A retrospective analysis of 24-month real-world glucose control for children and adolescents with type 1 diabetes using the MiniMed™ 670G insulin pump

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1 | INTRODUCTION

The MiniMed™ 670G insulin pump was the first hybrid closed-loop (HCL) system available for clinical use. Data on metabolic outcomes in children, adolescents and young adults over the first 12 months with auto-mode use of this device are available, but no data with longer follow-up have been published. We aimed to assess the metabolic outcomes in children and adolescents using the MiniMed™ 670G for 24 months.

2 | METHODS

The primary endpoint was change in glycated haemoglobin (HbA1c) levels. Continuous glucose monitoring (CGM) metrics were secondary endpoints.

This retrospective real-world study was conducted at 13 Italian paediatric diabetes clinics joining the **Italian** Society for **Pediatric** Endocrinology and **Diabetes** (**ISPED**). The study was performed in accordance with Italian law.

Prior 1-year HbA1c was calculated as the mean of the HbA1c measurements in the 12 months before initiation of 670G insulin pump use. Data were collected at baseline (at pump start and in the first 2-week run-in period with the system in manual-mode functionality), and in the prior 2-week period[1] before the visit every 6 months. Data are presented as mean ± SD, median (interquartile range), or percentage as appropriate. Further information is reported in the Supplementary file data.

3 | RESULTS

A total of 77 patients (pump start between November 2018 and February 2020) were recruited (Table 1). The supplementary file summarizes findings in patients below or above 13 years old.

TABLE 1 Features of the 77 patients included in the study cohort at initiation of MiniMed™ 670G pump use

Characteristic	Participants
Male	42 (54.5)
Female	35 (45.5)
Age at diabetes onset, years	7.0 ± 3.7
Age at MiniMed™ 670G pump initiation, n (%)	12.6 ± 3.3
7-12.9 years	46 (59.7)
13-20.9 years	31 (40.3)
TDD (n = 75), IU/kg/d	0.9 ± 0.3
Basal rate, %	48.7 ± 9.4
Pre-meal boluses, %	51.3 ± 9.4
HbA1c at baseline	
mol/mol	55 (50-64)
%	7.2 (6.7-7.8)
Prior 1-year HbA1c (n = 73)	
mmol/mol	58 ± 11
%	7.5 ± 1.1
Period on manual mode before starting the SmartGuard functionality, days	33 ± 37
Period of time on auto-mode functionality, years	2.04 ± 0.19
Prior treatment, n (%)	
MDI	30 (39.0)
MiniMed™ 640G pump	32 (41.5)
Other pump	15 (19.5)

Note: Values are reported as mean ± SD or median (interquartile range) or as number (percentage) as appropriate.
Abbreviations: MDI, multiple daily injections; n, number of patients with available data; TDD, total daily dose.

3.1 | Glycaemic control

Table 2 shows the glycaemic control results during the 24-month follow-up. At baseline, HbA1c was 55 mmol/mol (50-62 mmol/mol), higher than at 6 months (53 mmol/mol [48-60 mmol/mol]; $P = 0.005$) and 12 months (54 mmol/mol [49-63 mmol/mol]; $P = 0.042$), but not different from the values at 18 months (52 mmol/mol [51-64 mmol/mol]) and 24 months (56 mmol/mol [51-64 mmol/mol]; Figure S1). In patients with baseline values ≤58 mmol/mol, HbA1c levels did not change, but in patients with baseline values >58 mmol/mol, HbA1c levels significantly decreased after 6 (3 mmol/mol; $P = 0.006$), 12 (1.5 mmol/mol; $P = 0.013$) and 24 months (2 mmol/mol; $P = 0.017$). The baseline sensor glucose was 8.8 ± 1.1 mmol/L, with a significant decrease only at 12 months ($P = 0.004$). The baseline %CV was 33.4% (31.3-37%), higher than at 12 months ($P = 0.021$) and 24 months ($P = 0.036$).

3.2 | CGM metrics

The median time below range (TBR) was always below 4% during the study, with no statistically significant change. Time in range (TIR) was 66.1 ± 13.1% at baseline. TIR significantly improved at 6 ($P = 0.044$), 12 ($P < 0.001$) and 18 months ($P = 0.038$). Time above range (TAR; baseline 31.1 ± 14.1%) did not change during the study. TAR >250 mg/dL and TBR < 54 mg/dL did not change during the study. In patients with baseline HbA1c levels >7.5%, TIR significantly increased after 6 (+4.9%; $P = 0.021$), 12 (+9%; $P < 0.001$) and 24 months (+5.5%; $P = 0.025$). No differences were found in patients with baseline HbA1c ≤7.5%. The percentage of patients with TBR, TIR and TAR at target did not change during the follow-up. Glycaemia risk index (GRI) was 49.8 ± 18.0 at baseline, 46.8 ± 14.2 at 6 months, 44.2 ± 12.6 at 12 months (vs. baseline: $P = 0.007$), 45.2 ± 14.2 at 18 months, and 46.8 ± 15.3 at 24 months (Table 2, Figure S1).

