Articles

Continuous subcutaneous insulin infusion in type 1 diabetic Saudi children

A comparison with conventional insulin therapy

Bassam S. Bin-Abbas, MD, Nadia A. Sakati, MD, Hussein Raef, MD, Abdullah A. Al-Ashwal, MD.

ABSTRACT

Objective: To assess the efficacy and effectiveness of continuous subcutaneous insulin infusion (CSII) therapy in type 1 diabetic Saudi children in comparison with conventional insulin (CI) therapy.

Methods: Continuous subcutaneous insulin infusion was initiated in 14 Saudi children with type 1 diabetes mellitus (T1DM) through insulin pump therapy between October 2002 and June 2004. All children were followed at the Diabetes Clinic, King Faisal Specialist Hospital and Research Centre, Riyadh, Kingdom of Saudi Arabia. The patients were initially on CI therapy, which is usually defined as 2 or fewer insulin injections per day before shifting them to CSII. The patients were trained on carbohydrates counting and started on continuously basal insulin infusion aside from the meal and high blood glucose correction insulin boluses.

Results: The patients included in the study had T1DM for a mean duration of 6 years. The age of the children ranged from 4-18 years. They were followed on insulin pump therapy for a mean duration of 10 months. There was a significant reduction in hemoglobin A1c, mean blood glucose level, total insulin requirement, frequency of hypoglycemic episodes and frequency of diabetic ketoacidosis (DKA) events during CSII therapy.

Conclusion: Continuous subcutaneous insulin infusion improved the glycemic control in diabetic Saudi children with decreased frequency of hypoglycemic episodes and DKA events. Long follow-up studies are needed to confirm these results.

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Since the introduction of continuous subcutaneous insulin infusion (CSII) in the late 1970s, it has become apparent that the use of insulin pump therapy has many potential benefits for children with type 1 diabetes mellitus (T1DM). It offers a more physiological way to deliver insulin and, therefore potentially improves the long-term outcome.[1-3] Several studies showed that insulin pump therapy improves glycemic control, reduces hypoglycemia and decreases episodes of recurrent diabetic ketoacidosis (DKA).[4-7] This study describes the use of insulin pump therapy in Saudi children and shows its efficacy and safety.

Methods. Fourteen Saudi children (7 male, 7 female) with T1DM were selected and started on 508 MiniMed, insulin pump therapy (MiniMed, Sylmar, CA). Selection criteria included diabetic children with poor diabetic control (hemoglobin A1c [HbA1c] >8.5%) who had recurrent hypoglycemic episodes (more than 2 episodes per month). These patients were willing to monitor

From the Department of Pediatrics (Bin-Abbas, Sakati, Al-Ashwal) and Department of Medicine (Raef), King Faisal Specialist Hospital and Research Center, Riyadh, *Kingdom of Saudi Arabia*.

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Address correspondence and reprint request to: Dr. Bassam S. Bin-Abbas, Consultant, Section of Pediatric Endocrinology, Department of Pediatrics, MBC 58, King Faisal Specialist Hospital and Research Centre, PO Box 3354, Riyadh 11211, *Kingdom of Saudi Arabia*. Tel. +966 (1) 4427763. Fax. +966 (1) 4427784. E-mail: benabbas@kfshrc.edu.sa

blood glucose regularly and frequently, motivated to improve blood glucose control, willing to quantify food intake and count carbohydrates. They had adequate family support and were interested in preventing short and long-term diabetic complications. All patients were followed at the Diabetes Clinic, King Faisal Specialist Hospital and Research Centre, Riyadh, Kingdom of Saudi Arabia. All patients were on CI therapy that included 2 injections of insulin per day; NPH (intermediate-acting) and regular (short- acting) insulin before shifting them to CSII.

All patients were trained by a diabetic dietitian on carbohydrates counting and food nutrition labels reading. Fifty percent of their total caloric intake was from carbohydrates. The total daily carbohydrate intake calculated as grams was distributed into 3 meals and 3 snacks.

