

# Introduction of flash glucose monitoring in children with Type 1 diabetes: experience of a single-centre in Spain

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## 1. Background

The FreeStyle Libre flash glucose monitoring system is proven in the IMPACT and REPLACE studies<sup>1,2</sup> in adults with type 1 (T1D) or type 2 diabetes (T2D) on insulin to reduce time in hypoglycemia below 70 mg/dL by 38% (IMPACT) and 43% (REPLACE) over 26 weeks, compared to SMBG. In neither study was a significant change in HbA1c observed with flash glucose monitoring compared to SMBG. In the SELFY prospective interventional single-arm study<sup>3</sup> using the FreeStyle Libre system in 76 children and adolescents with T1D, mean HbA1c was reduced from 7.9% to 7.5% over 8-weeks compared to SMBG.

Flash glucose monitoring is now included in the Portfolio of Services of the Public Health System in Spain and Andalucía was a pioneer Spanish region in introducing flash glucose monitoring in the paediatric population. Here we report on the impact of flash glucose monitoring over 6 months on measures of glycaemic control in a paediatric T1D population being treated either with multiple daily injections of insulin (MDI) or with continuous subcutaneous infusion of insulin (CSII).

## 2. Aims

- To evaluate the relationship between change in HbA1c with treatment type (MDI vs CSII) following initiation of the FreeStyle Libre system
- To evaluate the relationship between change in HbA1c with prior metabolic control following initiation of the FreeStyle Libre system
- To evaluate the relationship between change in HbA1c with treatment type (MDI vs CSII) and prior metabolic control after starting the FreeStyle Libre system
- To evaluate the impact of the FreeStyle Libre system on measures of hypoglycaemia
- To understand the impact of daily sensor scan rates on hypoglycaemia.

## 3. Methods

We enrolled 145 paediatric T1D diabetes patients into a prospective, interventional study of the impact of the FreeStyle Libre system on HbA1c levels and on measures of hypoglycaemia. Subjects were trained in use of the FreeStyle Libre system and the LibreView data platform. Inclusion criteria were: the presence of T1D with disease duration >1 year; age 4–18 years. Patients were excluded if they were not adherent with routine clinical review or had previously used the FreeStyle Libre system. Mean age ( $\pm$  SD) of study subjects was 11.4 ( $\pm$  3.1) years and average duration of diabetes was 5.2 ( $\pm$  3.2) years. Patients were treated either with MDI (n=119) or with CSII (n=26). Metabolic control was stratified according to baseline HbA1c <7.5% (Good control; n=105) versus  $\geq$ 7.5% (Poor control; n=38).

Laboratory measurement of HbA1c was carried out at baseline, at 1, 3 and 6 months. Measures of hypoglycaemia were monitored using the LibreView platform, using the most recent 14 days of glycaemic data at 1 month, 3 months and at 6 months. Parameters measured included those accepted in international consensus guidelines for interpreting CGM data<sup>4,5</sup>:

- number of sensor scans per day;
- percentage of readings <70 mg/dL
- number of Level 1 hypoglycaemia events <70 mg/dL
- number of Level 2 hypoglycaemia events <54 mg/dL

The study was carried out in accordance with the regulations published in Boletín Oficial de la Junta de Andalucía (BOJA) for the inclusion of glucose monitoring systems in the Portfolio of Services of the Public Health System of Andalucía.

### References

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## 4. Results

**Table 1: Impact of FreeStyle Libre system on HbA1c levels in paediatric subjects with T1D on the basis of treatment type (MDI vs CSII)**

When stratifying study subjects by the type of treatment (CSII vs MDI), it was observed that in the patients on CSII therapy there was a significant and clinically relevant difference of 0.55% between the 6<sup>th</sup> and 1<sup>st</sup> month after starting the FreeStyle Libre system ( $p=0.032$ , Student's t-test, assuming homogeneity of variances).