3.3 | System usability

The proportion of time when CGM worked (%CGM) was 87.4 ± 13.4% at baseline, with no change during the study (Table 2). The HCL system was enabled for 84.8 ± 17.8% of the time at 6 months, with a decrease only at 18 months ($P = 0.032$). The frequency of system alarms was similar among the timepoints. The median number of daily fingersticks was 6.1 (4.7-7.7) at baseline, higher than at 12, 18 and 24 months ($P < 0.001$). The glucose sensor was calibrated 3.1 (2.6-3.6) times/d at baseline and less frequently at the other timepoints ($P \leq 0.02$).

3.4 | Correlation and regression analysis

Table S1 summarizes the correlation analysis results. Prior 1-year HbA1c, time in auto-mode functionality, 24-month proportion of time when the HCL was enabled (%HCL), and 24-month total daily dose (TDD) significantly predicted the 24-month HbA1c value ($R^2 = 0.632$, $P < 0.001$). The 24-month TIR was significantly predicted by baseline TIR, 24-month %CGM, age at pump start, system alarms and daily calibrations ($R^2 = 0.617$, $P < 0.001$). Baseline %CGM, age at diabetes onset and prior 1-year HbA1c value were predictors of 24-month % HCL ($R^2 = 0.471$, $P < .001$; Table S2).

4 | DISCUSSION

Our data show that HbA1c was significantly reduced up to 2 mmol/mol during the first year of treatment, but beyond 12 months no significant improvements were found. Our data confirm that the biggest decrease in HbA1c and increase in TIR occurred in patients with the highest baseline HbA1c levels. These findings are consistent with previous papers showing an HbA1c drop to between 53 and 58 mmol/mol after 3 months,[2-4] to 64 mmol/mol after 6 months,[5] and to between 54 and 56 mmol/mol after 12 months[6,7] of use. In our paper, TIR improved in parallel with HbA1c improvement, with a significant increase by 2.3% to 5.1% up to 18 months. This improvement appears to be clinically relevant to a minor extent only, although statistically significant.

TABLE 2 Hybrid closed-loop system characteristics during the follow-up

	Baseline	6 months	12 months	18 months	24 months
SG, mmol/l	8.8 ± 1.1	8.5 ± 1.1	8.5 ± 0.8[a]	8.6 ± 0.6	8.7 ± 1.1
	n = 77	n = 76	n = 75	n = 73	n = 76
%CV	33.4 (31.3-37)	33.9 (31.3-37.8)	33.1 (29.9-36)[a]	33.7 (30.0-36.7)	32.8 (30.6-35.4)[a]
	n = 77	n = 76	n = 75	n = 73	n = 76
GMI, %	7 (6.7-7.3)	7 (6.7-7.4)	6.9 (6.7-7.2)[b]	7 (6.7-7.3)	7 (6.7-7.3)
	n = 77	n = 73	n = 74	n = 72	n = 74
%CGM	87.4 ± 13.4	87.1 ± 14.8	85.9 ± 13.4	85.8 ± 15.0	82.9 ± 18.3
	n = 77	n = 76	n = 75	n = 73	n = 76
%HCL	n.a.	84.8 ± 17.8	81.9 ± 19.2	79.2 ± 24.3	79.9 ± 21.7[a]
		n = 75	n = 75	n = 73	n = 73
TBR, %	2 (1-3)	2 (1-3)	1 (1-3)	1 (1-3)	1.5 (1-3)
	n = 77	n = 76	n = 75	n = 73	n = 76
TBR < 54 mg/dL, %	0 (0-1)	0 (0-0)	0 (0-1)	0 (0-0)	0 (0-1)
TIR, %	66.1 ± 13.1	68.4 ± 11.2[a]	71.3 ± 9.0[b]	69.8 ± 11.2	67.9 ± 12.5
	n = 77	n = 76	n = 75	n = 73	n = 76
TAR, %	31.1 ± 14.1	29.2 ± 16.3	26.8 ± 9.7[b]	27.8 ± 11.6	29.5 ± 13.0
	n = 77	n = 76	n = 75	n = 73	n = 76
TAR >250 mg/dL, %	7.6 ± 7.0	7.3 ± 7.8	5.3 ± 4.1	6.5 ± 5.9	6.8 ± 6.4
HbA1c at target (<7%), %	37.7	45.3	43.2	30.7	35.1
Daily fingersticks	6.1 (4.7-7.7)	5.3 (3.9-7.6)	5.2 (3.8-6.6)[c]	4.9 (3.3-7.0)[c]	4.8 (3.2-7.2)[c]
	n = 77	n = 76	n = 75	n = 73	n = 75
Daily sensor calibrations	3.1 (2.6-3.6)	3.0 (2.4-3.4)	2.9 (2.3-3.3)[b]	2.9 (2.4-3.3)[b]	2.7 (2.3-3.2)[b]
	n = 77	n = 76	n = 75	n = 73	n = 75
System alarms (assessed over a 2-week period)	8 (5-12)	9 (4-12)	9 (4-12.75)	8 (4.5-14)	8 (5.5-14)
	n = 77	n = 76	n = 75	n = 72	n = 72
Active insulin time, h	3 (2-3)	3 (2-3)	2.75 (2-3)	2.5 (2-3)	2.5 (2-3)
	n = 77	n = 76	n = 75	n = 73	n = 76
SmartGuard mode suspensions, daily number per person	n.a.	0.10	0.11	0.10	0.11
		n = 76	n = 75	n = 72	n = 72

