ORIGINAL ARTICLE

Continuous subcutaneous insulin infusion versus multiple daily injections

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Abstract

Background and aim: Continuous Subcutaneous Insulin Infusion (CSII) and Multiple Daily insulin Injections (MDI) are both strategies aiming to achieve a tight glycemic and metabolic control. However, the choice between them remains controversial. The aim of the present study was to compare the efficacy of MDI (three or more injections daily) with CSII on glycemic control in patients with Type 1 Diabetes Mellitus and assess satisfaction from treatment in the CSII group.

Material and Methods: Seventeen patients with Type 1 Diabetes Mellitus on CSII (previously on MDI) and 17 patients on MDI, matched for age, gender, BMI and duration of diabetes, were retrospectively studied. Glucosylated Hemoglobin A1c (HbA1c), frequency of hypoglycaemias (assessed as self reported episodes), BMI and total units of insulin per day were evaluated at baseline and after 6 months in both groups. CSII group completed a questionnaire concerning motive for treatment selection, advantages, deficiencies and inconvenience at the end of the study. Satisfaction from treatment was assessed with a scale from 0 to10.

Results: CSII group had more hypoglycaemic episodes at baseline than MDI group (16.2±2.8 vs 2.8±1.3, $p<0,001$). HbA1c (8.4±0.5 before vs 7.3±0.4 after, $p<0.05$) and total hypoglycaemic episodes per month (16.2±2.8 before vs 8.7±2.3 after, $p<0.05$) significantly decreased in CSII group 6 months after baseline. On the contrary, total hypoglycaemic episodes per month were increased in MDI group (2.8±1.3 before vs 10.8 ±2, 6 after, $p<0.05$) in order to maintain HbA1c levels. No significant differences were observed in BMI in both groups. Total insulin demands were reduced in the CSII group (49.4±3.3 before vs 39.0±4.6 after, $p<0.05$) and remained unchanged in MDI group. None of the patients discontinued CSII therapy, while overall satisfaction rate in this group was high. The main motive for CSII selection was frequent hypoglycaemic episodes and glucose fluctuations (10/17). The majority of patients expressed their wish for incorporating glucose trend indicator and/or continuous glucose measurement into pump and reducing pump size (15/17). Most commonly stated advantage was improved flexibility, followed by greater freedom and decreased sense of physical restrictions (10/17). Inconvenience mainly derived from alarm malfunction and catheter or needle occlusion and was reported from a minority of patients (4/17).

Conclusion: CSII group reported more hypoglycaemias than MDI group at baseline but 6 months later had significantly less hypoglycaemic events, while on the contrary, MDI group 6 months after baseline had more frequent and more severe hypoglycaemias. Although baseline hypoglycaemias are not equal between the two groups, we can assume that CSII group achieved less hypoglycaemic events along with significant reduction in HbA1c while utilising less insulin units. Hippokratia 2009; 13 (2): 93-96

Key words: continuous insulin infusion; diabetes mellitus; hypoglycaemia; HbA1c; insulin; insulin pump, intensified insulin treatment

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Intensive insulin therapy has been documented by Diabetes Control and Complications Trial (DCCT) (1) and U.K Prospective Diabetes Study (UKPDS)[2] as the cornerstone for tight glycemic control leading in less long-term complications. Advances in technology have allowed individuals with diabetes to choose insulin delivery modes in order to achieve tight glycemic control: Multiple Daily insulin Injections (MDI) or Continuous Subcutaneous Insulin Infusion (CSII). The magnitude of benefit and appropriateness of each mode are still an issue of debate. Both intensified modes of treatment require training, motivation and ability to adjust treatment needs in everyday life. The limitations for both schemes are set[3,4].

Disadvantages of MDI include: self monitoring blood glucose (SMBG), self regulation of insulin dose prior to physical activity and meals, in case of holidays and illness; actions in case of hypoglycaemia or hyperglycaemia, which can affect treatment goals.

On the other hand, CSII increase the cost and self care demands comparing to MDI.