Insulin pump therapy using the ultra short-acting Lispro (Humalog®) insulin was started as continuous basal insulin infusion and distributed into 1-2 basal insulin infusion rates. The total insulin dose through the CSII was calculated as 80% of the total pre-pump total insulin dose. Fifty percent of that was given as basal continuous infusion over 24 hours. Additional insulin doses for meal carbohydrates coverage were calculated by dividing 500 by the total insulin units per day. One unit of Lispro insulin was required to cover for 10-30 grams of carbohydrates (meal insulin bolus). Additional insulin doses for high blood glucose correction were calculated by dividing 1500 by the total insulin units per day. One unit of Lispro insulin was required to correct for 50-100 mg/dl above 150 mg/dl (correction insulin bolus). Prior to insulin pump initiation, all patients were trained on insulin pump operation and programming and were psychologically accepting it and had realistic expectations of CSII. They were instructed to change the infusion set every 2-3 days. Younger children required 2-3 days of hospitalization for insulin basal rates, meal and correction insulin boluses adjustment. The patients were asked to maintain ordinary lifestyle activities and to adjust insulin dose in relation to glucose level, physical activities, extra meals, illness and other significant daily events.

All patients were initially instructed to check blood glucose 8 times per day; pre and post-meals, bed time and early in the morning for the first few days of CSII initiation, and then 5 times of blood glucose monitoring were required. Continuous glucose monitoring was performed in 4 children by using continuous glucose monitoring system (CGMS®) (MiniMed, Sylmar, CA). Continuous glucose monitoring system is a lightweight, portable, minimally invasive system which measures subcutaneous interstitial glucose level every 5 minutes. All children faxed their blood glucose record sheet to the health care team or phone for consultation whenever having difficulties in controlling blood glucose levels. All children had a weekly clinic visit and every 2 months for HbA1c monitoring. In young children, the parents used MiniMed insulin pumps with external remote control devices that can be locked. Special belts and pouches to secure placement of pumps were recommended and used by some children.

Statistical analyses were performed using the paired comparison T test to evaluate the differences between CSII and CT treatment levels of HbA1c, blood glucose levels, hypoglycemic episodes and total insulin requirement as well as changes in body weight. The tests were 2 tailed, and p value of <0.05 was chosen to indicate significant deviation from the null hypothesis.

Results. All patients had T1DM for a mean duration of 6 years ± 4.3 (range from 0.3-15 years). The age of the children ranged from 4-18 years (mean 12.8 ± 4.3). They were followed on insulin pump therapy for a mean duration of 10 months ±5.9 (range from 2-20 months). All children had no diabetic complications and biochemically had normal thyroid function tests, anti-celiac disease antibodies, urine microalbumin, lipid profile and retinal examination. One female patient was diagnosed with celiac disease based on elevated anti-celiac disease antibodies and villous atrophy on intestinal biopsy (**Table 1**).

During the 6-12 months prior to insulin pump therapy initiation (**Table 2**), the mean HbA1c was 10.2% ± 1.2 (range from 8.5-12.5%), the mean blood glucose level was 233 mg/dl ± 39 (range from 169-311 mg/dl), the frequency of hypoglycemic episodes (defined as a blood glucose level of ≤40

Table 1 - Clinical features of the patients.

Patients	Age (years)	Duration of diabetes (years)	Duration of insulin pump therapy (months)
1	4	0.3	2
2	8	5	6
3	9	2	11
4	11	5	5
5	11	6	7
6	11	9	18
7	13	11	18
8	15	2	7
9	18	3	18
10	18	8	7
11	18	8	20
12	18	15	7
13	12	9	7
14	13	0.6	6
Mean	12.8	6	10
SD	4.3	4.3	5.9

mg/dl) ranged from 2-5 episodes per month (mean 2.8 ± 1.1) and the mean daily total insulin requirement was 1.2 units/kg body weight (range from 0.8-2.2). The total numbers of hypoglycemic convulsive were 3 and DKA were 12 episodes in the 14 patients during the 12 months period prior to insulin pump initiation.

