Effects of Continuous Subcutaneous Insulin Infusion on Glycaemic Control and Acute Complications in Young People with Type 1 Diabetes in Bangladesh

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Keywords

Continuous subcutaneous insulin infusion · Type 1 diabetes · Glycaemic control · Young people · Bangladesh

Abstract

Objective: The objective of this study was to assess the effects of continuous subcutaneous insulin infusion (CSII) therapy on glycaemic control and acute complications in children, adolescents, and young adults with type 1 diabetes mellitus (T1DM). **Methods:** The prospective observational study was done in patients on multiple daily injection (MDI) switching to pump system. All patients were followed at the Paediatric Diabetes Clinic at BIRDEM Hospital. They were trained on carbohydrates counting and started on continuous basal insulin infusion in addition to meal and high blood glucose correction insulin boluses. They were followed on insulin pump therapy for a 6-month period. **Results:** Twenty patients were analysed, from baseline to visit 2 after 6 months. The patients included in the study had T1DM for a mean duration of 4.7 ± 3.1 years. The age ranged from 3 to 25 years (mean 13.7 ± 6.1). There was 1% reduction in haemoglobin A1c (HbA1c) after 6 months, though it did not reach the statistical significance ($p = 0.084$). There was sig-

nificant reduction of mean fasting blood glucose level 13.4 ± 7.0 versus 6.9 ± 1.6 mmol/L ($p = 0.001$), total insulin requirement ($p = 0.043$), frequency of hypoglycaemic episodes ($p = 0.006$), and diabetic ketoacidosis ($p = 0.002$) events during CSII therapy. **Conclusion:** In our study, we found that switching young T1DM patients from MDI to insulin pump had been effective with achievement of a reduction in fasting blood glucose, HbA1c, and acute complications.

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Introduction

Continuous subcutaneous insulin infusion (CSII) therapy has been used to treat diabetes since the late 1970s [1–3]. The increasing use of insulin pump therapy over the last 15 years, particularly in children, has been driven by improvements in pump technology and the availability of insulin analogues, along with the results of the Diabetes Control and Complications Trial (DCCT), which established the benefit of improved glycaemic control [4, 5]. The advantage of CSII is its ability to better mimic physiological insulin release. It is able to closely simulate the normal pattern of insulin secretion, namely, continu-

ous 24-h adjustable “basal” delivery of insulin upon which are superimposed prandial “boluses,” which may provide a more efficient supply of insulin to the tissues and minimize the risk of hypoglycaemia events [6, 7]. In addition, CSII offers the possibility of more flexibility and more precise insulin delivery than multiple daily injection (MDI). Various studies in paediatric patients showed that there were improvements in haemoglobin A1c (HbA1c), along with lower glycaemic variability, less complication events and improved long-term glycaemic control [8–17]. Although most studies report an improvement in HbA1c associated with pump therapy [18–20], some reports showed no improvement or an initial improvement followed by a return to pre-pump levels after a short time [21–23]. There are few reports on long-term effects on glycaemic control or complications of CSII. In a recent prospective cohort study, it was shown that CSII use was associated with lower rates of early microvascular complications in type 1 diabetes (T1D) [24]. Though insulin pumps have been used for the management of type 1 diabetes mellitus (T1DM) over decades in developed countries, multi-dose insulin injections are the mainstay of management of T1DM in Bangladesh like other developing countries. The objective of this study was to determine the short-term effects of continuous insulin infusion on glycaemic control and acute complications in youth with diabetes in Bangladesh.

Materials and Methods

This is a prospective observational study which was conducted among youths using the insulin pump continuously for more than 6 months in BIRDEM (Bangladesh Institute of Research and Rehabilitation of Diabetes, Endocrine and Metabolic Disorders) hospital (October 2016–September 2018). BIRDEM is the only paediatric diabetes centre with multidisciplinary team management in Bangladesh. Firstly, pump therapy was introduced at our centre in 2016. Data were collected prospectively at each visit and entered into the CDiC database. Consent for data to be entered into the database was obtained from all parents. Data were recorded as pre-pump and post-pump values. Data included HbA1C, insulin dose, weight, BMI, episodes of diabetic ketoacidosis (DKA), hypoglycaemia (just before initiation of pump therapy and 6 months after initiation) and demographic details. Severe Hypoglycaemia was defined as either altered sensorium or seizures associated with low blood glucose level. HbA1c was assessed by Clover A1C using Photo Electric Method.