Guidelines for patient selection for a CSII trial have been set, addressing the four main problems (frequent unpredictable severe hypoglycaemia, elevated glucosylated haemoglobin A1c (HbA1c), glycemic fluctuations and a marked dawn phenomenon)[3]. Factors as local resources, patient preferences and expertise may affect decision for treatment selection[3]. Given the complexity of schemes and prerequisites, assessment of quality of life, satisfaction from treatment and effectiveness is necessary.

The objective of this study was to compare the glycemic control and hypoglycaemias after CSII or MDI in patients with Type 1 Diabetes Mellitus (T1DM) and assess satisfaction from treatment in CSII group.

Material and Methods

This was a retrospective study conducted in an outpatient basis at the Diabetes Centre of Hippocratio General Hospital, Thessaloniki. Patients previously on MDI were put on CSII (CSII group), whereas others remained on MDI (MDI group) with non-randomized selection. Consent was required by the patients subsequently treated with MDI and CSII before insulin pump treatment. MDI group continued to use human insulin analog (lispro/aspart-detemir/glargine) and human insulins (actrapid/regular, NPH/Protaphane).

The groups were matched for age, gender, body mass index (BMI) and duration of diabetes. Newly diagnosed T1DM (6 months before baseline) and pregnant women were excluded. HbA1c, frequency and severity of hypoglycaemic episodes (self-reported), BMI and total units of insulin per day were evaluated for both groups at baseline and after 6 months for both groups. Major hypoglycaemia was defined by requirement of third party assistance, whereas minor hypoglycaemia as a self-controlled condition.

CSII group completed a questionnaire concerning motive for treatment selection, advantages, deficiencies and inconvenience at the end of the study. Satisfaction from treatment was assessed with a scale from 0 to10.

Statistical analysis

Numeric data are presented as mean ± standard error of the mean. Categorical data are presented as numbers and/or percentages. Chi-square or Fisher's exact test were used to compare categorical variables between or within the groups. Mann-Whitney test was used to identify differences between the two groups in cases of numeric variables. Wilcoxon Signed Ranks Test was used to identify differences within each group in cases of numeric variables. A p value less than 0.05 was considered statistically significant in all tests. Statistical analysis was performed with SPSS 13.0 for Windows (SPSS Inc., Chicago, Illinois, USA).

Results

Thirty-four patients with T1DM were totally reviewed. Seventeen (12 women and 5 men) patients were subsequently treated with MDI and CSII, whereas 17 (12 women, 5 men) continued to be treated with MDI. None of the patients discontinued CSII therapy. Data of both CSII and MDI groups at baseline and at the sixth month are presented in Table 1. CSII group had more hypoglycaemic episodes (major, minor, total) at baseline than MDI group. HbA1c and total hypoglycaemic episodes per month significantly decreased in CSII group at 6 months. On the contrary, hypoglycaemic episodes (major, minor, total) were increased in MDI group trying to retain HbA1c levels. Total insulin demands were significantly reduced in CSII group and remain unchanged in MDI group. No significant differences were observed in BMI in both groups. Overall satisfaction rate in CSII group was high (8.1±0.3).

CSII group questionnaire

The main motive for CSII selection was frequent hypoglycaemic episodes and glucose fluctuations (10/17). The majority of patients expressed their wish for incorporating glucose trend indicator and/or continuous glucose measurement into pump and reducing pump size (15/17). Most commonly stated advantage was improved flexibility, followed by greater freedom and decreased sense of physical restrictions (10/17). Inconvenience mainly derived from alarm malfunction and catheter or needle occlusion and was reported from a minority of patients (4/17).

Discussion

CSII group had lower HbA1c combined with reduced rate of hypoglycaemia at the end of the study, suggesting lower glycemic variability which is a major issue when attempting to tighten control with MDI[4-7]. Achieving the lowest possible HbA1c level without frequent or severe hypoglycaemia could be defined as quality diabetes management. Moreover, lower HbA1c is expected to reduce long-term complications in a certain number of patients. Total insulin demands were fewer in the CSII group after 6 months compared to baseline, resulting in less hyperinsulinemia, which according to literature might additionally lead in atherosclerosis rate reduction[8,9].

