Day-to-day variability of fasting self-measured blood glucose associates with risk of hypoglycaemia in adults with type 1 and type 2 diabetes

Background

- The relationship between glycaemic variability and the risk of hypoglycaemia has not yet been well established.
- Hypoglycaemia has significant negative effects on patient health and quality of life, and is a major concern to both patients and physicians.1
- Day-to-day variability can be assessed as the variation in glucose level at a given time-point over a series of days, as a measure of glycaemic variability.2

Methods

- A post hoc analysis was performed to investigate the association between day-to-day variability of fasting SMBG (with hypo-, normo- and hyperglycaemic rates using data from two 64-week, randomised, multicentre, controlled, double-blind, treat-to-target, two-period crossover trials with insulin degludec (Deg) once daily (OD) and insulin glargine 100 units/ML (Glar 100 OD). One trial comprised adult patients with T1D (SWITCH 1 [NCT02034513], n=501), the other insulin- experienced patients with T2D (SWITCH 2 [NCT03103600]), n=721.

- The trial design used for both SWITCH 1 and SWITCH 2 is shown in Figure 1. In both studies, the 64-week trial period consisted of two 16-week treatment periods, one on each of the comparator basal insulins. Each treatment period consisted of a 16-week titration period (Weeks 1–16 and Weeks 32–48) and a 16-week maintenance period (Weeks 16–32 and Weeks 48–64). The fasting pre-breakfast SMBG variables in this post hoc analysis were retrieved from the two 16-week maintenance periods of both treatments (Weeks 16–32 and Weeks 46–64) in both trials (Figure 1). The data were pooled for the two treatment arms, but analysed separately for T1D and T2D.
- A schematic illustration of the data collection for day-to-day glycaemic variability of fasting SMBG values is shown in Figure 2.

- For patients with T1D, the fasting pre-breakfast SMBG measurements were used for weekly titration of basal insulin and also daily glycaemic control. For patients with T2D, three fasting pre-breakfast SMBG measurements were used for weekly titration of basal insulin. Therefore, up to seven SMBG measurements were available for patients with T1D and up to three SMBG measurements were available for patients with T2D.

- The available pre-breakfast SMBG variables in each week of the 16-week maintenance period were used to determine a log- transformed weekly standard deviation for each patient and treatment combination, the day-to-day variability (for each patient and treatment combination) was defined as the geometric mean of these data. The day-to-day variability data were then grouped into equally sized tertiles for the analyses. This method of grouping patients by tertiles was based on a previous study.3

- The number of hypoglycaemic events was analysed using the pre-specified primary model1 with the fasting SMBG as an additional factor.

- Hypoglycaemic episodes were defined as:
  - Overall symptomatic: severe or blood glucose (BG)-confirmed (<3.1 mmol/L) symptomatic hypoglycaemia, 00:01–05:59 (both tertiles).
  - Nocturnal symptomatic: severe or BG-confirmed (<3.1 mmol/L) symptomatic hypoglycaemia, 00:01–05:59 (both tertiles).

- The available pre-breakfast SMBG values in each week of the 16-week maintenance period were used to determine a log-transformed weekly standard deviation for each patient and treatment combination, the day-to-day variability (for each patient and treatment combination) was defined as the geometric mean of these data. The day-to-day variability data were then grouped into equally sized tertiles for the analyses. This method of grouping patients by tertiles was based on a previous study.3

- Severe hypoglycaemic episodes requiring third-party assistance (based on the ADA definition 6) and confirmed by a blinded independent adjudication committee.

Results

- Baseline characteristics of the SWITCH 1 and SWITCH 2 study cohorts are shown in Table 1.
- Day-to-day glycaemic variability was significantly associated with the risk of overall and nocturnal hypoglycaemia in patients with T1D and T2D (Table 2, Figures 3 and 4).
- In patients with T1D, this significant association was also observed for severe hypoglycaemia, whereas in patients with T2D, no significant difference was found across tertiles for severe hypoglycaemia, likely due to the low number of severe hypoglycaemic events (Table 2, Figures 3 and 4).

Conclusions

- Day-to-day variability in pre-breakfast SMBG values was significantly related to the risk of overall and nocturnal symptomatic hypoglycaemia in patients with T1D or T2D, and severe hypoglycaemia in patients with T1D.
- Treatment choices that reduce day-to-day glycaemic variability may contribute to a reduction in the risk of hypoglycaemia.

References


The studies were sponsored by Novo Nordisk and are registered with ClinicalTrials.gov (NCT02034513 and NCT02030600). The authors acknowledge the medical writing assistance of Watermead Medical, an Ashfield company. Presented at the American Diabetes Association’s Annual Meeting, 10–16 November 2017, London, UK.