Original Article

Impact of insulin pump therapy on glycemic control among adult Saudi type-1 diabetic patients. An interview-based case-control study

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Abstract

Context: Diabetes is associated with several potential preventable complications like the efficacy of insulin pump over multiple daily insulin injections (MDI) in glycemic control. **Aims:** To assess the outcomes of insulin pump as compared to insulin injection therapy. **Setting and Design:** Case-control study conducted among adult type-1 diabetic patients using insulin pump therapy and alternative insulin injection therapy from the University Diabetes Center (UDC), King Saud University, Riyadh, Saudi Arabia during 1st June–30th October, 2017. **Materials and Methods:** Interview-based questionnaires were used on of 200 subjects using insulin therapy and control (conventional and MDI). Results of each were compared. **Statistical Analysis Used:** *t*- test was used for continuous variables and Chi-square test was used for categorical variables. *P* value less than 0.05 was considered statistically significant. **Results:** Patients on pump therapy showed a non-significant higher mean of hypoglycemic episodes per week and a lower mean of diabetic ketoacidosis (DKA) episodes per year as compared to the injection therapy patients 1.97 vs. 1.77 and 0.35 vs. 0.37, respectively. However, statistically significant differences were found between the pump and MDI, the pump and conventional, and the MDI and conventional when HbA1c levels were tested. **Conclusion:** Among adult patients with type-1 diabetes, insulin pump as compared to insulin injection was associated with better glycemic control. However, for acute complications, non-significant higher mean of hypoglycemic episodes per week and a lower mean of DKA episodes per year were reported in pump therapy as compared to the injection therapy patients.

Keywords: Conventional insulin therapy, insulin pump therapy, MDI therapy, type-1 diabetes

Introduction

Type-1diabetes (T1D) is an autoimmune disease with a strong genetic component, characterized by destruction of pancreatic β-cells, culminating in absolute insulin deficiency.[1] Globally, approximately 425 million adults (20–79 years) lived with diabetes in 2017, of which T1D accounts for 5% to 10%.[2] Diabetes complications continue to be the major cause of morbidity and mortality in patients with T1D. For instance, intensive insulin therapy was found effective to prevent progression of diabetes-related complications, thereby resulting in good glycemic control.[3] This intensive glycemic control is generally achieved through multiple daily insulin injections (MDI) or continuous subcutaneous insulin infusions (CSII) through an insulin pump.[4]

However, it is evident that better metabolic controls were achieved by CSII when compared with MDI in type-1 diabetic patients.[5] On the other hand, use of insulin pumps for intensive insulin therapy was substantially increased from 0.6% to 1.3% in 1995 to 44% to 47% in the period between 2012 and 2016 among T1D patients.[6] Generally, the aim of using insulin

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pump treatment is to decrease glucose level variability through the use of rapid-acting insulin that allows more physiologic insulin replacement, thereby avoiding the development of long-term diabetic complications.[7] Furthermore, insulin pump therapy can provide great flexibility during meal times, in addition to optimization of overnight glycemic control through programmable basal rates. It can also reduce the risk of exercise-induced hypoglycemia and has enhanced ability to achieve acceptable diabetic control.

Nevertheless, glycemic control is an important modifiable risk factor that influences the developmental rate of diabetic complications. However, hypoglycemia is a serious concern for diabetic patients, and fear of hypoglycemia can negatively affect the acceptance of insulin therapy and the ability to lower HbA1c levels effectively through intensive treatment. The previous studies have demonstrated the superiority of CSII over MDI and highlighted its efficacy in glycemic control with lower rates of severe hypoglycemic episodes.[8] Researchers have also studied the effectiveness of insulin pump therapy in youth with T1D and found that CSII improves glycemic control in children and adolescents with T1D, especially those with a history of moderate to poor glycemic control. This improvement was associated with decreased rates of severe hypoglycemia, and absence of significant increase in diabetic ketoacidosis (DKA), major catheter-site infection, or weight gain.[9] In addition, it has been observed during recent years that there has been decline in severe hypoglycemic frequency through the use of insulin pumps.[10] However, several studies have r eported an increased risk of DKA associated with the use of insulin pump therapy in pediatric patients, raising concerns about its safety.[11,12]

Data regarding the efficacy of insulin pump to reduce glycemia and the risk of severe diabetic complications (hypoglycemia and DKA), as compared to alternative insulin injection therapy, is scarce in Saudi Arabia. Therefore, this study was conducted to assess the outcomes of insulin pump therapy as compared to alternative insulin injection therapy, in Saudi adults with type-1 diabetes. It was hypothesized that insulin pump therapy would be associated with reduced rates of hypoglycemia and DKA, and lower HbA1c levels in comparison to injection therapy.

