DIABETES CLINICAL SUMMARIES

ASPIRE IN-HOME (2013): BENEFIT OF SAP WITH LGS COMPARED TO STANDARD SAP

STUDY RATIONAL

- Hypoglycaemia is a major burden for people with Type 1 diabetes. It can cause confusion, disorientation, loss of consciousness and in the worst cases coma and even death.
- Highest risk to patient is at night when they are likely to be asleep and unaware of any symptoms[1].
- Automated suspension of insulin delivery, also known as Low Glucose Suspend (LGS), in response to hypoglycaemia detected by Continuous Glucose Monitoring (CGM) when sensors glucose values fall below a pre-set threshold is designed to minimise the risk of hypoglycaemia. Sensor Augmented Pump (SAP) therapy with and without the LGS feature was evaluated in patients with nocturnal hypoglycaemia.

OBJECTIVES

- The study aimed to evaluate the clinical effectiveness of SAP therapy with the LGS feature, as compared to SAP without LGS feature, on nocturnal hypoglycaemia and HbA1c levels in patients with documented nocturnal hypoglycaemia.

DESIGN AND METHODS

- The study was a randomised controlled trial comparing SAP therapy with LGS turned ON vs SAP therapy with LGS turned OFF over 3 months. It was run in 19 sites in the USA.
- Subjects eligibility criteria: Type 1 diabetes for ≥2 years; aged 16 to 70; on CSII for ≥6 months; HbA1c value between 5.8% and 10%.
- All subjects were trained on the insulin pump and the CGM that would be used during the study.
- A 2-week run-in phase aimed to establish patients' eligibility for the study. Subjects were required to use CGM for at least 80% of the time and must have experienced ≥2 nocturnal hypoglycaemic episodes. An episode of nocturnal hypoglycaemia was defined as a sequence of sensor glucose (SG) values ≤65 mg/dL (3.6 mmol/L) lasting >20 minutes and that began between 10:00 PM and 8:00 AM.
- Subjects were randomised to either SAP therapy with LGS ON (LGS Group) or SAP therapy with LGS OFF (Control Group) for 3 months.
- Both groups had phone contacts after 1 and 4 weeks and came back to the clinic after 12 weeks for the end of study visit.
- The LGS threshold was initially set at 70 mg/dL after which the setting could range from 70 to 90 mg/dL. Subjects in the LGS Group were instructed to have the LGS feature ON between 10 p.m. and 8 a.m.; it was optional at other times.
- The primary efficacy endpoint was the Area Under the Curve (AUC) for nocturnal hypoglycaemic events. The primary safety endpoint was the change in HbA1c from randomisation to study end.

KEYPOINTS

- 37.5% reduction of nocturnal hypoglycaemia (AUC)
- 29.8% overall reduction of hypoglycaemic events
- No increase in HbA1c
- No severe hypoglycaemic events

STUDY TYPE

- Randomised Controlled Trial
- SAP with LGS vs SAP without LGS
- 3 months duration
- 247 subjects (aged 16-70) with documented nocturnal hypoglycaemia

ENDPOINTS

- Nocturnal hypoglycaemia AUC and events
- Combined nighttime and daytime hypoglycaemia AUC and events
- HbA1c levels

REFERENCE

Threshold-Based Insulin-Pump Interruption for Reduction of Hypoglycemia. Bergenstal R.M. et al. N Engl J Med 369:224-32, 2013.

Medtronic
Further, Together

FIGURE 1: Study Design

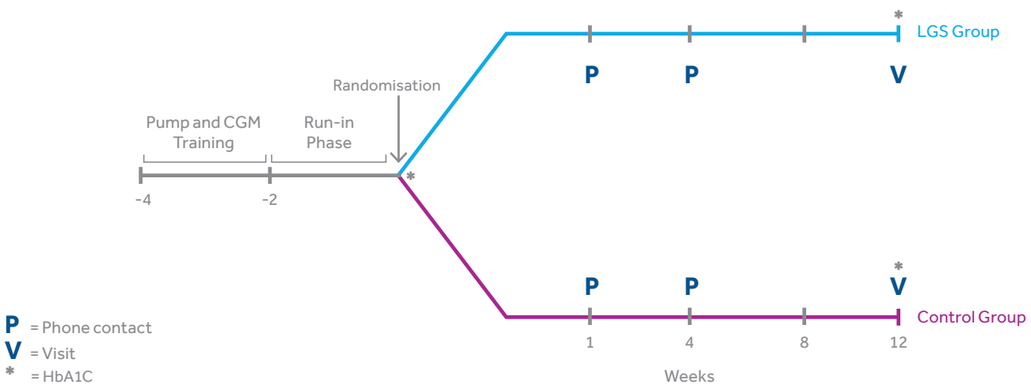
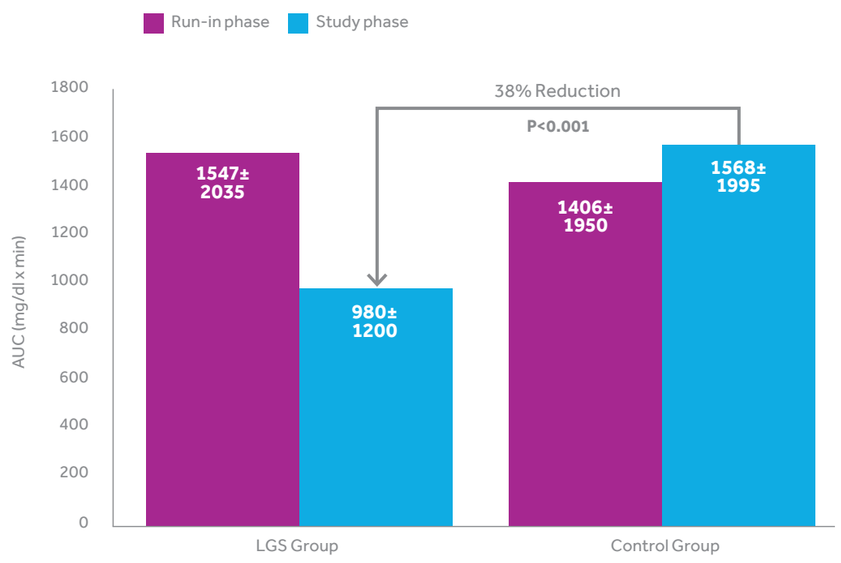


