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Original Research Article

Prospective study of comparing efficacy of Continuous Subcutaneous Insulin Infusion of Insulin Aspart versus Multiple Daily Injection of Insulin Aspart/Insulin Glargine in patients of Type 1 Diabetic mellitus

Rakesh Kumar Shahi[1*], Rajendra Rai[2], P Nigam[3]

[1]Professor of Medicine, B.R.D Medical College, Gorakhpur, UP, India
[2]Assistant professor, B.R.D Medical College, Gorakhpur, UP, India
[3]Retired Professor, B.R.D. Medical College, Gorakhpur, UP, India

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Abstract

Background: Intensive insulin therapy is an aggressive treatment approach to control the blood sugar levels of diabetic patient. Multiple daily injection (MDI) therapy and continuous subcutaneous insulin infusion (CSII) are current methods of it. Intensive insulin therapy requires close monitoring of blood sugar levels along with multiple doses of insulin.**Aims and Objective:** To compare the CSII of insulin aspart with MDI of insulin aspart / insulin glargine in type 1 diabetic (T1DM) patients previously treated with CSII.**Materials and Methods:** Eighty T1DM patients were randomly selected. Initially for first week all subjects were kept on insulin aspart by CSII. After one week 40 subjects shifted to MDI therapy i.e. insulin aspart before meal and insulin glargine at bedtime and 40 subjects remained with CSII. After 5 weeks of first treatment subjects were shifted to the alternate treatment for 5 weeks. During the last week of each treatment blood glucose was monitored for 48 to 72 h continuously.**Results:** Mean serum fructosamine levels were significantly lower after CSII therapy than after MDI therapy (343 ± 47 vs. 355 ± 50 μmol/l, respectively; P = 0.0001). Continuous glucose monitoring profiles over a 24-h time period showed that glucose exposure was 24 and 40% lower for CSII than MDI. Hypoglycemic episodes were reported as 92% in CSII and 94% in MDI.**Conclusion:** Subject on CSII therapy with insulin aspart showed lower glycemic exposure without enhanced risk of hypoglycemia, as compared to the subjects on MDI with insulin aspart and insulin glargine.

Keywords: Hypoglycemic episodes, Basal insulin, bolus insulin, intensive insulin treatment.

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Introduction

Multiple daily injection (MDI) therapy and continuous subcutaneous insulin infusion (CSII) with an external pump are prominent ways of intensive insulin therapy (IIT) for diabetes mellitus.

**Correspondence*
Dr. Rakesh Kumar Shahi
Professor of Medicine, B.R.D Medical College, Gorakhpur, UP, India
E- mail: drrkshahigkp@gmail.com

Multiple daily injection (MDI) therapy and continuous subcutaneous insulin infusion (CSII) with an external pump are prominent ways of intensive insulin therapy (IIT) for diabetes mellitus. MDI therapy included the bolus injection of short or rapid-acting insulin at each meal, along with long acting insulin once or twice a day for basal insulin coverage. [1] Rapid-acting insulin analogue are administered as meal-time boluses to control the postprandial glycemic excursions are proven to be more effective than human insulin.[1] The long-acting insulin analogue, insulin glargine has long pharmacodynamics that makes it suitable to use as a basal insulin. [2]CSII therapy is getting popularity due

to its established efficacy, improved pump technology and patient preference. Sometimes patients on CSII therapy discontinuesit temporarily because of pump malfunction, skin problems or physical activity. During such periods, type 1 diabetic patients (T1DM) switching to MDI therapy could continue to use insulin aspart as the mealtime insulinand could use insulin glargine as the basal insulin. [3]Past researches have proven that the CSII is equivalent to and a lot more effective than MDI therapy. The use of an analogue only MDI regimen consisting of basal glargine and meal time rapid-acting analogue has been nick named as "poor man's pump. [3]

Hence, in present study we tried to compare CSII of insulin aspart with MDI of insulin aspart / insulin glargine in T1DM patients previously treated with CSII