Materials and Methods

It was an interview-based case-control study conducted among adult type-1 diabetic patients using insulin pump therapy and alternative insulin injection therapy (either multiple daily injections MDI: taking more than two insulin doses per day, or conventional: taking two or less insulin injection per day) from the University Diabetes Center (UDC), King Saud University, Riyadh, Saudi Arabia during 1st June–30th October, 2017. Ethical approval was obtained from King Saud University on 19th October 2013, with approval number 13/3808/IRB.

At UDC, pump therapy is preceded by a training program for patients and their families. Such training program is conducted by the clinic multidisciplinary team for in and out-patient setting. During the pump use and after a period of stabilization on pump therapy, patients are seen routinely at two to three month's intervals. At each visit, HbA1c, weight, and height are measured, and insulin adjustments are made. Insulin dose adjustments are guided by the observed pattern of blood glucose and the target levels.

The inclusion criteria for the patients were that they should be Saudi, patients with T1D, and aged 18 years and above, whereas exclusion criteria were non-Saudi patients, type-2 DM, age <18 years, and pregnant women. The patients were then divided into two groups: (1) Cases who were recruited in this study were transitioned to insulin pump for ≥6 months, irrespective of the type of insulin infusion pump used, between the period from 1993–2013, and still following in UDC. And (2) control group who had never been treated with insulin pump and had been receiving at least one insulin injection per day for ≥6 months. Control patients were enrolled in a ratio of 1: 2 (Case: Control).

The data collection tool was an interview-based data collection sheet, which consisted of three main sections: the first section was for the sociodemographic data and clinical characteristics including age, gender, marital status, level of education, and occupation. The second section consisted of more specific questions regarding duration of diabetes, type of insulin regimen, duration of pump use, history of diabetes-related acute complications like hypoglycemic episode and DKA, in addition to associated co-morbid diseases. The third section was for anthropometrics parameters such as weight, height, and BMI and laboratory characteristic data such as HbA1c, fasting blood sugar, two hours postprandial (2hpp) sugar level, lipid profile, and renal and liver function test for 1 year before current insulin regimen and at 6 months, 1 year after that, and then at the last available follow-up visit. Insulin regimens in the current study were defined as following: insulin pump, conventional insulin therapy (≤ two injections per day), and multiple-dose insulin injection therapy (MDI) (three or more injections per day of basal and prandial insulin). Hypoglycemia was classified as mild (blood sugar 50–70 mg/dl or symptoms which were relieved by the ingestion of glucose or food), moderate (blood sugar level 30–49 mg/dl or any hypoglycemic event that required assistance from another person), and severe (blood sugar <30 mg/dl or event resulting in seizure or coma). DKA was defined as the presence of hyperglycemia and/or ketosis that required emergency medical treatment or inpatient hospitalization. The study included a total of 200 subjects. Out of which, there were 66 cases who were using insulin pump and had active follow-up at UDC, and 134 control patients, on either conventional (39) or MDI (95) insulin therapy.

Data were analyzed by using Statistical Package for Social Studies (SPSS 22; IBM Corp., New York, NY, USA). Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as percentages. t-test was used for continuous variables and Chi-square test was used for categorical variables. *P* value less than 0.05 was considered statistically significant.

Results

The total sample size was 200 adult type-1 diabetic patients with 83 males and 117 females, with a mean age of 27.16 ± 7.97 years. Statistically significant differences ($P < 0.05$) were found between the two groups in terms of educational level, dietary compliance, and following carbohydrate count (CC) diet. On the other hand, non-significant differences were found between the groups when compared marital status, smoking, body mass index (BMI), hypertension, hyperlipidemia, and hypothyroidism, as shown in Table 1.