FIGURE 2: Mean AUC of nocturnal hypoglycaemia



RESULTS

247 patients were randomised: 121 in the LGS Group and 126 in the Control Group.

Nocturnal hypoglycaemia

- The mean AUC for nocturnal hypoglycaemic events was 37.5% lower in the LGS Group than in the Control Group (980 vs 1,568 mg/dLxmin respectively, p<0.001) (Figure 2).
- The rate of nocturnal hypoglycaemic events was 31.8% lower in the LGS Group that in the Control Group (1.5 vs 2.2 events per patient-week respectively, p<0.001).
- In the LGS Group, 6.0% of nocturnal SG values were <70 mg/dL, versus 10.0% in the Control Group, which represent a 40.0% reduction. The biggest reduction was observed for more severe hypoglycaemia (Figure 3):
  - 26.8% (p<0.001) reduction in SG readings 60 – 70 mg/dL
  - 41.9% (p<0.001) reduction in SG readings 50 – 60 mg/dL
  - 57.1% (p<0.001) reduction in SG readings <50 mg/dL

Combined daytime and nighttime hypoglycaemia

- The mean AUC for combined daytime and nighttime hypoglycaemic events was 31.4% lower in the LGS Group than in the Control Group (798 vs 1,164 mg/dLxmin respectively, p<0.001).
- The rate of combined daytime and nighttime hypoglycaemic events was 29.8% lower in the LGS Group that in the Control Group (3.3 vs 4.7 events per patient-week respectively, p<0.001).
- In the LGS Group, 5.3% SG values were <70 mg/dL, versus 8.1% in the Control Group, which represent a 34.6% reduction (Figure 3).

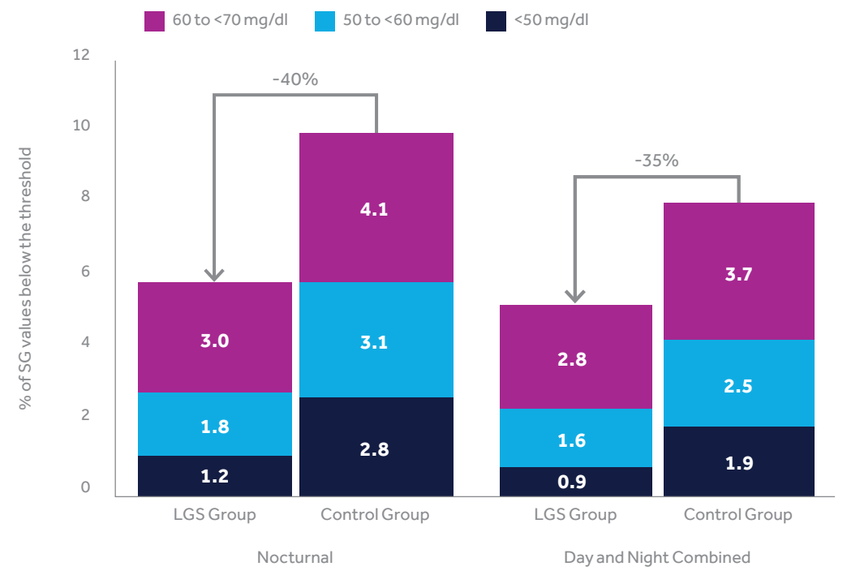
HbA1c

There was no significant change in HbA1c level from randomisation to end of the study in either group (0.00% in LGS Group vs -0.04% in the Control Group, 0.05% between groups difference).

Safety

- No severe hypoglycaemia was reported in the LGS Group; 4 subjects had a severe hypoglycaemia in the Control Group.
- No subjects had diabetic ketoacidosis.

FIGURE 3: Sensor Glucose values <70 mg/dL



CONCLUSIONS

- Sensor Augmented Pump therapy with the Low Glucose Suspend (LGS) technology was associated with significant reduction in hypoglycaemia without increasing HbA1c levels.

Additional References

1. Raju B. et al. Nocturnal hypoglycemia in type 1 diabetes: an assessment of preventive bedtime treatments. J Clin Endocrinol Metab. 2006; 91 (6); 2087-2092.