DIABETES CLINICAL SUMMARIES

STAR 3 (2010): BENEFIT OF SAP THERAPY VS MDI

STUDY RATIONAL

- Improved glycaemic control can reduce the microvascular and macrovascular complications associated with type 1 diabetes mellitus[1] and diabetes practitioners are continuously challenged to optimise glucose control while minimising hypoglycaemia.
- Sensor Augmented Pump (SAP) therapy is the combination of Continuous Subcutaneous Insulin Infusion (CSII) therapy and Continuous Glucose Monitoring (CGM). It is designed to assist patients with Type 1 diabetes in safely reaching glycaemic goals.
- Whether, and to what extent, switching directly from Multiple Daily Injections (MDI) to SAP therapy might improve metabolic control in patients with type 1 diabetes who were previously unable to reach glycaemic targets with a regimen of MDI and conventional blood-glucose monitoring is unknown.

OBJECTIVES

- The study aimed to evaluate the clinical effectiveness of Sensor Augmented Pump (SAP) therapy in HbA1c reduction compared to Multiple Daily Injection (MDI) therapy, in inadequately controlled type 1 diabetes patients.

DESIGN AND METHODS

- The study was a randomised controlled trial comparing SAP therapy vs MDI therapy over 12 months. It was conducted at 30 diabetes centres in the United States and Canada.
- Subjects eligibility criteria: Type 1 diabetes; aged 7 to 70; on MDI therapy for ≥3 months; HbA1c level between 7.4% and 9.5%; documented Self-Monitoring of Blood Glucose (SMBG) ≥4 times daily during the 30 days prior to enrolment.
- All enrolled patients received training in intensive diabetes management including carbohydrate counting and the administration of correction doses of insulin.
- Subjects were randomly assigned to SAP therapy (SAP group) or to MDI therapy (MDI group) for 12 months. The randomisation was stratified according to subjects' age (7-18 and 19-70 years) to ensure a proper balance of children and adults in each group.
- Visits were scheduled for all subjects at 3, 6, 9 and 12 months where glucose data were reviewed, therapy adjusted and HbA1c measured.
- Subjects in the SAP group started with CSII therapy alone for two weeks after which CGM was introduced. 3 additional visits were performed during the first 5 weeks to train the subjects on the insulin pump and the CGM.
- Sensor glucose values were collected in both groups for a 1-week period at baseline, 6 months and 1 year.
- The primary endpoint was the mean between-group change in HbA1c level from baseline to 12 months. Secondary endpoints included the rate of severe hypoglycaemia, area under the curve (AUC) in hypoglycaemia and AUC in hyperglycaemia.

KEYPOINTS

- 0.6% HbA1c reduction between-group
- Increased CGM usage results in greater HbA1c reduction
- Reduction in hyperglycaemia
- No increase in hypoglycaemia

DESIGN AT A GLANCE

- Randomised controlled Trial
- SAP vs MDI
- 12 months duration
- 485 subjects (aged 7-70) previously unable to achieve glycaemic control

ENDPOINTS

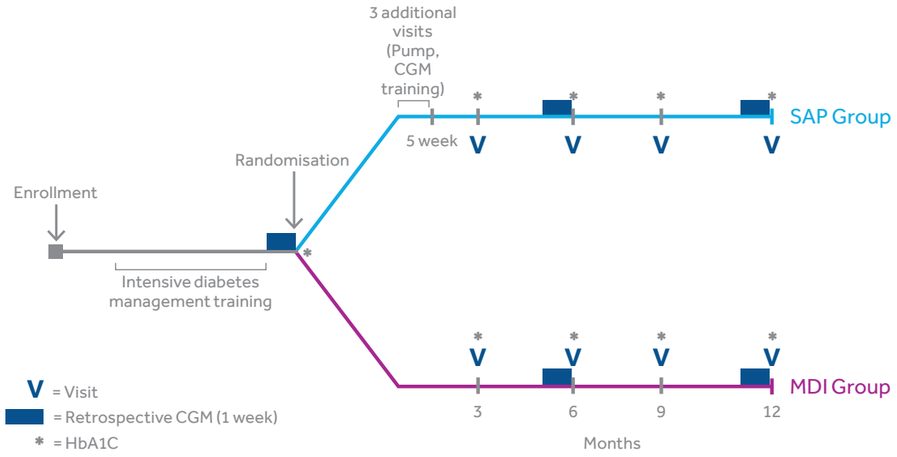
- Change in HbA1c level
- Rate of severe hypoglycaemia
- AUC in hypoglycaemia
- AUC in hyperglycaemia

