CASE REPORT

Basal insulin regime change from Lantus to Toujeo resulted in fewer hypoglycaemic episodes in a 28-year-old man with diabetes mellitus

Alexandra Shields, Sailesh Sankaranarayanan

University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK

Correspondence to
Alexandra Shields,
a.shields@warwick.ac.uk

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SUMMARY

An active 28-year-old man with type 1 diabetes mellitus reported a reduced number of hypoglycaemic episodes following change in basal regime insulin glargine from U100 Lantus to U300 Toujeo. Consequently, an improved quality of life was also reported. Flash-based glucose monitoring was utilised to record 24-hour continuous glucose levels throughout two comparable 60-day periods before and after the change in regimen. Low blood glucose was most likely between 03:00 and 08:00. Nocturnal hypoglycaemic episodes (≤ 3.9 mmol/L) reduced by an average of 2.5 episodes per week. Severe hypoglycaemic episodes (≤ 2.9 mmol/L) reduced to an average of 0.4 per week, down from 1.5 per week. Nocturnal hypoglycaemic episodes reduced in frequency and severity. Furthermore, nocturnal hypoglycaemia episodes occurred in a more predictable time window. This was especially important in the reported reduction of impact on the patient's quality of life, as the episodes tended to be associated with anxiety and low mood. Patient education needed to facilitate this change was minimal, and benefits to the patient were great, including decreased sleep disturbances and reduced risk of associated anxiety symptoms.

BACKGROUND

Type 1 diabetes mellitus is an autoimmune condition in which the ability to regulate blood glucose is lost due to the immune system destroying insulin-producing pancreatic β cells.¹ The condition is most commonly diagnosed in childhood or adolescence, and presents with excessive thirst, tiredness, polyuria and unexplained weight loss.¹

Owing to the destruction of the body's insulin source, management is by insulin administration via pump or injection. By injection, basal-bolus insulin regimens are recommended as they closely mimic physiological insulin action in patients without diabetes.^{2,3} A rapid or short-acting bolus insulin dose is injected subcutaneously before meals, aiming to control prandial blood glucose.¹

Basal insulins are long-acting, working in the background to control fasting blood-glucose and suppress hepatic ketogenesis; the main options are: twice-daily insulin detemir or once-daily insulin glargine.² Insulin glargine is usually taken at the same time each night, creating a peakless profile—this feature is popular with patients as it helps to control nocturnal hypoglycaemia.¹

The European Union-wide standard for insulin is 100 units/mL⁴ of, for example, insulin glargine

(Lantus or Abasaglar). Three types of insulin have been approved at higher strengths: insulin degludec 200 units/mL (Tresibo), insulin lispro 200 units/mL (Humalog) and insulin glargine 300 units/mL (Toujeo).⁴

Insulin glargine, as Lantus and Toujeo, has been authorised in the European Union since June 2006. Both brands have the same composition, except Toujeo has three times the amount of active ingredient and zinc content.³ Toujeo delivers a more regular serum insulin glargine level, with a lower peak to trough fluctuation ratio and more tightly controls blood glucose over a 36-hour period, compared to Lantus.³

Lantus and Toujeo have very similar prescribing information, including administration guidelines, drug interactions and adverse reactions. Toujeo has not been approved for paediatric use, whereas Lantus can be used for paediatric patients.^{5,6}

Changing from Lantus to Toujeo requires little additional patient knowledge, but may greatly improve the patient experience of living with type 1 diabetes mellitus.

CASE PRESENTATION

A 28-year-old man, diagnosed with type 1 diabetes mellitus in December 2011 (aged 24 years), experienced self-managed nocturnal hypoglycaemic episodes that interrupted sleep cycles and consequently caused symptoms of anxiety. To manage these episodes, his basal insulin glargine regime was changed from U100 Lantus to U300 Toujeo on 5 November 2015. The patient used a FreeStyle Libre monitoring device to capture flash-based blood glucose data, which were used in analysis. For the purposes of this report, any blood glucose episode under 3.9 mmol/L is defined as a hypoglycaemic episode, blood glucose under 2.9 mmol/L as a 'severe' hypoglycaemia episode and blood glucose under 1.9 mmol/L as 'very severe', in order to quantify the effect of reduction in severity.