In post-insulin therapy (**Table 2**), the mean HbA1c was 7.5 % ± 0.7 (range from 6.5-9%), the mean blood glucose level was 156 mg/dl ± 32 (range from 111-201 mg/dl), the frequency of hypoglycemic episodes ranged from 0-2 per month (mean 0.6 ± 0.6) and the mean daily total insulin requirement was 0.9 unit/kg body weight (range from 0.7-1.5). Hemoglobin A1c level improved significantly during CSII treatment in the study group ($p<0.001$). Mean blood glucose level was significantly lower during CSII compared with CI therapy ($p<0.001$). A significant decrease in the frequency of hypoglycemic episodes ($p<0.001$) and total insulin requirement ($p<0.002$) was observed in children treated with CSII. There was no significant difference in body mass index pre and post insulin pump therapy. There was no report of hypoglycemic convulsion or coma or diabetic ketoacidosis in children on CSII. The children on insulin pump therapy required 0.1-1.2 units of continuous insulin per hour as a basal rate. All children were started initially on one basal insulin rate throughout the day, and then additional basal rates were added according to the blood glucose levels. One unit of Lispro insulin was required to cover 10-30 grams of carbohydrates as meal boluses and one unit of Lispro insulin was needed to correct for 50-100 mg/dl of blood glucose as correction boluses. Pump performance was without mechanical or electrical fault throughout the study. There was no report of local skin infection related to the catheter insertion site. All children admitted their wish to continue on pump therapy and there was no report of discontinuation of pump therapy throughout the study.

Discussion. A tremendous amount of data suggests that near-normal glycemic control prevents, or delay complications of diabetes, which has led to dramatic increase in CSII or insulin pump use. The worldwide popularity of CSII has increased dramatically, and the number of insulin pump users among adults and children has doubled over the last several years. However, the number of insulin pump users among Saudi children is still small. Lack of patient/family motivation, health care team enthusiasm and proper technical support are among the contributing factors for that. This article reports our experience with 14 Saudi children on insulin pump therapy that proves that CSII is extremely effective in treating T1DM Saudi children. Intensive diabetes management with CSII provides better glycemic control than does conventional therapy.[8,9] It also provides as good and

Table 2 - Pre-insulin pump therapy and post-insulin pump therapy results.

Patients	Pre-insulin pump therapy				Post-insulin pump therapy			
	Mean HbA1c (%)	Mean (range) blood glucose level (mg/dl)	Mean hypoglycemic episodes/month	Mean total insulin dose (unit)/Kg	Mean HbA1c (%)	Mean (range) blood glucose level (mg/dl)	Mean hypoglycemic episodes/month	Mean total insulin dose (unit)/kg
1	9.1	209 (50-351)	2	1.0	8	170 (66-222)	1	0.5
2	11.2	251 (23-365)	4	1.1	8	143 (60-189)	0	0.9
3	8.8	169 (35-228)	4	0.8	7	144 (58-188)	1	0.7
4	11.5	231 (60-396)	3	0.9	6.9	122 (45-222)	0	0.7
5	11.2	245 (36-412)	2	2.2	7.1	189 (55-202)	1	1.3
6	9	201 (33-389)	4	1.1	8	188 (45-269)	0	0.8
7	11.3	261 (69-450)	2	1.1	8	201 (49-301)	0	0.9
8	9.3	271 (45-333)	2	1.0	7.3	124 (44-188)	0	0.9
9	9.2	258 (41-444)	3	1.2	6.5	111 (38-159)	2	1.0
10	9.9	255 (31-365)	5	1.0	7.2	158 (66-321)	0	0.9
11	10	222 (31-356)	2	1.2	7	174 (53-245)	1	1.0
12	12.5	311(37-500)	2	1.5	9	201 (56-288)	1	1.2
13	11	199 (55-303)	2	1.5	7.8	150 (33-254)	1	1.5
14	8.5	177 (60-288)	2	0.8	7.0	112 (60-288)	1	0.8
Mean	10.2	233	2.8	1.2	7.5	156	0.6	0.9
SD	1.2	39	1.1	0.4	0.7	32	0.6	0.3