Visit	Treatment type (CSII or MDI)	n	% HbA1c (Mean $\pm$ SD)
Baseline	CSII	26	7.13 $\pm$ 0.67
	MDI	117	7.10 $\pm$ 0.83
1 month	CSII	9	7.16 $\pm$ 0.50
	MDI	42	6.95 $\pm$ 0.84
3 months	CSII	21	6.83 $\pm$ 0.72
	MDI	87	7.25 $\pm$ 0.72
6 months	CSII	17	6.79 $\pm$ 0.55
	MDI	687	7.34 $\pm$ 0.78

**Table 2: Impact of FreeStyle Libre system on HbA1c levels in paediatric subjects with T1D stratified on basis of starting HbA1c**

Patients with a baseline HbA1c  $\geq$ 7.5% had a significant reduction in mean HbA1c at 3 months (8.11 $\pm$ 0.71% vs 7.7 $\pm$ 0.6%;  $p=0.04$ ). In contrast, those with a baseline HbA1c <7.5% showed a significant increase in HbA1c at 3 months (6.75 $\pm$ 0.48% vs 6.98 $\pm$ 0.69%;  $p=0.03$ ).

Visit	HbA1c <7.5% at baseline			HbA1c $\geq$ 7.5% at baseline		
	% HbA1c (Mean $\pm$ SD)	n	p	% HbA1c (Mean $\pm$ SD)	n	p
Baseline	6.75 (0.48)	105	0.77	8.11 (0.71)	38	0.48
1 month	6.69 (0.54)	36	0.68	7.68 (0.86)	15	0.31
3 months	6.98 (0.69)	81	0.03	7.70 (0.60)	27	0.04
6 months	7.01 (0.59)	65	0.24	7.97 (0.85)	19	0.36

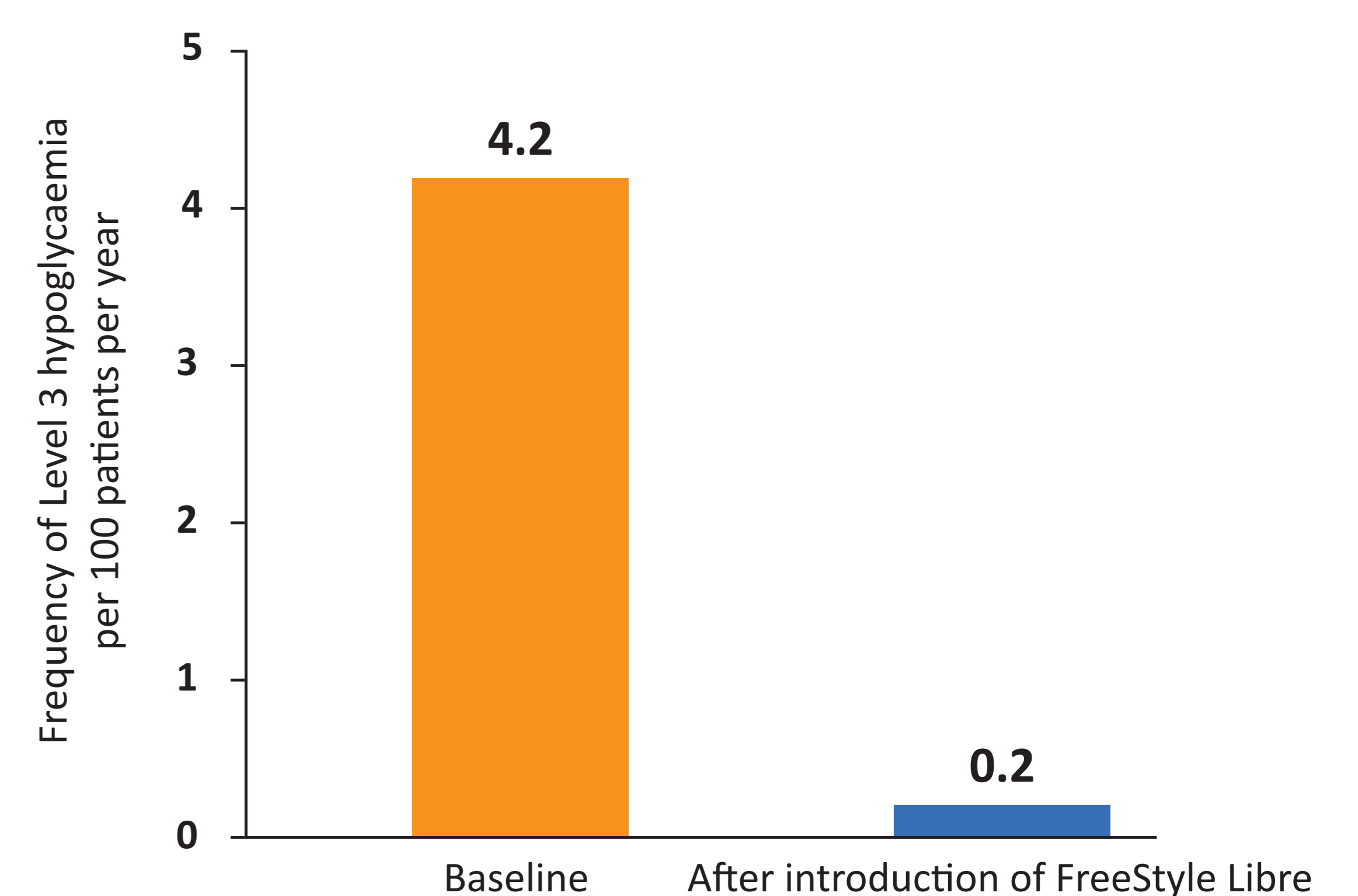
**Table 3: Change in HbA1c in paediatric subjects with T1D and baseline HbA1c  $\geq$ 7.5%, stratified on basis of treatment type**