Two time periods of data were analysed to determine the effect of this change in basal insulin regime. First, during the period the patient was prescribed U100 Lantus, from 12 July 2015 to 4 November 2015, and second, while the patient was prescribed U300 Toujeo, from 5 November 2015 to 29 February 2016.

On the previous regime of U100 insulin, the patient was self-administered 14 units of glargine (long acting) at 21:00 daily with 1 unit of Humalog

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(rapid acting) insulin to every 20 g of carbohydrate (~12 units per day). On days of heavy exercise, he reduced his basal dose by 2 units.

While prescribed U100 Lantus, the patient's daily blood glucose averaged 6.8 mmol/L and an average glycated haemoglobin (HbA1c) was recorded as 41 mmol/mol. During this period, there were, on average, 4.8 hypoglycaemic events per week, of these, an average of 1.5 per week were severe hypoglycaemic episodes.

No very severe hypoglycaemic episodes were recorded.

Eighty-eight per cent of recordings below 3.9 mmol were recorded during the night (between 21.00 and 09.00 hours); 92% of the severe hypoglycaemic episodes occurred between these times (8% of severe hypoglycaemic episodes occurred during daytime hours).

On the new regimen of U300 insulin, the patient was self-administered 14 units of glargine (long acting) at 21:00 daily with 1 unit of Humalog (rapid acting) insulin to every 17 g of carbohydrate (14 units/day). This represents an increase of ~2 units of rapid acting insulin per day, which is a typical amendment made when changing from U300 to U100.⁷ On days with heavy exercise, the patient reduced his basal dose by 2 units. While prescribed U300 Toujeo, daily blood glucose averaged 6.9 mmol/L and an average HbA1c was recorded as 42 mmol/mol.

During this period, an average of 2.3 hypoglycaemic events per week were recorded, of which 0.4 per week were severe hypoglycaemic episodes. No very severe hypoglycaemic episodes were recorded.

Seventy per cent of the hypoglycaemic events were recorded during the night (between 21.00 and 09.00 hours). All severe hypoglycaemic episodes were recorded between 00.00 and 03.00 hours—highlighting the increased predictability of U300.

For both periods, the most likely time to record a blood glucose <3.9 mmol/L was between 22:00 to 08:00 hours (period between evening meal and breakfast).

OUTCOME AND FOLLOW-UP

The results indicate:

Both frequency and severity of nocturnal hypoglycaemia episodes were reduced while on the new U300 Toujeo regimen, when compared to similar periods on the previous U100 Lantus regime. The hypoglycaemic episodes that occurred under the new regime tended to be within a narrower time frame, indicating increased predictability.

- ▶ HbA1c measurements recorded differ by 1 mmol/mol while prescribed Lantus (41 mmol/mol) and Toujeo (42 mmol/mol).
- ▶ Daily blood glucose recordings differed by +0.1 mmol/L while prescribed Lantus (6.8 mmol/L) and Toujeo (6.9 mmol/L).

Table 1 Number of blood glucose recordings <3.9 mmol/L/month. Complete data for August 2015 were not available

Month	Low-glucose recordings
July 2015	19
September 2015	15
October 2015	16
November 2015	8
December 2015	6
January 2016	10
February 2016	11

Figure 1 Low-glucose events 12 July 2015 to 8 August 2015. Figure from FreeStyle Libre data analysis.

- ▶ There was a reduced average number (difference of 8.25/month) of total hypoglycaemic episodes (<3.9 mmol/L) on Toujeo compared to on Lantus (table 1).
- ▶ There was a reduced average number (difference of 3/month) of blood glucose recordings ≤2.9 mmol/L on Toujeo compared to on Lantus (figures 1–3)
- ▶ There was a reduced number of nocturnal hypoglycaemic episodes (comparing <3.9 mmol/L episodes between 00:00 and 09:00) on Toujeo compared to on Lantus.
- ▶ Blood glucose ≤2.9 mmol was only recorded between night-time hours of 00.00 and 03.00 when the patient was prescribed Toujeo.
- ▶ No blood glucose recordings ≤2.9 mmol/L were noted between 16 November 2015 and 24 December 2015 (figure 2).
- ▶ Hypoglycaemic episodes (<3.9 mmol/L) were more likely at night (00:00–09:00) for both periods.

DISCUSSION

Daily blood glucose and repeated HbA1c measurements would need to be monitored over future months to determine if average blood glucose and HbA1c is affected by the change in basal insulin regime.

