Increased time in range observed after introduction of a connected insulin pen

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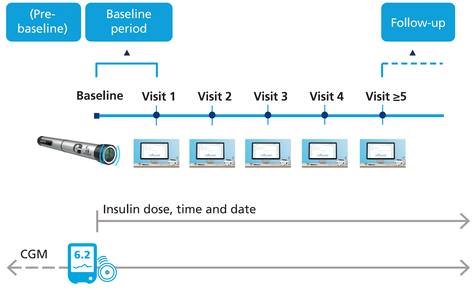
Background

- Insulin pens have become the most widely used devices for delivering insulin. Despite their convenience, however, there are shortcomings. In particular, poor documentation of insulin therapy can result in inadequate glycaemic control for patients with diabetes. Smart insulin pens offer automatic access to insulin injection data, and could help overcome barriers of poor adherence, clinical inertia and incorrect dosing.[1]
- The smart connected NovoPen® 6 collects and stores data on the date and time of insulin injections and the number of units administered. These data are then downloaded using near field connectivity to a centralised database. This allows healthcare professionals (HCPs) and patients to look at injection data together when discussing insulin treatment. If the injection data are further combined with glucose/continuous glucose monitoring (CGM) data the potential to improve patient-HCP dialogue is thought to be even greater.
- The possibility to have a combined view of insulin injections and CGM data gives the HCP and the patient a more complete picture of current glycaemic status. Thus, both patient-HCP dialogue and treatment approaches can be improved.
- An engaging and open patient-HCP dialogue has been identified as highly important for optimal disease management. Therefore, the NovoPen® 6 has the potential to improve glycaemic control.[2,3]

Figure 1: Study design

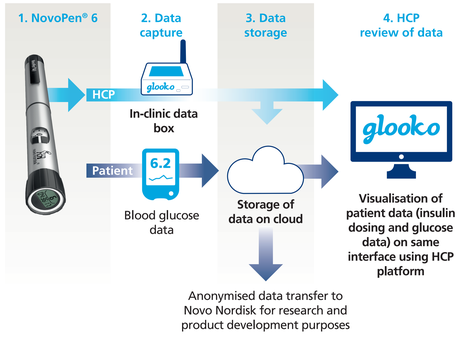


Pre-baseline was the period before study commencement where patients were already using CGM, but without concurrent use of the NovoPen® 6.
CGM, continuous glucose monitoring.

Aim

- The objective of this non-interventional study was to investigate how a smart connected insulin pen (NovoPen® 6) influences glycaemic control in patients with type 1 diabetes (T1D) in a real world setting.

Figure 2: Using NovoPen® 6 with the Glooko/Diasend® system



HCP, healthcare professional.

Methods

- This pilot study was a prospective, non-interventional study running from May 2017–Nov 2018. Twelve diabetes clinics from different parts of Sweden participated. Patients with T1D using CGM were included if their treating physicians decided to offer them a NovoPen® 6.
- At baseline, patients received a NovoPen® 6 for basal and/or bolus insulin injections. Baseline was then followed by a baseline period between pen introduction and visit 1, during which the patient started to use the NovoPen® 6 but without access to downloads of injection data. The first data download occurred at visit 1, using the Glooko/Diasend® in-clinic system to transfer data from the pen to the Glooko/Diasend® server. From here the data were accessed via the Glooko/Diasend® HCP web portal and the patient and HCP had the first chance to look at the data together.
- Hereafter, the study continued with HCP visits according to clinical practice. At each visit, pen data were available for download and use by the patient and HCP during the consultation (Figures 1 and 2).
- This study design permitted comparison between the baseline and follow-up periods. CGM and dosing data from the first 14 days following a clinic visit were used in the analyses. The 14-day period was chosen to be in line with the international consensus on the use of CGM.[4] Visit 5 was chosen as the earliest point for follow-up, as patients would on average have been in the study for ≥180 days, allowing for sufficient interaction with HCPs and discussion of available pen data. Time in range (TIR), time spent in hyperglycaemia and time spent in L1 (3.0–<3.9 mmol/L) and L2 hypoglycaemia (<3.0 mmol/L) were compared between the baseline and follow-up periods, which was defined as any point after the fifth HCP visit.

Table 1: Baseline levels and estimated changes to follow up of key glycaemic parameters

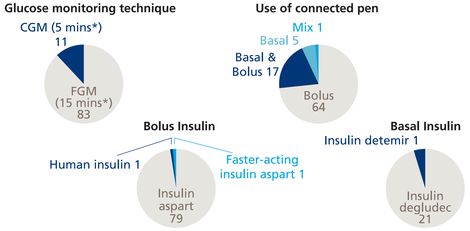
	Baseline level [95% CI]	Estimated mean change [95% CI]	*p*-value
TIR (3.9–10.0 mmol/L) (hours)	9.19 [8.28; 10.10]	1.89 [0.79; 2.99]	0.0009
TIHyper (>10.0 mmol/L) (hours)	11.80 [10.81; 12.79]	–1.78 [–2.96; –0.60]	0.003
TIHypo L1 (3.0–<3.9 mmol/L) (hours)	0.69 [0.55; 0.83]	–0.15 [–0.36; 0.07]	0.181
TIHypo L2 (<3.0 mmol/L) (hours)	0.47 [0.32; 0.61]	–0.33 [–0.56; –0.10]	0.005
Mean glucose (mmol/L)	11.09 [10.53; 11.64]	–0.34 [–0.96; 0.28]	0.279
Coefficient of variation (%)	35.89 [34.33; 37.45]	–3.84 [–6.12; –1.56]	0.001