Note: [a] vs. baseline: $P < 0.05$; [b] vs. baseline: $P \leq 0.002$; [c] vs. baseline: $P < 0.001$.
All variables were assessed for a 14-day period.
Abbreviations: %CGM, proportion of time when CGM worked; %CV, glycaemic variability; %HCL, proportion of time when the hybrid closed-loop system was enabled; CGM, continuous glucose monitoring; GMI, glucose management indicator; n, number of patients; n.a., not assessed; SG, sensor glucose; TAR, time above range; TBR, time below range; TIR, time in range.

The straightforward difference from previous papers is that the relative decrease in HbA1c and the relative increase in TIR in this study are smaller. We suggest that the better metabolic control in our patients at baseline, in agreement with previous data,[8,9] could account for this finding. On the other hand, we have previously reported a better improvement in TIR in Italian patients treated with a different HCL system (+11% after 6 months).[10]

Similarly to previous papers reporting a decline in auto-mode use over time,[5,11,12] overall, the children and adolescents in our study presented a decrease in glucose calibrations and daily fingersticks, and thus in CGM and HCL use, confirming that the burden of technology may lead to underutilization of the system functionalities. As higher auto-mode use and lower HbA1c level are correlated,[5,12] we suggest that the progressive underutilization of system functionality accounts for lack of improvement in HbA1c at 24 months. The MiniMed™ 780G system addressed the usability issues, with fewer exits than the 670G system.[13]

The regression analysis suggests that patients with greater use of this technology at baseline have better glucose control at the end of the study. On the other hand, a lower compliance to the pump requirements (calibrations, CGM and HCL use) may worsen the glucose control. This finding confirms that greater use of system functionality allows greater improvement in glucose control.[5,14]

All these data support the key role of education in the use of technology. The patients need appropriate education and periodic reinforcement to properly use HCL and to take advantages from these systems as much as possible.

Our results confirm that the MiniMed™ 670G seems effective to reach the targeted TBR. Furthermore, the GRI values suggest that this system may reduce the overall risk of hypoglycaemia, if only to a minor extent, during the first year of follow-up. These are points in favour of the safety of this device and may reduce the psychological distress for the patients.

This study has some limitations. First, it is a retrospective study. Second, the run-in time before starting auto-mode was longer than expected (COVID-19 pandemic caused rescheduling of several appointments). Third, we were not able to assess whether the COVID-19 pandemic affected blood glucose control. The study also has two key strengths: it is a real-world study and is the first study evaluating metabolic outcomes up to 24 months.

Our data confirm that the MiniMed™ 670G system may improve metabolic outcomes overall in patients with the highest baseline HbA1c levels in the first year of utilization, with less evident benefits in the second year. The clinical significance of this improvement appears to be poor. Unfortunately, the patients reduced their use of the technology, probably because it was burdensome to use. Better blood glucose control and better use of the device at baseline play a key role in glucose management after 24 months.

AUTHOR CONTRIBUTIONS

Maurizio Delvecchio and Elvira Piccinno conceptualized and designed the study; Claudio Maffeis, Riccardo Bonfanti, Claudia Piona and Marco Marigliano made substantial contributions to interpreting the data. Stefano Passanisi, Roberto Franceschi, Gianluca Tornese, Elena Calzi, Angela Zanfardino, Giulia Patrizia Bracciolini and Alessio Galati made substantial contributions to data acquisition; Alberto Sabbion, Fortunato Lombardo, Elena Fornari, Giuseppina Salzano, Andrea Rigamonti, Francesco Scialabba, Vittoria Cauvin, Elena Faleschini, Dario Iafusco, Caterina Grosso, Cinzia Ciullo, Graziella Fichera, Irene Rutigliano and Giulia Patrizia Bracciolini were involved in clinical follow-up of the patients. Maurizio Delvecchio and Alessio Galati were involved in drafting the paper. All the authors listed on the title page and as ISPED Diabetes Study Group members approved the final version of the paper.

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DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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