Material and Method

It was a cross sectional observational study which ran for 10 weeks. It was divided in to two periods during which outcomes of CSII therapy on T1DM patients were compared with outcomes of MDI therapy in two 5-weeks treatment periods. All 80 subjects of this study were T1DM patients.A written informed consent was obtained before the start of the present study. All patients were adults of age 18 years or more, having body mass index (BMI) less than or equal to 41 kg/m^2 and glycated hemoglobin (HbA1c) ≤9%. All subjects were formerly treated with CSII for at least 100 days before the sampling. Subjects with weakened hepatic, weakened renal function, decreased cardiac function, hypoglycaemia or frequent hypoglycaemia were excluded from the study. Pregnant, breast-feeding or not practicing contraception were also excluded. In a first week of study subjects were switched from use of their CSII insulin to insulin aspart. The mealtime insulin coverage with insulin aspart during MDI and CSII treatments were adjusted based on the carbohydrate counting and a pre-prandial blood glucose levels. During therapy cross-over subjects were either emained on CSII with insulin aspart or were swapped to MDI therapy using a single basal bedtime injection of insulin glargine.Overall glycemic control in subjects was assessed by fructosamine measurements taken at the beginning and end of each treatment period. The normal fructosamine level range from 0 to 285μmol/l. HbA1c was recorded at the beginning and end of the study. During the last week of each treatment period (5 week each), subjects were kept on continuous monitoring to keep track of blood glucose. General physical examinations were conducted at the beginning and end of the study and critical situations were monitored during the study. Hypoglycemic episodes were monitored as minor hypoglycaemic episodes (asymptomatic blood glucose measurement <50 mg/dl) and major hypoglycemic episodes (blood glucose <50 mg/dl).All the data analysis was [performed using IBM SPSS ver. 20 software. Frequency distribution and cross tabulation was used to prepare the tables. Quantitative data is expressed as mean ± standard deviation (SD). Student t test was used to compare the means. P value of <0.05 is considered as significant.

Results

Mean HbA1c at the end of the 10^{th} week was similar as at the end of each therapy period i.e. at the time of CSII to MDI shifting it was 7.3±0.7% and at MDI to CSII shifting it as 7.1± 0.7% (P>0.05). It shows that patients have maintained the overall glycemic control during both therapy periods.

At the end of study, combined HbA1c value (7.2 ± 0.7) of all the patients was significantly lower than the baseline value of 7.5± 0.8%.

Total daily insulin doses taken by subjects in both CSII and MDI treatments were similar as their baseline daily insulin dose.

Table 1: Comparing mean fructosamine (μmol/l) levels

Treatment Sequence	Baseline	CSI	MDI
CSI to MDI	349± 43	350± 45	358± 48
MDI to CSI	343±47	332± 47	347± 49

Data is expressed as mean±SD, MDI; multiple daily injection, CSII; continuous subcutaneous insulin infusion

Table 2: Comparing daily insulin dose (units) requirement

Treatment Sequence	Baseline	CSI	MDI
CSI to MDI	42.1± 17.7	42.2±18.9	45.9± 18.1
MDI to CSI	41.5± 16.9	39.4± 17.6	46.1± 20.5

Data is expressed as mean ± SD, MDI; multiple daily injection, CSII; continuous subcutaneous insulin infusion

Out of 80 patients, 74 had experienced the hypoglycemic episodes during the CSII treatment and 73 during the MDI therapy ($p>0.05$). Five major hypoglycemic episodes were reported; two in CSII-treated patients and three in MDI-treated subjects.

Discussion

Intensive diabetes management can be done either with the CSII or with MDI. Intensive diabetes management required to achieve near normal glycemia, to avoid short-term crises such as hypoglycemia requiring third part assistance or intervention, to minimize longterm complications and to improve the quality and length of life in persons suffering from diabetes. [4]Disadvantages of MDI are the need for patients to take three or even more injections per day by syringe or pen, resulting in poor compliance, and to use modified insulin intermediate or long acting insulins that must be injected to reach basal concentration of insulin to keep blood glucose within normal limits between meals. It has been clearly shown that absorption of modified insulin varies from 19% to 55% in the same individual, which could be the reason for blood glucose variability. [5]However, the absorption of short-acting insulins that are used in CSII varies by less than 3% daily. As the result of CSII insulin pump therapy and use of a continuous glucose sensor, achievement of the main goals in diabetes treatment could rather become an achievable task. [6, 7]In current study, during the 5-week cross-over therapy HbA1c wasn't changed significantly in patients and can't be used for concluding the efficacy of treatment. Though the considerably lower fructosamine values and significantly lower glucose during the CSII treatment shows that the CSII therapy with insulin aspart provides better glycemic control than MDI therapy with insulin aspart and insulin glargine.CSII permits the regulation of night time basal insulin rate and therefore it have advantage over MDI therapy by providing the ability to control the dawn phenomenon and restrain the exacerbation of postprandial hyperglycemia at breakfast. [8, 9]Cross sectional nature was the main limitation of the present study; a large randomized clinical trial is needed to strengthen the present study findings.

Conclusion

CSII was a more optimal therapy than MDI, resulting in lower glycemic exposure without an increased risk of hypoglycemia. To conclude CSII therapy with insulin aspart provides better glycemic control as compared to the MDI therapy with insulin aspart and insulin glargine. Statistical mean of fructosamine calculated after the CSII treatment for all subjects was considerably lesser than the calculated mean after the MDI therapy.

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