Subjects with baseline HbA1c <7.5% showed no change in HbA1c based on treatment type (data not shown). Patients with baseline HbA1c  $\geq$ 7.5% had a significant reduction of 1.96% from baseline at 3 months with MDI therapy (9.66 $\pm$ 0.80% vs 7.70 $\pm$ 0.85%;  $p=0.04$ ). No significant change in HbA1c was seen in patients with baseline HbA1c  $\geq$ 7.5% on CSII therapy.

Visit	HbA1c $\geq$ 7.5% at baseline + CSII therapy			HbA1c $\geq$ 7.5% at baseline + MDI therapy		
	% HbA1c (Mean $\pm$ SD)	n	p	% HbA1c (Mean $\pm$ SD)	n	p
Baseline	7.93 (0.35)	8	0.34	9.66 (0.80)	38	0.21
1 month	7.47 (0.38)	4	0.31	7.68 (0.86)	15	0.19
3 months	7.60 (0.76)	5	0.27	7.70 (0.60)	27	0.04
6 months	7.56 (0.56)	3	0.21	7.97 (0.85)	19	0.23

**Figure 1. Reduced rate of Level 3 hypoglycaemia following introduction of FreeStyle Libre**

Prior to introduction of the FreeStyle Libre system, baseline data was collected from a sample of 357 patients. The rate of Level 3 hypoglycaemia (with convulsion or loss of consciousness) in the 12 months prior to starting the Free Style Libre system was 4.2 episodes per 100 patients per year. In the 12 months following introduction of FreeStyle Libre, the rate of Level 3 hypoglycaemia was reduced to 0.2 episodes per 100 patients per year.



**Table 4. Time below range and sensor scan rates.**

There was no significant change in time below range <70 mg/dL. This may be attributed to the fact that was no masked baseline and any changes would have occurred within two days of the first sensor wear. However, the frequency of Level 1 (<70 mg/dL) and Level 2 (<54 mg/dL) hypoglycaemia was lowest in subjects who scanned their sensors >10 times per day ( $p=0.05$ ).

Glycaemic	Month 1	Month 3	Month 6	p	n
% readings <70mg/dL	6.18 (6.5)	5.52 (4.56)	5.23 (4.17)	0.183	84
Number of events <54mg/dL	3.76 (4.01)	3.55 (3.70)	3.68 (3.89)	0.685	27
Number of events <70mg/dl	11.73 (8.77)	11.13 (7.80)	9.83 (6.89)	0.25	28

## Conclusions

- The FreeStyle Libre system can be beneficial in some paediatric subjects with T1D to reduce HbA1c.
- The benefits of the FreeStyle Libre are emphasised in paediatric subjects with T1D with poor metabolic control (baseline HbA1c  $\geq$ 7.5%).
- In our study, paediatric subjects with T1D on CSII therapy show a reductions in HbA1c at 6 months.
- Amongst patients with baseline HbA1c  $\geq$ 7.5% there was a significant reduction in HbA1c for those on MDI therapy.
- The rate of Level 3 hypoglycaemia is significantly reduced amongst subjects following introduction of the FreeStyle Libre system, from 4.2 to 0.2 events per 100 patient per year.
- The frequency of Level 1 (<70 mg/dL) and Level 2 (<54 mg/dL) hypoglycaemia was lowest in subjects who scanned their sensors >10 times per day.
- Additional investigation is required to identify which individuals are most likely to benefit from use of the FreeStyle Libre system.