Careful patient selection is widely recognized as an important factor in treatment with CSII and may have biased the results of the study[10]. Patients who choose CSII usually are motivated, they often reevaluate their previous strategies for diabetes management, including learning new skills, increasing awareness of insulin to carbohydrate ratios, monitoring blood glucose values more frequently, all of which result in better glycemic control and potentially affect the quality of life[11].

Satisfaction rate from pump was rather high. Concerning inconvenience from CSII treatment, practical matters were raised regarding advances in technology that would help simplify glucose control (trend indicator

and/or continuous glucose measurement, size of pump) and improve utility of pump-especially during summer. Relative disadvantages of CSII compared to MDI include extra cost and supervision, although CSII may be cost effective when improved quality of life and reduced tissue complications are taken into account[12].

Patients that are well controlled, without hypoglycaemic problems on MDI, may receive no significant benefit from treatment change, regarding metabolic control, but lifestyle indications such as varied work shifts, desire for flexibility and inconvenience from multiple daily injections, can affect decision for switching from MDI to CSII.

Our study involved patients both on insulin analogs and human insulins. Modern insulin analogs can contribute in improving glycemic control according to literature[13-16]. Comparative studies concerning their use in CSII and MDI along with continuous glucose monitoring would provide stronger evidence regarding patient selection and optimal benefit.

Limitations of the study are: retrospective analysis; MDI group used both insulin analogs and human insu-

Table 1: Baseline and final data of both MDI and CSII groups.

	MDI Group	**CSII Group**	**p-value (*)**
N (Male)	17 (5)	17 (5)	1.000
Age	30.4±1.8	31.6±2.0	0.743
Years after diabetes diagnosis	14.6±2.2	14.8±2.2	0.822
HbA1c before	8.8±0.6	8.4±0.5	0.782
HbA1c after	7.9±0.4	7.3±0.4(a)	0.127
BMI before	24.6 ± 0.9	26.8±2.8	0.931
BMI after	25.0±0.9	27.4±2.8	0.973
Insulin Units before	49.4±4.8	49.4±3.3	0.717
Insulin Units after	49.6±4.4	39.0±4.6(a)	0.082
Hypoglycaemias before	5 (29%)	16 (95%)	0.001
Hypoglycaemias after	11 (65%)(a)	14 (82%)	0.462
Major Hypoglycaemias before	1 (6%)	11 (65%)	0.002
Major Hypoglycaemias after	7 (41%)(a)	8 (47%)	0.951
Minor Hypoglycaemias before	5 (29%)	16 (95%)	0.001
Minor Hypoglycaemias after	10 (59%)(a)	11 (65%)(a)	0.759
Total Hypoglycaemias/Month before	2.8±1.3	16.2±2.8	<0.001
Total Hypoglycaemias/Month after	10.8±2.6 (a)	8.7±2.3(a)	0.486
Major Hypoglycaemias/Month before	0.0±0.0	4.0±1.2	0.001
Major Hypoglycaemias/Month after	2.8±0.9(a)	2.8±1.4	0.502
Minor Hypoglycaemias/Month before	2.8±1.3	12.2±2.2	0.002
Minor Hypoglycaemias/Month after	8.1±1.8(a)	5.9±2.0	0.204
Satisfaction (#)		8.1±0.3	

Data are presented as mean ± standard error of the mean for numeric and number (percentage) for categorical variables
(*): p-value between groups (Mann-Whitney test for numeric and chi-square test or Fisher's exact test for categorical variables)
(a): p<0.05 within groups (before vs. after) (Wilcoxon signed ranks test for numeric and chi-square test or Fisher's exact test for categorical variables)
(#): Satisfaction was measured only in CSII group. A 0 to 10 categorical scale was used (0=no satisfaction after the pump; 10=maximum satisfaction after the pump)
Abbreviations: BMI: Body Mass Index; CSII: Continuous Subcutaneous Insulin Infusion; HbA1c: Glucosylated Hemoglobin A1c; MDI: Multiple Daily insulin Injections; N: Number of patients

lins; CSII group utilized different pumps (Deltec Cosmo, Roche, Medtronic); and baseline hypoglycaemias were not equal between two groups.