REFERENCE

Effectiveness of Sensor-Augmented Insulin Pump Therapy in Type 1 Diabetes. Bergenstal RM, et al. N Engl J Med 363:311-20, 2010.

Medtronic
Further, Together

FIGURE 1: Study design



RESULTS

485 subjects (156 children aged 7-18 and 329 adults aged 19-70) were randomised to the SAP group (247 subjects) or to the MDI group (248 subjects). 443 subjects (224 in the SAP group; 219 in the MDI group) completed the study and were evaluable for the primary analysis.

HbA1c levels

- The HbA1c level at baseline was 8.3% in both groups. At 12 months, the HbA1c level decreased to 7.5% in the SAP group (0.8% reduction) as compared to 8.1% in the MDI group (0.2% reduction). This represents a 0.6% between-group reduction in HbA1c in favour of the SAP group ($p<0.001$) (Figure 2A).
- HbA1c reduction in favour of the SAP group was observed in both children, 0.5% ($p<0.001$, Figure 2B) and adults, 0.6% ($p<0.001$, Figure 2C).
- In both adults and children, the HbA1c level in the SAP group fell rapidly from baseline to 3 months and then remained lower than the MDI group HbA1c level for the remainder of the study.
- In the SAP group 27% (67 out of 244) of the subjects reached an HbA1c level of ≤7% as compared to 10% (23 out of 241) of the subjects in the MDI group ($p<0.001$).

Impact of sensor usage

Increased frequency of sensor usage was associated with greater reduction in HbA1c level at 12 months. Subjects using sensor >80% of the time had an HbA1c reduction of 1.21% from baseline to 12 months (Figure 3). This represents an HbA1c reduction of 1% in favour of this SAP sub-group vs MDI.

Hyperglycaemia

- AUC above 250 mg/dL at 12 months was reduced by 45.8% in the SAP group compared to no reduction (+0.7%) in the MDI group ($p<0.001$, Figure 4).
- With a threshold at 180 mg/dL the reduction was 36.8% in the SAP group as compared to 3.4% in the MDI group ($p<0.001$).

Hypoglycaemia

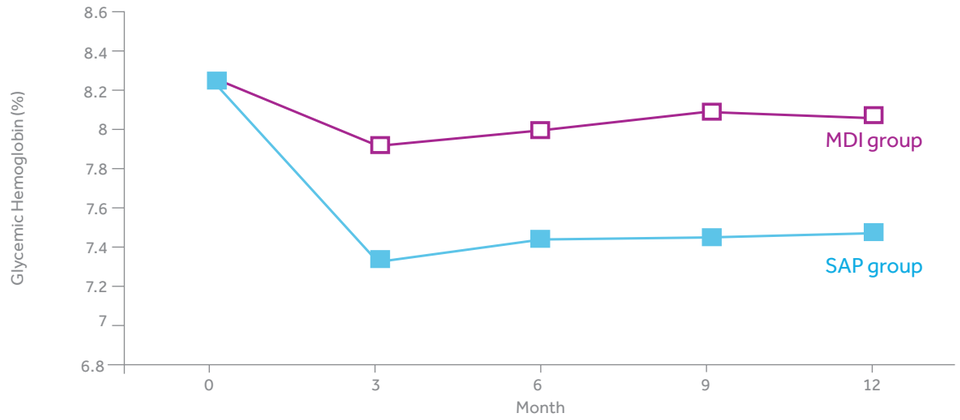
No significant difference was observed in the AUC below 70mg/dL at 12 months between both groups (0.24 vs 0.28 mg/dL/min, SAP group and MDI group respectively, $p=0.54$)