Moreover, it was also found that T1D patients on pump therapy had a non-significant higher mean of hypoglycemic episodes per week and a lower mean of DKA episodes per year as compared to the injection therapy patients (1.97 vs. 1.77) and (0.35 vs. 0.37), respectively. However, when analysis for hypoglycemia and DKA was carried out for pump, MDI, and conventional therapy groups, the highest mean for hypoglycemic episodes per week was for conventional therapy at 2.69, followed by MDI at 1.97 and pump therapy at 1.39 were obtained, with statistically significant differences between: the pump and MDI, the pump and conventional, and MDI and conventional. But for the number of DKA per year, there was no significant difference between the three groups as shown in Figure 1.

Participants in each of the two groups (Pump and injection therapy groups) were again subgrouped according to their HbA1c (as an indicator of diabetes control) levels: (1) patients with HbA1c <7 mmol/l (controlled) and (2) patients with HbA1c ≥7 (uncontrolled). The results revealed that after using pump for 6 months, the percentage of patients on insulin pump who achieved HbA1c <7 mmol/l (30.6%) was highly significant ($P = 0.002$) as compared to those who achieved it in the injection group (6.6%). Similar results were obtained in the 1-year visit and the last visit obtained from the patients. When this analysis was carried out for the three groups (pump, MDI, and conventional), highly significant ($P < 0.001$) percentages of patients in pump group were achieved when compared to those on MDI, that is 30.6% vs. 2.6% at the 6 months follow-up, 27.9% vs. 1.9% at the 1-year follow-up, and 20.0% vs. 6.6% at the last follow-up visit. In contrast, for the pump group and the conventional, the only significant difference was for the last follow-up visit. However, there was no statistically significant difference

Table 1: Baseline characteristics of the study population

Baseline Characters	All (200) (%)	Pump Therapy (66) (%)	Injection Therapy (134) (%)	*P*
Age	7.97	9.07	7.14	0.009*
Body Mass Index	4.98	4.45	5.24	0.891
Gender				
Male	41.5	37.9	43.3	0.466
Female	58.5	62.1	56.7	
Marital status				
Single	64	54.5	68.7	0.158
Married	33.5	43.9	28.4	
Divorce	2	1.5	2.2	
Widow	0.5	0	0.7	
Education level				
Less than high school	6	0	9	<0.001*
High school	25	12.1	31.3	
University & above	69	87.9	59.7	
Hypertension	4	3	4.5	0.474
Dyslipidemia	11.5	10.6	11.9	0.781
Hypothyroidism	19	18.2	19.4	0.836
Dietary compliance				
None	26	10.6	33.6	<0.001*
Partial	54.5	53	55.2	
Full	19.5	36.4	11.2	
Follow-up Carbohydrate Count Diet				
None	62.5	12.1	87.3	<0.001*
Irregular	11.5	22.7	6	
Regular	26	65.2	6.7	
Exercise				
None	39	37.9	39.6	0.208
Irregular	42	36.4	44.8	
Regular	19	25.8	15.7	

*Significant *P*

between the MDI and the conventional group in achieving the metabolic control, as shown in Table 2.

When laboratory results were compared before the pump use, only HbA1c, total cholesterol and triglyceride showed significantly lower differences in the pump therapy group as compared to the injection therapy one. And when insulin pump use was started, patients on insulin pump showed significantly lower levels of HbA1c, 2hrpp, serum glutamic-oxaloacetic transaminase (SGOT), also called aspartate aminotransferase (AST), alkaline phosphatase, TG, and LDL. When followed up for 6 months of the use of insulin pump, patients showed significantly lower levels of HbA1c (7.43 vs. 9.89, $P < 0.001$), FBS (8.62 vs. 11.16, $P < 0.05$), creatinine (60.70 vs. 67.43, $P < 0.5$), alkaline phosphatase (80.53 vs. 126.59, $P < 0.001$), total cholesterol (4.38 vs. 4.91, $P < 0.05$), and TG (0.90 vs. 1.32, $P < 0.05$), when compared to patients on insulin injection therapy. However, when tested after 1 year of using insulin pump, similar results to that of 6 months were obtained, except for the creatinine level which did not show any significant difference in addition to significantly lower levels of 2hrpp, urea, and serum glutamate-pyruvate transaminase or serum glutamic-pyruvic transaminase (SGPT), also called alanine transaminase (ALT), at 11.11 vs. 14.40, 3.6 vs. 4.23, and 13.83 vs. 21.47, respectively, were obtained after comparing with patients on insulin injection therapy, as shown in Table 3.