often better glycemic control than intensive diabetes management with multiple daily insulin (MDI) injection.[7-10] In our group of children, the blood glucose level, blood glucose variability and HbA1c significantly improved on CSII therapy. Hypoglycemia is a serious risk associated with intensive therapy and occurs with both CSII and MDI. Early studies suggested that the risk of hypoglycemia with CSII was greater or similar to that of conventional diabetes management and MDI.[11] Recently, reports have suggested that severe hypoglycemia may be reduced by CSII as much as 4-fold compared with MDI treatment with no reduction in glycemic control.[12,13] Reduced frequency of hypoglycemia was observed in our patients on insulin pump therapy and none of them developed a hypoglycemic coma or convulsion. Disabling hypoglycemia defined as a state of neuroglycopenia leading to impairment or loss of consciousness was reported 3 times in our patients during the 12 months period of CI therapy and none was reported during CSII period. Among the possible hazards of CSII is the susceptibility of these patients to rapidly develop attacks of DKA. Children on CSII have reduced tolerance to the interruption of CSII due to small amount of insulin deposited in the subcutaneous tissue. Several studies showed that DKA is more common in CSII patients than in those using CI therapy.[14-16] The most common cause of DKA in children on insulin pump is interruption of insulin delivery caused by catheter occlusion, catheter disinsertion, battery failure, depleted insulin supply, patient error or inadequate training.[17] 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 hyperglycemia. In our group of patients, none of them develop DKA on CSII therapy; however, 12 episodes of DKA were reported in the year prior to CSII initiation. The effectiveness of intensive insulin therapy including CSII appears to decrease with a decreased frequency of blood glucose self-monitoring (BGSM) and insulin dose adjustment.[18,19] Our patients were instructed to check their blood sugar at least 8 times per day, and the majority of them were checking their blood sugar more than 10 times per day. The favorable results achieved in this study may have been promoted by high frequency of BGSM. Blood glucose was controlled in the majority of children by one basal insulin infusion rate. Some of the children required a higher basal insulin infusion rate during the early hours of the morning to cover for the early morning hyperglycemia secondary to counter-regulatory hormones rise (dawn phenomenon) and other children required a lower basal insulin infusion rate during sleeping hours to avoid hypoglycemia at nighttime. The most common metabolic adverse effect of improved glycemic control is weight gain. Participants in the DCCT who used intensive management gained approximately 4.5 kg than conventional treatment group.[3,11] Our CSII patients were instructed not to exceed the recommended total caloric intake per day to avoid excessive weight gain. There was no significant change in BMI in the studied children pre and post insulin pump therapy. Meal boluses for carbohydrates coverage ranged from one unit of Lispro insulin for every 10-30 grams of carbohydrates. Younger children required less insulin to carbohydrates ratio coverage (one unit to 30 grams carbohydrates) and older children required higher doses (one unit to 10 grams carbohydrates). One of the advantages of CSII therapy that it provides eating flexibility. Children can eat freely and cover what they ate with insulin. This advantage can be misused and lead to overeating and weight gain. The most common complication associated with CSII is infection at the infusion site.[20] This is one of the most common causes listed for discontinuation of CSII.[21] In our series, all children were instructed to change the infusion set every 2-3 days and none of them developed skin infection or contact dermatitis related to infusion site.

The present short-term study showed that CSII is effective in improving the metabolic control in type 1 diabetic Saudi children. The results of this local experiment are encouraging to implement this mode of intensive insulin therapy in all candidate diabetic Saudi children and longer follow-up studies are needed to confirm these results. Patient motivation, the availability of medical, technical and family support are necessary for this modality of insulin therapy to succeed.

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