Protocol for pump therapy – prior to commencing pump therapy all patients were assessed by the multidisciplinary team for suitability for pump therapy. Selection criteria included diabetic children with poor diabetic control, less compliant with MDIs, who had recurrent hypoglycaemic episodes. The patient and family received outpatient education with the dietitian and educators

Table 1. Demographic characteristics of patients with CSII

Demographs	Mean $\pm$ SD or count (%)
Age at diagnosis, years	9.8 $\pm$ 4.2
Age at pump start, years	13.7 $\pm$ 6.1
Sex, <i>n</i> (%)	
Male	8 (40)
Female	12 (60)
Diabetes duration at pump start, years	4.7 $\pm$ 3.1

Table 2. Clinical characteristics of pre-pump versus post-pump patients

	Pre-pump	Post-pump	<i>p</i> value
BMI, mean $\pm$ SD	21.1 $\pm$ 5.8	21.9 $\pm$ 5.0	0.130
Insulin dose, μ /kg, mean $\pm$ SD	1.6 $\pm$ 1.5	1.2 $\pm$ 1.0	0.043
FBS, mmol/L, mean $\pm$ SD	13.4 $\pm$ 7.0	6.9 $\pm$ 1.6	0.001
HbA1c, %, mean $\pm$ SD	10.2 $\pm$ 1.8	9.2 $\pm$ 1.3	0.084
Acute complications, <i>n</i> (%)			
Hypoglycaemia count	7 (35)	3 (15)	0.006
DKA count	2 (10)	1 (5)	0.002

SD, standard deviation; DKA, diabetic ketoacidosis; Hb, haemoglobin.

prior to commencing pump therapy. All patients had their continuous glucose monitoring system (CGMS) done prior to CSII initiation. Instruction was given to monitor blood glucose at least 3 times daily. Pump trial started for 2 weeks initially in an outpatient set-up day care, and patients had their blood glucose monitoring and further education during that period. Patients were then followed with daily telephone calls and were seen in the clinic within 3 days. Post-CGMS was advised in patients 4–6 weeks after the initiation of pump therapy, and dose adjustment was done accordingly.

Summary statistics were reported as mean $\pm$ SD. The normality test, Shapiro-Wilk test, was done to know whether the data were normally distributed before doing statistical test. Paired-sample *t* test was done for comparing pre- and post-pump variables. Categorical variables were analysed by the McNemar’s test. A two-tailed *p* value <0.05 was considered to be significant.

Results

Twenty-eight patients were enrolled. Six patients discontinued the pump after trial; 2 patients missed the last follow-up. Analysis data set (complete data for baseline and visit) comprised of 20 patients.

Twenty patients (8 male and 12 female) on insulin pump were included in this study. Mean age at diagnosis

Fig. 1. Pre-pump CGMS in a patient.

Fig. 2. Post-pump CGMS after 6 months.

was 9.8 ± 4.2 years. Age of the patients at initiation of insulin pump ranged from 3 to 25 years (mean 13.7 ± 6.1) (Table 1). They were followed up for 6 months, majority of these patients were regular on follow-up.

Pre-insulin pump therapy, mean HbA1c was 10.2 ± 1.8 (%) and during pump therapy was 9.2 ± 1.3 (%) ($p = 0.084$) after 6 months. The mean fasting blood glucose level was 13.4 ± 7.0 mmol/L which was reduced to 6.9 ± 1.6 mmol/L ($p = 0.001$) at follow-up. The mean daily total insulin requirement was 1.6 ± 1.5 unit/kg body weight which was reduced to 1.2 ± 1.0 unit/kg body weight after 6 months ($p = 0.043$) (Table 2).

Pre-pump CGMS showed marked glucose variability in all patients. Most of the CGMS showed marked hyperglycaemia with few episodes of hypoglycaemia (Fig. 1). The post-pump CGMS was analysed with daily lay out and showed marked improvement of glucose variability (Fig. 2). Prior to insulin pump therapy initiation, the frequency of hypoglycaemic episodes (defined as a blood glucose level of 4 mmol/L or less) ranged from 2 to 3 episodes per month. There were frequent hypoglycaemic episodes in 3 patients, among them 2 patients had severe hypoglycaemia. One patient had H/O frequent episodes of severe hypoglycaemia and required admission several times. The frequency of hypoglycaemic episodes reduced

to 1 per month. There were 2 episodes of DKA among these patients prior to pump therapy. During pump therapy, only one patient had mild episode of DKA which could be managed by increasing the rate of basal insulin infusion rate. There was no report of hypoglycaemic convulsion or coma or severe DKA requiring hospitalizations in children on CSII during this 6-month period.