Safety

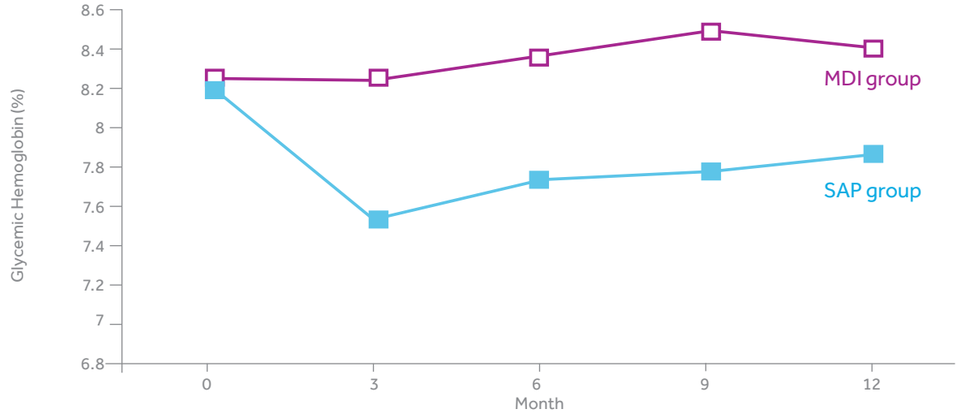
Rates of severe hypoglycaemia were similar in both groups (13.31 vs 13.48 events per subject-year in the SAP group and MDI group, respectively, $p=0.58$). Severe hypoglycaemia was defined as an episode requiring assistance and was confirmed by documentation of a blood glucose value of less than 50 mg/dL or recovery with restoration of plasma glucose.