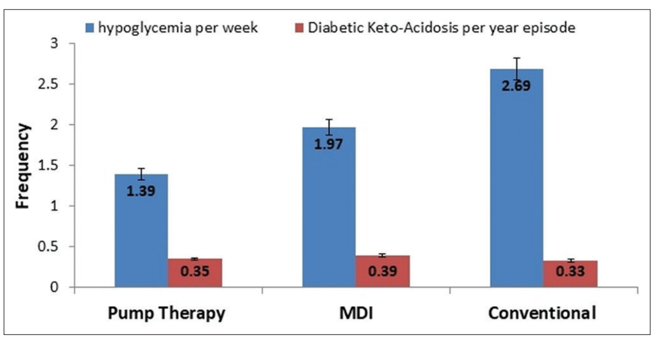

Figure 1: Hypoglycemia and diabetic ketoacidosis for pump, MDI, and conventional therapy

The results also showed that the mean of the total daily insulin dose was significantly higher in the MDI group (68.73 ± 21.33) than the conventional group (59.79 ± 13.89), with a P value of 0.032.

Discussion

The findings of the current study showed that pump therapy was associated with lower HbA1c levels reflecting improved metabolic control than in MDI adults.[13,14] This is in agreement with what had been previously reported in a similar study.[15] In a systematic review and meta-analysis, it was reported that in randomized controlled trials, CSII and MDI have similar effects on hypoglycemia and glycemic control, except that CSII has a favorable effect on glycemic control in adults with type-1 diabetes mellitus, a finding which is in line with the results of the current study.[16]

Likewise, another study showed that insulin pump therapy significantly and safely improved diabetes with less usage of insulin along with the maintainable reduction of lipid profile and blood pressure in patients of type-2 diabetes.[17] One more study confirmed that insulin pump therapy provides possible benefits for control of diabetes.[18]

In another study of cluster randomized trial that compared the effectiveness of insulin pumps with MDI for adults with type-1 diabetes, both the groups received equivalent training in flexible insulin treatment and it was found that both groups (insulin pumps and MDI) showed clinically relevant and long-lasting decreases in HbA1c and severe hypoglycemia rates. In addition, it was also reported that adding pump treatment did not substantially enhance educational benefits on glycemic control or hypoglycemia among adults with type-1 diabetes.[19]

Another study that compared insulin pump and multiple daily injection regimens in 22 T1D Saudi children came up with the finding that both CSII and MDI were efficacious in glycemic control in type-1 pediatric patients.[20] However, CSII had more favorable effect on HbA1c reduction than MDI therapy.[19] The present study was in accordance with this study. Whereas, in

Table 2: HbA1c status indicating metabolic control for pump, MDI, and conventional therapy

HbA1c Status	Pump Therapy (66) (%)	MDI (95) (%)	$P^†$	Conventional (39) (%)	$P^‡$	$P^§$
HbA1c at time start Insulin regimen						
<7%	13.5	4.1	0.060	10.7	0.512	0.209
≥7%	86.5	95.9		89.3		
HbA1c after 6 months						
<7%	30.6	2.6	0.001*	13.6	0.125	0.129
≥7%	69.4	97.4		86.4		
HbA1c after 1 year						
<7%	27.9	1.9	<0.001*	13.0	0.143	0.077
≥7%	72.1	98.1		87.0		
HbA1c at last follow-up visit						
<7%	20.0	6.6	0.012*	5.4	0.038*	0.579
≥7%	80.0	93.4		94.6		

*Significant P. †P value was calculated between Pump and MDI, ‡P value was calculated between Pump and Conventional, §P value was calculated between MDI and Conventional

Table 3: Assessment of laboratory values (mean) for injection therapy vs. pump therapy

