DIABETES CLINICAL SUMMARIES

CSII META–ANALYSIS: BENEFIT OF CSII VS MDI

STUDY RATIONAL

- Severe hypoglycaemia is a devastating complication of Type 1 diabetes that can cause loss of consciousness, coma and even death. It is also a significant barrier to achieving glycaemic control which is critical to minimise long-term complications[1].
- A meta-analysis combining data from recent clinical studies was performed to clarify the role of Continuous Subcutaneous Insulin Infusion (CSII) in reducing severe hypoglycaemia frequency and HbA1c levels.

OBJECTIVES

This meta-analysis aimed to evaluate the clinical effectiveness of CSII therapy in reducing severe hypoglycaemia frequency and HbA1c levels, as compared to MDI therapy.

DESIGN AND METHODS

Studies addressing all the following criteria were considered for inclusion in the meta-analysis:

- Randomised Controlled Trial (RCT) or before/after (B/A) design comparing MDI and CSII
- Evaluating severe hypoglycaemic events and glycaemic control
- Type 1 diabetes population
- CSII therapy treatment period ≥6 months
- Rate of severe hypoglycaemia with MDI therapy >10 events per 100 subject-years
- Published between 1996 and 2006

Severe hypoglycaemia was defined as that requiring third-party assistance, including unconsciousness, seizure, glucagon administration and emergency attendance or admission to hospital. Glycaemic control was assessed by HbA1c levels.

The primary endpoint was the rate ratio of severe hypoglycaemic events between MDI therapy and CSII therapy. The secondary endpoint was the mean difference in HbA1c levels between MDI therapy and CSII therapy.

KEYPOINTS

- 4.19 times less severe hypoglycaemia with CSII
- 0.62% lower HbA1c levels with CSII

STUDY TYPE

- Meta-analysis of 22 RCTs or B/A studies
- CSII vs MDI
- CSII therapy duration between 6 to 48 months
- 1414 subjects with Type 1 diabetes

ENDPOINTS

- Rates of severe hypoglycaemic events
- Difference in HbA1c levels

REFERENCE

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.

Medtronic
Further, Together

RESULTS

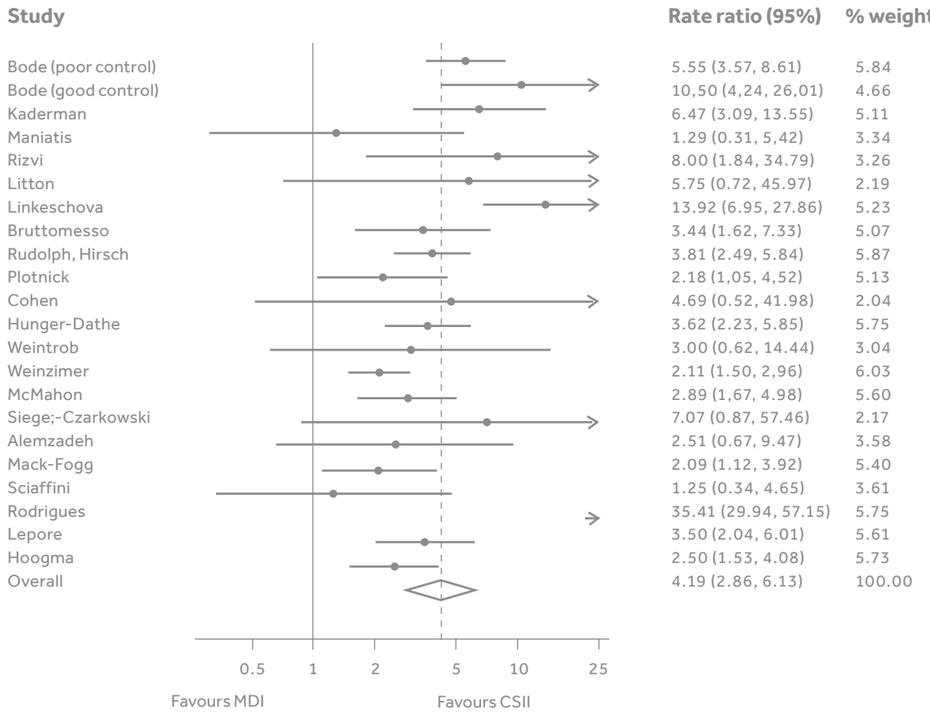
Twenty-One studies corresponding to the inclusion criteria were included in the meta-analysis. One study reported results in 2 groups (according to subjects' HbA1c level at baseline) and was considered as 2 studies. Thus a total of 22 clinical studies (10 in children and 12 in adults for a total of 1414 subjects) were analysed for the primary endpoint.