Estimated mean baseline level and change between the follow-up period (visits ≥5) and the baseline period with 95% CI. Linear mixed model, with visit number (baseline, 1, 2, 3, 4, 5+) as fixed effect, patient and visit nested in patient as random effects, and with exponential covariance function. N=94, visits=231, CGM days=2552.
CGM, continuous glucose monitoring; CI, confidence interval; TIR, time in range; TIHyper, time in hyperglycaemia; TIHypo L1, time in L1 hypoglycaemia; TIHypo L2, time in L2 hypoglycaemia.

Results

- Ninety-four adults with T1D with a mean [min; max] age of 40.1 years [18; 83] were included in the analyses. A total of 64 patients used NovoPen® 6 for bolus insulin only, 17 for basal and bolus insulin and 5 for basal insulin only. For the majority, insulin degludec was the basal insulin and insulin aspart was the bolus insulin. Seven patients did not have connected pen data in the 14-day periods studied and 1 patient used biphasic insulin aspart 30, neither bolus nor basal insulin (Figure 3).
- A significant increase of 1.9 hours per day (~21% of the baseline level) in mean TIR from the baseline period to the follow-up period was observed (p=0.0009; Figure 4 and Table 1).
- Accordingly, a significant reduction in mean time spent in hyperglycaemia (>10.0 mmol/L) and L2 hypoglycaemia (<3.0 mmol/L) of –1.8 hours per day (p=0.003) and –0.3 hours per day (p=0.005), respectively, was also observed (Figure 4 and Table 1).
- There was no significant change in mean time spent in L1 hypoglycaemia (3.0–<3.9 mmol/L; p=0.181; Figure 4 and Table 1).
- While the mean glucose level did not change significantly, the coefficient of variation was reduced by 3.8% from the initial level of 35.9% (Table 1). This shows that the improved TIR is obtained primarily by more stable glucose levels over the day.
- In terms of bolus insulin dose (n=81), a significant increase from the baseline period to the follow-up period of 28%, to a dose of 32.1 U/day was observed. There was no significant change in mean basal insulin dose (n=22).

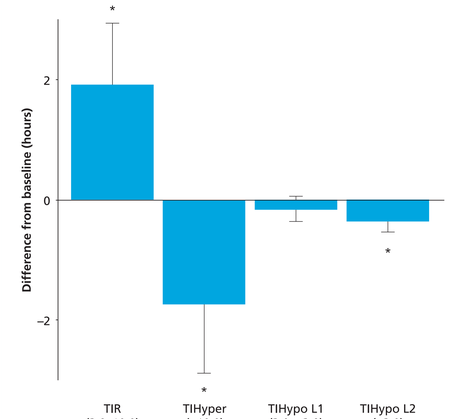
Figure 3: Patient treatment characteristics



*Interval between CGM readings. Numbers indicate numbers of patients. Seven patients did not have connected pen data at any of the CGM days studied. One patient used biphasic insulin aspart 30 that is neither considered bolus nor basal insulin in the analysis.
CGM, continuous glucose monitoring, FGM, flash glucose monitoring.

Figure 4: Mean difference in the time spent in glycaemic ranges from the baseline period to the follow-up period

Key result



*p<0.05. Estimated mean difference in time spent in glycaemic ranges with 95% CI. The difference is observed between the baseline period and the follow-up period (≥5 visits). Baseline is the period after treatment initiation but before the first visit. Analysis is based on CGM data from a 14-day interval after each visit (≥70% coverage).
CGM, continuous glucose monitoring; CI, confidence interval; TIR, time in range; TIHyper, time in hyperglycaemia; TIHypo L1, time in L1 hypoglycaemia; TIHypo L2, time in L2 hypoglycaemia. Patients above 18 years (n=94) are included.

Conclusion

- These real-world findings in patients with T1D highlight the potential benefit to glycaemic control when connected pen data contribute to the patient-HCP dialogue.
- Patients with a smart connected pen obtained more stable CGM profiles, with more time in range and less time spent in hyperglycaemia and hypoglycaemia.

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References: (**1**) Klonoff and Kerr. *J Diabetes Sci Technol* 2018;12:551–3; (**2**) Heisler *et al. J Gen Intern Med* 2002;17:243–52; (**3**) Ritholz *et al. Chronic Illn* 2014;10:303–13; (**4**) Danne *et al. Diabetes Care* 2017;40:1631–40.