In conclusion, CSII group reported more hypoglycaemias than MDI group at baseline but 6 months later had significantly less hypoglycaemic events, while on the contrary MDI group 6 months later had more frequent and severe hypoglycaemias. Although baseline hypoglycaemias are not equal between the two groups, we can assume that CSII group achieved less hypoglycaemic events along with significant reduction in HbA1c while utilising less insulin units.

References

1. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993; 329: 977-986
2. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. Lancet. 1998; 352: 837-853
3. Pickup J, Keen H. Continuous subcutaneous insulin infusion in type 1 diabetes. BMJ 2001; 322: 1262-1263
4. Pickup J, Keen H. Continuous subcutaneous insulin infusion 25 years: evidence base for the expanding use of insulin pump therapy in type 1 diabetes. Diabetes Care 2002; 25: 593-5988
5. Pickup JC: Are insulin pumps underutilized in type 1 diabetes? Yes. Diabetes Care 2006; 29: 1449-1452
6. Pickup J, Mattock M, Kerry S. Glycemic control with continuous subcutaneous insulin infusion compared with intensive insulin injections in patients with type 1 diabetes: meta-analysis of randomized controlled trials. BMJ 2002; 324: 1-6
7. Linkeschova R, Raoul M, Bott U, Berger M, Spraul M. Less severe hypoglycaemia, better metabolic control and improved quality of life in type 1 diabetes mellitus with continued subcutaneous insulin infusion (CSII) therapy: an observational study of 100 consecutive patients followed for a mean of 2 years. Diabet Med 2002; 19: 746-751
8. Hunger-Dathe W, Braun A, Muller UA, Schiel R, Femerling M, Risse A. Insulin pump therapy in patients with type 1 diabetes mellitus: results of the nationwide Quality Circle in Germany (ASD) 1999-2000. Exp Clin Endocr Metab 2003; 111: 428-434
9. Stout RW. Insulin and atheroma: 20-year perspective. Diabetes Care 1990; 13: 631-654
10. Retnakaran R, Hochmann J, DeVries H, et al. Continuous subcutaneous insulin iInfusion versus multiple daily injections: the impact of baseline A1c.Diabetes Care 2004; 27: 2590-2596
11. Pickup JC, Kidd j, Burmiston S, Yemane N. Determinants of glycemic control in type 1 diabetes during intensified therapy with multiple daily insulin injections or continuous subcutaneous insulin infusion: importance of blood glucose variability. Diabete Metab Res Rev 2006; 22: 232-237
12. Scuffham P, Carr L. The cost effectiveness of continuous subcutaneous insulin infusion compared with multiple daily injections for the management of diabetes. Diabet Med 2003; 20: 586- 593
13. Raskin P, Guthrie RA, Leiter L, Riis A, Jovanovic L. Use of insulin aspart, a fast acting insulin analogue, as the mealtime insulin in the management of patients with type 1 diabetes. Diabetes Care 2000; 23: 583-588
14. Ciofetta M, Lalli C, Del Sindaco P, et al. Contribution of postprandial versus interprandial blood glucose to HbA1c in type 1 diabetes on physiologic intensive therapy with lispro insulin at mealtime. Diabetes Care 1999; 22: 795-800
15. Home P, Bartley P, Russell-Jones D, et al. Insulin detemir offers improved glycemic control compared to NPH insulin in people with type 1 diabetes. Diabetes Care 2004; 27: 1081-1087
16. Warren E, Weatherley-Jones E, Chilcott J, Beverley C. Systematic review and economic evaluation of a long acting insulin analogue, insulin glargine. Health Technol Assess 2004; 8: 1-57