DIABETES CLINICAL SUMMARIES

CSII LONG-TERM: LONG TERM BENEFIT OF CSII IN CHILDREN COMPARED TO INJECTION THERAPY

STUDY RATIONAL

- Delivering insulin with an insulin pump, also known as Continuous Subcutaneous Insulin Infusion (CSII) therapy, has been shown to reduce severe hypoglycaemia and to improve glycaemic control compared to Multiple Daily Injection (MDI) therapy[1].
- There is a need to further evaluate the long term effect of CSII therapy in children in conditions reflecting real life experience, as compared to injection therapy.

OBJECTIVES

- This study aimed to evaluate the long-term clinical effectiveness of CSII therapy in improving glycaemic control and reducing severe hypoglycaemia and DKA hospitalisation as compared to insulin injection therapy in children with Type 1 diabetes.

DESIGN AND METHODS

- This was an observational retrospective study with a case-control design comparing subjects on CSII therapy (CSII group) to matched subjects on injection therapy (injection group).
- Subjects eligibility criteria: Type 1 diabetes; children aged up to 18; ≥6 months experience with CSII; started CSII therapy ≥6 months after diagnosis.
- Subjects included in the study were matched to subjects on injection therapy according to age (within 1 year), duration of diabetes (within 2 years) and HbA1c at the start of CSII therapy (within 1.5%). Data were collected from the Western Australian Childhood Diabetes Database (WACDD) and were only displayed at each time point when available for both matched subjects.
- The injection group was further subdivided into 3 sub-groups according to subjects' therapy at the time their matched CSII subject started CSII therapy: injection twice daily (BD), three times daily (TDS) and ≥4 injections daily (basal/bolus) also known as Multiple Daily Injection (MDI).
- As this is an observational study where the source of data is a paediatric clinical database, the data are subject to natural attrition (e.g. subject data collection ceased when a subject left the state or were transferred to an adult clinic).
- Subjects starting CSII therapy were trained on the insulin pump and glucose monitoring and were then followed daily by telephone calls for 1 week.
- HbA1c levels were measured every 3 months. Baseline level for HbA1c was measured at the start of CSII therapy.
- Episodes of severe hypoglycaemia and episodes of hospitalisation for Diabetic Ketoacidosis (DKA) were collected throughout the study duration. Baseline rates of severe hypoglycaemia and rate of hospitalisation for DKA were measured during the 1-year period prior to start of CSII therapy.
- Severe hypoglycaemia was defined as an event resulting in convulsion or coma.
- The endpoints were the change in HbA1c levels, rate of severe hypoglycaemic episodes and rate of hospitalisations for DKA between the CSII group and the injection group.

KEYPOINTS

- 0.6% reduction in HbA1c compared to injection therapy
- 51% reduction in the rate of severe hypoglycaemia
- No increase in hospitalization for DKA

STUDY TYPE

- Observational retrospective case control study
- CSII vs injection therapy
- 7 years duration
- 345 children (aged up to 18)

ENDPOINTS

- HbA1c levels
- Rate of severe hypoglycaemia
- DKA hospitalisation

REFERENCE

Long-term outcome of insulin pump therapy in children with type 1 diabetes assessed in a large population-based case-control study. Johnson SR, Cooper MN, Jones TW, Davis EA. Diabetologia 56:2392-2400, 2013.

Medtronic
Further, Together

RESULTS

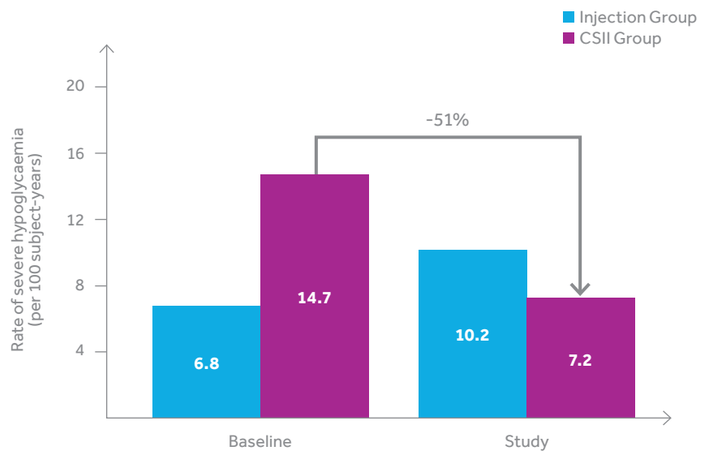
345 subjects on CSII therapy were included in the study and matched to subjects on injection therapy. The study lasted for up to 7 years with an average duration of 3.5 years per subject.

