DM) is a controversial topic. An analysis of data from the Diabetes Control and Complications Trial (DCCT) suggests that long-term glycemic instability increases the risk of retinopathy and nephropathy in such patients.

The DCCT was a 9-year study that compared the effects of conventional and intensive glycemic control on the development of microvascular complications in 1,441 diabetic individuals. Kilpatrick *et al.* examined variability in quarterly HbA_{1c} measurements as an indicator of glycemic instability. HbA_{1c} variability was higher in conventionally treated patients than in those treated intensively. Whether measured as updated HbA_{1c}, SDs of HbA_{1c} levels across all follow-up visits, or an updated, time-dependent SD, variability was an independent predictor of retinopathy and nephropathy: every 1% increase in the HbA_{1c} SD was associated with a hazard ratio of 2.26 for development of retinopathy, and 1.80 for nephropathy. A patient whose HbA_{1c} variability was in the 97.5th centile had more than three times the risk of developing retinopathy, and more than twice the risk for nephropathy, of a patient whose variability was in the 2.5th centile.

The authors conclude that, in contrast to the apparent lack of effect of short-term (daily) changes in blood glucose, long-term fluctuations in serum HbA_{1c} levels increase the risk of microvascular complications in patients with T1DM. Regular measurements of HbA_{1c} levels might help to monitor at-risk patients.

Original article Kilpatrick ES *et al.* (2008) A1c variability and the risk of microvascular complications in type 1 diabetes: data from the Diabetes Control and Complications Trial. *Diabetes Care* **31:** 2198–2202

Once-weekly exenatide reduces HbA_{1c} more than the twice-daily formulation

The glucagon-like peptide 1 receptor agonist exenatide improves glycemic control and reduces body weight in patients with type 2 diabetes mellitus. Exenatide is currently given twice daily by injection; however, this formulation does not provide continuous glucagon-like peptide 1 receptor activation. Drucker *et al*. report that a long-acting-release (LAR) formulation of exenatide, which can be given once weekly by injection, provides superior glycemic control compared with that of the twice-daily formulation.

The 30-week, randomized, noninferiority study included 295 patients with type 2 diabetes mellitus who were naive to drug treatment or were receiving ≥1 oral antidiabetic agent. Participants were randomly allocated to receive 2 mg LAR exenatide once weekly or 10 µg exenatide twice daily.

Compared with the twice-daily formulation, LAR exenatide produced greater declines in HBA_{1c} levels and significantly increased the proportion of patients who achieved a target HbA_{1c} level of ≤ 7.0% (77% versus 61%). Body weight declined to a similar extent in the two groups. The two regimens also showed comparable results in terms of safety and tolerability, although treatment-related nausea occurred in fewer patients treated once weekly.

Drucker and colleagues conclude that the once-weekly formulation of exenatide might be a convenient treatment option for patients with type 2 diabetes mellitus. Future studies are required to compare the efficacy of LAR exenatide with that of other classes of antidiabetic agents.

Original article Drucker DJ *et al*. (2008) Exenatide once weekly versus twice daily for the treatment of type 2 diabetes: a randomised, open-label, non-inferiority study. *Lancet* **372:** 1240–1250