Hypoglycaemic episodes throughout the day and night were reduced, and less severe hypoglycaemic episodes recorded, with none recorded in the last month of analysis. This reduced hypoglycaemic-related morbidities, including sleep disturbances, and so also the risk of heightened anxiety levels for the patient. The levels of blood glucose while the patient was prescribed Toujeo were increasingly stable and predictable. There were reduced peak-to-trough fraction variations, reducing the risk of hyperglycaemic and hypoglycaemic episodes, and reducing uncertainty for the patient. This was particularly important in this case, as the patient was a young man who would need a degree of 'flexibility' with his blood glucose control, to allow him to have a good quality of life and to enjoy activities with peers, such as sports and eating out at restaurants, where very tight blood glucose control may be challenging. This is a very common situation, particularly in this population.

Current guidelines for type 1 diabetes mellitus control specify a target HbA1c of 48 mmol/mol (6.5%) or lower.² This patient's HbA1c was significantly lower at ~42 mmol/mol, so it is reasonable to suggest that, to avoid hypoglycaemia, the Lantus U100

Figure 2 Low-glucose events 16 November 2015 to 24 December 2015. Figure from FreeStyle Libre data analysis.

Figure 3 Low-glucose events 26 January 2016 to 26 February 2016. Figure from FreeStyle Libre data analysis.

regime could have been reduced in absolute terms, and still have been within the target HbA1c. However, as shown in this report, U300 Toujeo greater suited this patient's individual requirements. The patient exercised regularly, primarily in the evening, when the previous day's Lantus U100 dose would be running out. Toujeo U300 has a flatter mode of action, avoiding a sudden drop in blood glucose a few hours later. The patient reported that this led to a beneficial effect of stability and predictability, as his exercise varied in intensity and duration

from day to day. By switching to U300 Toujeo, the preferable lower HbA1c level of 42 mmol/L was maintained while still reducing the impact of hypoglycaemia episode load on the patient. We propose that, in many other patients who lead similar lifestyles, this change could lead to similar beneficial effects.

Toujeo and Lantus are very similar products, with the main education point to patients being that, during the change-over period, there should be an initial 10% reduction in long-acting insulin, with titration upwards, to achieve fasting blood glucose within 5–7 mmol/L. This is to reduce the risk of hypoglycaemia during the transition phase. The main difference patients should notice is the extended time of action. To patients already managing their diabetes regimen to a high standard, this would not be too challenging to comprehend and should not discourage the practitioner.

Further study would incur the cost of these two products and would benefit from, if financially viable, more patients.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Patient's perspective

I am a 28-year-old student who has had type 1 diabetes for 4 years. During this time, I had grown in diligence in monitoring my condition and last year I found it very helpful to switch to using a free-style libre device that monitors blood sugars in a few seconds without a finger prick. The upshot was that my control became quite fine-tuned, and as I am active and play a lot of sports I would frequently find that, on the Lantus regime, I would experience night-time lows. This had a very big effect on my life and I would frequently become so anxious I'd wake myself up once or twice a night to check. I became very tired because of this. My consultant and I agreed on a trial of splitting the dose of Lantus between morning and evening, but this didn't suit me because it caused erratic high-blood sugar and was yet more to think about. Following this, my consultant switched me onto Toujeo, which worked much better. Whereas before, once injecting Lantus, I would notice a quite significant blood sugar drop, especially if post exercise. I noticed fairly straight away that this didn't happen with Toujeo. In fact, I noticed that my blood sugars were far more stable overnight and also throughout the following day. In the evenings, I noticed fewer high-blood sugars as well. Since changing to Toujeo, the quality of life improvement has been huge, I'm now no longer staying up late and not waking up in the night to check. I feel more confident in managing my diabetes and consequently much happier because of the change. I think that I have benefitted because I control my diabetes very strictly, and possibility too strictly, but I find it hard not to.

Learning points

- In this active young patient, hypoglycaemic episodes were most likely during the night.
- Nocturnal hypoglycaemic episodes disrupt quality of life for people with diabetes mellitus.
- Adjusted selection of basal insulin significantly influenced hypoglycaemic frequency and severity in this patient. Plus, hypoglycaemic episodes tended to be in a more predictable time window.
- Management of diabetes mellitus is specific to each individual; mental health and quality of life should be considered to guide insulin regimen choice.

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