Laboratory Tests	Pump Therapy (66) (%)	Injection Therapy (134) (%)	*P*
HBA1c at time start insulin regimen	8.39	10.29	<0.001*
HBA1c after 1 year	7.49	9.74	<0.001*
HBA1c at last follow-up visit	7.54	9.25	<0.001*
FBS at time start insulin regimen	11.36	11.24	0.909
FBS after 1 year	8.35	10.55	0.013*
FBS at last follow-up visit	7.88	10.93	<0.001*
2HPP at time start insulin regimen	11.21	15.34	0.027*
2HPP after 1 year	11.11	14.4	0.023*
2HPP at last follow-up visit	11.51	12.37	0.508
Creatinine at time start insulin regimen	62.81	65.02	0.425
Creatinine at last follow-up visit	62.62	61.67	0.67
SGPT at time start insulin regimen	16.59	20.98	0.148
SGPT after 1 year	13.83	21.47	0.012*
SGPT at last follow-up visit	16.48	18.19	0.441
SGOT at time start insulin regimen	15.49	20.21	0.041*
SGOT after 1 year	15.34	18.28	0.084
SGOT at last follow-up visit	14.82	18.96	0.135
Alkaline phosphatase at time start insulin regimen	86.29	122.13	<0.001*
Alkaline phosphatase after 1 year	83.67	119.72	<0.001*
Alkaline phosphatase at last follow-up visit	73.73	92.94	<0.001*
Total Cholesterol at time start insulin regimen	4.31	9.74	0.441
Total Cholesterol after 1 year	4.22	4.74	0.017*
Total Cholesterol at last follow-up visit	4.29	4.88	<0.001*
TG at time start insulin regimen	0.88	1.2	0.011*
TG after 1 year	0.83	1.19	0.002*
TG at last follow-up visit	0.84	1.21	<0.001*

*Significant *P*

addition, it was also found that there was a significant decrease in the levels of TG, total cholesterol, and LDL levels at 6 months, 1 year, and last follow-up visits with CSII, as compared to the injection therapy group, thereby giving a faster improvement in the lipid profile.

Evidence suggests that CC diet may have positive effects on metabolic control and on reducing HbA1c. In addition, CC might reduce the frequency of hypoglycemia.[21] In the current study, a higher percentage of patients in the pump group were following CC diet as compared to the injection therapy group.

Overall, in the current study, it was observed that the risk of hypoglycemia was non-significantly higher and the risk of DKA was non-significantly lower with insulin pump therapy as compared to insulin injection therapy. These results were in contrast with the results reported by Karges *et al.*, in which pump therapy was associated with a lower rate of DKA and severe ketoacidosis in injection therapy.[15] On the other hand, a meta-analysis by Misso *et al.*, included 23 studies with randomized 976 type-1 diabetic participants to either intervention [continuous subcutaneous insulin infusion (CSII) or multiple insulin injections] found that there were no obvious differences between the interventions for non-severe hypoglycemia, but severe hypoglycemia appeared to be reduced in those using CSII.[4] This study showed similar results as the current study. In addition, in the observational METRO study among young adults with type-1 diabetes, it was found that the use of CSII was associated with overall hypoglycemic events than MDI during a 2-year period of follow-up.[22] Despite the fact that CSII has the ability to better mimic physiological insulin release, it may provide a more efficient insulin supply to the tissues and minimize the risk of hypoglycemic events.[23,24] However, some patients in the intensive treatment group of the Diabetes Control and Complications Trial (DCCT) who were using CSII showed no benefit over MDI patients.[3]

The current study has several limitations. This was a non-randomized, case-control study and thus was prone to residual selection biased. The individual insulin pump use duration was not considered in the analyses, and patient adopting such technology might have a higher frequency of short-term complications. In addition, the use of continuous glucose monitoring that had been shown to improve glycemic control and reduce HbA1c levels and hypoglycemic events was not analyzed in the current study.[25,26] The intensity of diabetes education, motivation, and family support were not addressed, despite the fact that all of them are relevant to hypoglycemia and ketoacidosis risk.[27-29] Moreover, the risk of hypoglycemia was not analyzed according to the degree of hypoglycemic events severity. Further studies are recommended to address these limitations while analyzing the efficacy of insulin pumps in T1D patients.

Conclusion

Thus, in public health perspective, the insulin pump therapy is associated with better and sustainable glycemic control in both type 1 and 2 diabetic patients of all ages as it is evident from different studies as discussed earlier.[18] This is important because glycemic control is required to avoid diabetic complications both at macro and micro levels, in addition to the increased mortality rates, that are the important factors contributing in compromised quality of life and increased burden on economy. Thereby, it was concluded that insulin pump therapy was associated with better glycemic control during the first year of therapy when compared to insulin injection therapy among adult type-1 diabetic patients.

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Conflicts of interest

There are no conflicts of interest.

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