FIGURE 2: HbA1c levels at 3, 6, 9 and 12 months

A. All Patients



B. Children, 7 -18 Yr



C. Adults, 19-70 Yr

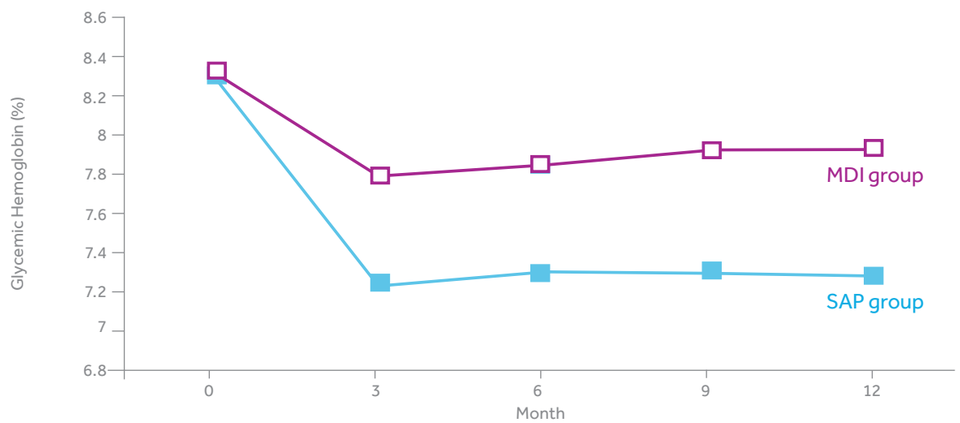


FIGURE 3: Sensor Use and Change in HbA1c levels

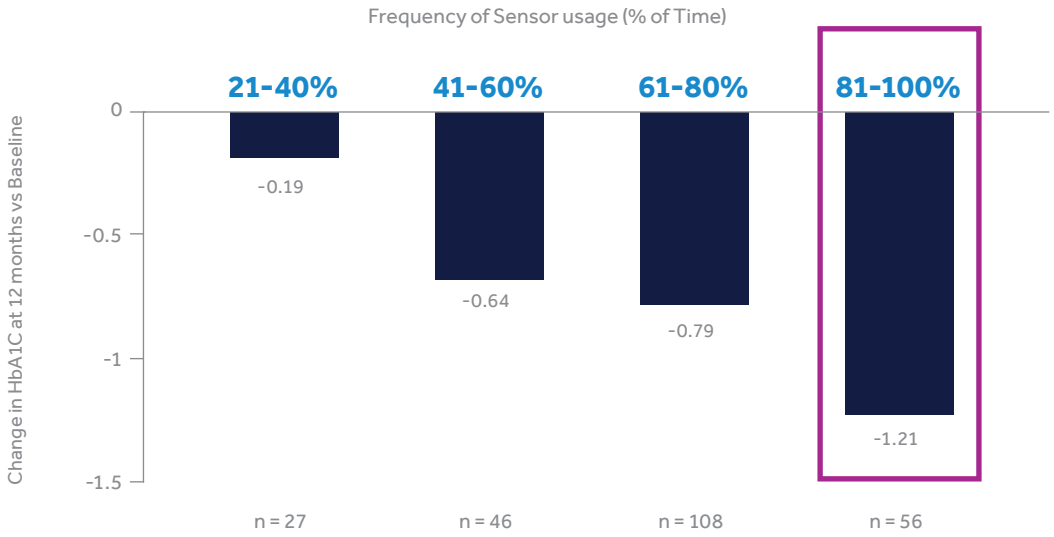
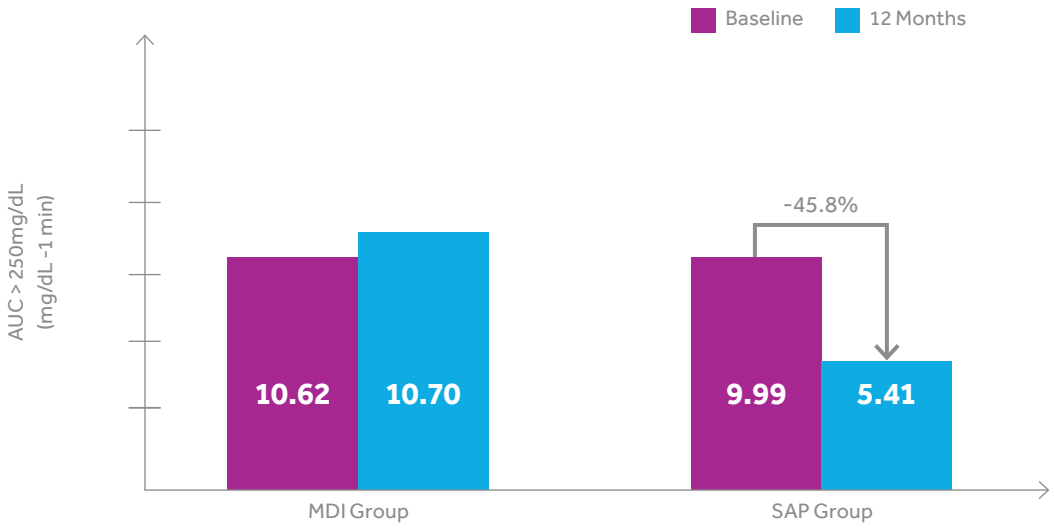


FIGURE 4: Continuous Glucose Monitoring data



CONCLUSIONS

- SAP therapy was associated with a significant HbA1c reduction from baseline to 12 months compared to MDI.
- Increased frequency of sensor usage was associated with greater reduction in HbA1c level.
- SAP therapy was associated with a significant reduction in hyperglycaemia while not increasing hypoglycaemia.

Additional References

1. Diabetic complications: the importance of glucose control. Skyler JS. Endocrinol Metab Clin North Am. 25(2):243-54, 1996.