Out of these 22 studies, 3 were RCTs with a crossover design and 19 were B/A studies.

Severe Hypoglycaemia

- The mean rate of severe hypoglycaemic events with MDI therapy was 62 events per 100 subject-years. Severe hypoglycaemic events were reduced by 4.19 times with CSII therapy (4.34 and 2.89 in B/A studies and RCTs, respectively) (Figure 1).
- Larger reductions in rates of severe hypoglycaemic events were observed for higher initial severe hypoglycaemia frequency, older subjects and longer duration of diabetes.

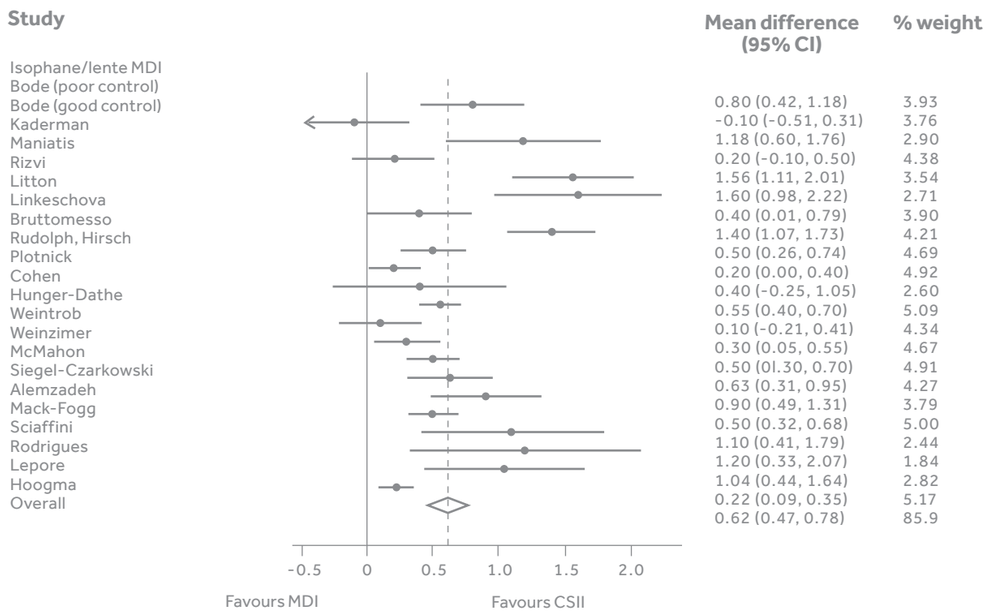
FIGURE 1: Rate ratios of severe hypoglycaemic events between CSII and MDI



HbA1c

- The mean HbA1c level was 0.62% lower with CSII therapy compared to MDI therapy (0.72% and 0.21% in B/A studies and RCTs, respectively) (Figure 2).
- Larger difference in HbA1c levels were observed for higher initial HbA1c levels.

FIGURE 2: Mean difference in HbA1c levels between CSII and MDI



CONCLUSIONS

- CSII therapy was associated with significant reduction in the rate of severe hypoglycaemia vs MDI, with the largest reduction in those with the most severe hypoglycaemia on MDI and with the longest duration of diabetes.
- CSII therapy was also associated with significant reduction in HbA1c levels vs MDI, with the largest reduction in those with the highest HbA1c level on MDI.

Additional References

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