At baseline, no significant difference was observed between the CSII group and the injection group in age, duration of diabetes, HbA1c level or rate of hospitalisation for DKA. The CSII group had a significant higher rate of severe hypoglycaemia compared to the injection.

Severe hypoglycaemia

- The rate of severe hypoglycaemia was reduced by 51% in the CSII group (14.7 to 7.2 events per 100 subject-years from baseline to study period). In comparison, the rate of severe hypoglycaemia increased by 50% in the injection group (6.8 to 10.2 events per 100 subject-years from baseline to study period) (Figure 1).
- The overall rate of severe hypoglycaemia was 29% lower in the CSII group during the 7-years study period.

FIGURE 1: Rates of severe hypoglycaemia in injection group and CSII group



Hospitalisation for DKA

- The rate of hospitalisation for DKA increased in the injection group (1.1 to 4.7 events per 100 subject-years from baseline to study period) while it stayed at a similar level in the CSII group (2.0 to 2.3 events per 100 subject-years from baseline to study period).
- The overall rate of hospitalisation for DKA was 51% lower in the CSII group during the 7-years study period.

HbA1c levels

- Both the CSII therapy group and the injection group had similar HbA1c levels at baseline (8.0%). There was an overall 'between-group' reduction of 0.6% over the 7 years study duration in favour or the CSII group. This reduction was observed after 3 months, decreased after 2 years (0.3%) and then constantly increased until 7 years, with a maximum of 1% HbA1c reduction at 6 years (Figure 2).
- When compared to the MDI sub-group, the CSII group showed an overall HbA1c reduction of 0.7% over 5 years with a maximum of 1.8% reduction at 5 years (Figure 3). This sub-analysis was limited to 5 years as less than 5 matched pairs' data were available after 5 years.
- When compared to the BD/TDS subgroup, the CSII therapy group showed an overall HbA1c reduction of 0.5% over 7 years.

FIGURE 2: Mean HbA1c difference between CSII group and injection group

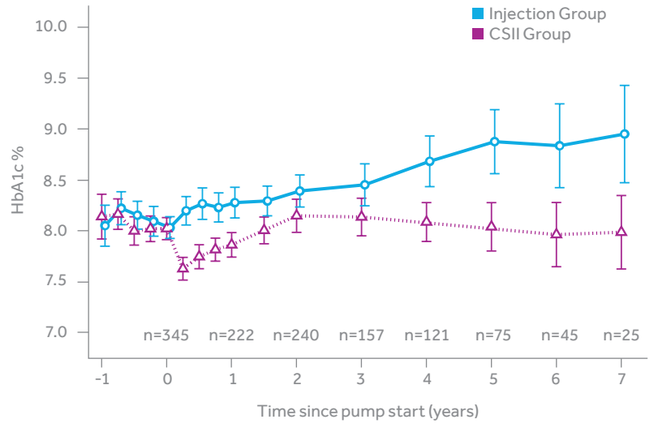
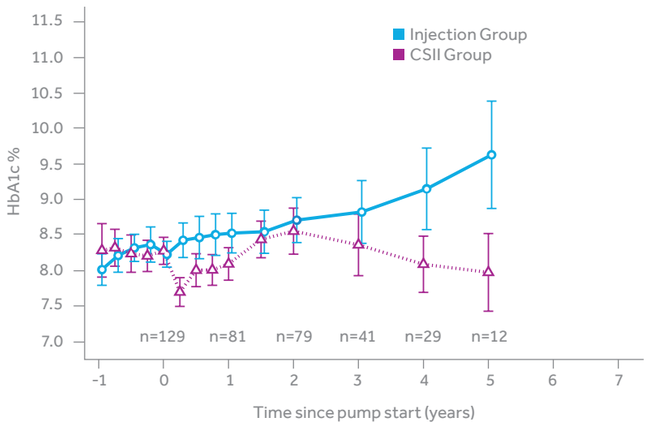


FIGURE 3: Mean HbA1c difference between CSII group and MDI sub-group



CONCLUSIONS

- CSII therapy was associated to a significant reduction in HbA1c levels compared to injection therapy. This reduction was observed after 3 months and sustained over 7 years.
- Significant HbA1c reduction was observed compared to both MDI and BD/TDS sub-groups.
- CSII therapy was associated with a significant reduction in the rate of severe hypoglycaemia compared to injection therapy.
- No significant increase in the rate of hospitalisation for DKA was observed with CSII therapy.

Additional References

1. Severe hypoglycaemia and glycaemic control in Type 1 diabetes: meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. Pickup J.C., Sutton A.J. Diabetes Medicine 25(7):765-774, 2008.