Discussion

Several studies suggest that near normal glycaemic control prevents or delays complications of diabetes, which has led to dramatic increase in CSII or insulin pump use. This study showed our experience in 20 Bangladeshi T1DM patients with CSII for 6 months, who had improvement in glycaemic control along with a decrease in daily insulin dose. Although there was 1% reduction of HbA1c values, it did not reach the normal target level. High baseline level HbA1c probably a reason for not achieving the target level. Most of other studies reported a lesser improvement, a meta-analysis reported for the paediatric part improvements of 0.32% [10]. In another study done in 25 Saudi children, it showed better metabolic effect of insulin pump therapy maintained for 2 years [25]. Post-pump CGMS showed marked reduction of glucose variability in most of our patients. Although HbA1c is currently the gold standard for assessing glycaemic control, it does not provide a measure of the magnitude or frequency of fluctuations in blood glucose throughout the day. The adverse effect of glycaemic variability is increasingly becoming recognized [26]. Some patients were less compliant with frequent blood glucose monitoring, but most of them were checking blood glucose at least 3 times a day and did not miss their boluses, which might have contributed in reduction of glucose variability in CGMS. In our study patients, insulin dose has been reduced significantly after pump start. In a large cohort study with longer duration, the insulin dose was reduced significantly in CSII compared to MDI users [27].

Hypoglycaemia is a serious risk associated with intensive therapy and occurs with both CSII and MDI. Early studies suggested that the risk of hypoglycaemia with CSII was greater or similar to that of conventional diabetes management and MDI [28]. More recently, however, reports have suggested that severe hypoglycaemia may be reduced by CSII as much as 4-fold compared with MDI treatment with no reduction in glycaemic control [29, 30]. In the observational METRO study among young

adults with T1D, it was found that the use of CSII was associated with overall hypoglycaemic events than MDI during a 2-year period of follow-up [31]. Reduced frequency of hypoglycaemia was observed in our patients on insulin pump therapy and none of them developed severe hypoglycaemia, rather one patient who had recurrent episodes of severe hypoglycaemia and required hospitalization several times, had no episode of severe hypoglycaemia within 6 months of pump therapy. In a recent study, insulin pump as compared to insulin injection was associated with better glycaemic control, but for acute complications, non-significant higher mean of hypoglycaemic episodes per week and a lower mean of DKA episodes per year were reported in pump therapy as compared to the injection therapy patients [32].

Among the possible hazards of CSII is the susceptibility of these patients to rapidly develop attacks of DKA. The risk of DKA can be minimized by frequent self-monitoring of blood glucose and taking the emergency necessary steps in the event of unexplained hyperglycaemia. In our group of patients, none developed severe DKA; however, mild episode of DKA was successfully managed by increasing the rate of basal insulin infusion rate in one patient.

The present study showed that CSII is effective in improving the metabolic control in Bangladeshi youth with diabetes. In our group of patients, none developed severe hypoglycaemia or DKA, where hospitalization is required. The study design of inclusion criteria and lack of comparison between users of the pump with MDI or conventional regimen were the limitations of our study.

In conclusion, we have shown that patients using CSII in a clinic population with T1D had short-term improvement in glycaemic control with marked improvement of glucose variability and reduction of episodes of severe hypoglycaemia with DKA. Longitudinal studies on CSII comparing with MDI users, with inclusion of continuous glucose monitoring data, will provide long-term benefits of CSII. This is the first study of CSII demonstrating improvement of the metabolic control and acute complications in Bangladeshi type 1 diabetic children, adolescents, and young adults.

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Statement of Ethics

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Conflict of Interest Statement

The authors declare that they have no conflict of interest.

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Author Contributions

B.Z., J.N., N.I., K.A., and K.D.: conceived and designed the study; B.Z.: analysed the data; and B.Z., J.N., and K.D.: wrote the paper.

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