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First Libyan Experience with Insulin Pump Therapy: Impact on Glycemic Control and Patients Satisfaction

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Abstract

Background: The mainstay of contemporary management of type 1 diabetes mellitus (T1DM) is "physiological insulin replacement". Regimens based on multiple daily injections (MDI) of insulin improve glycemic control and increase the frequency of hypoglycemia. Insulin pump therapy also improves glycemic control, and reduces the within-day and between-day glycemic variability that is seen with insulin injections. **Objectives:** We aimed to evaluate out first experience with insulin pump therapy by 1) assessing the glycemic control on insulin pump therapy compared to MDI based therapy and 2) to learn the attitude of patients and families towards the use of insulin pump. **Patients and Methods:** A prospective observational study involving 37 patients who used insulin pump between March & November 2013. Patients were selected according to certain criteria set up by treating physician. Data collected included demographic, clinical and biochemical data before, during and after insulin pump therapy use. Severe hypoglycemia requiring hospital management and diabetic ketoacidosis (DKA) were documented. Health-related quality of life, diabetes knowledge and patient's attitude towards pump therapy were captured before and after pump use. **Outcome measures:** Change HbA1c, occurrence of severe hypoglycemia and DKA. Change of body mass index (BMI) and difference in score results of health quality questionnaire. **Results:** 51.4% were males; mean age was 15 years (86.5% of them were between 2 and 22 years. About 94.4% had diabetes for a mean of 6.9 (range 1-14) years. The indications of insulin pump were high HbA1c (29.7%), wide variation of blood glucose (10.8%), severe hypoglycemia and/or hypoglycemic unawareness (18.9%), recurrent DKA (5.4%) and other indications (8.1%). However, 27.0% had a good metabolic control but multiple daily injections (MDI) was reportedly "compromising" their quality of life. The mean HbA1c level decreased from 9.1% to 7.4% (P = 0.001). The mean BMI increased from 21.2 to 22.0 kg/m^2 (P=0.026) independent of age (r = 0.180,

P = 0.295). Two episodes of DKA in one patient who had severe contact dermatitis at the site of cannula & sensor and one severe hypoglycemia, which required hospital admission due to unmatched carbohydrate intake to insulin dose due to incorrect carbohydrate counting. The health quality questionnaire scores revealed an improvement from 34.2 to 46.7 (P = 0.001). **Conclusions**: Our first experience with insulin pump therapy was positive in terms of achieving and maintaining good glycemic control in most of patients, it for more contact between patients and health providers and created better opportunities for diabetes education and support.

Key words: Insulin pump therapy, Type 1 diabetes mellitus, HbA1C, Hypoglycemia, Diabetic ketoacidosis.

Introduction

Duration of diabetes and quality of glycemic control are well established determinants of the risk of long term microvascular complications in T1DM (1). There have been renewed efforts to help patients achieve near- normal glycemia. The mainstay of current management of T1DM is the "physiological insulin replacement" by administering multiple daily injections (MDI) of insulin (2-3). However, as glycemic control improves with intensified insulin therapy, the frequency of hypoglycemia increases (1-4). Hypoglycemia causes stress and anxiety, impaired well-being and poor quality of life. About 35- 40% of patients with T1DM regularly suffer have episodes of severe hypoglycemia necessitating third party assistance and about 25% of these have blunting of the symptoms of hypoglycemia "hypoglycemia unawareness" (5-7). Continuous subcutaneous insulin infusion (CSII) or insulin pump therapy or was introduced over 30 years ago as a procedure for improving glycemic control in patients with T1DM by mimicking the insulin-delivery patterns of persons without diabetes (8,9). Pump therapy can improve glycemic control in patients with T1DM by reducing the within-day and between-day glycemic variability that is often seen with insulin injections (10-12). This beneficial effect of CSII over MDI may be attributed to a) the smaller subcutaneous depot of insulin during pump therapy and b) the low coefficient of variation for absorption during the basal rate infusion being about 3% in CSII compared with 50% in a large dose of isophane insulin (13). This reduction in glycemic fluctuations allows patients to achieve lower HbA1C levels without increasing the risk of hypoglycemia (11). Established indications for initiation of insulin pump therapy in patients with T1DM include continued elevated HbA1c levels despite best attempts with multiple daily insulin injections, continued disabling hypoglycemia, in the first trimester of pregnancy or before conception; when target HbA1c levels cannot be achieved without disabling hypoglycemia and young children especially infants (14). Diabetic ketoacidosis (DKA) may occur with insulin- pump therapy if insulin delivery is interrupted because of a pump mal-function or insulin demand is increased because of an intercurrent illness. The frequency of DKA is similar with the two treatment modalities. Self-monitoring of blood glucose (SMBG) and a prompt response to hyperglycemia are key components of modern diabetes practice (15-18). The frequency of DKA can even be lower with CSII than with MDI regimens (18). Localized skin infections at the infusion site occasionally occur with insulin-pump therapy, but they are rarely serious (18). Other possible reasons for unexplained hyperglycemia include problems with the cannula (kinked, blocked, or leaking cannula or failure of the cannula to prime after change), problems at infusion site (infection, lipohypertrophy, dislodgment of the infusion set, or leaving the set place for longer than 3 days) (14). These are known to be less frequent in diabetic units with established pump practices. We have just acquired insulin pump therapy in the public health facilities in Tripoli, Libya for the first time. Therefore, we wished to subject our practice to scrutiny and share our first experience with pump therapy. We evaluated the magnitude of improvement in glycemic control on pump therapy and assessed the perceptions of patients and families towards the use and perceived advantages of pump therapy.

Patients and methods

Settings and design

A prospective observational study included a total of 37 patients using insulin pump was conducted. Patients were selected to change to insulin pump therapy according to specific indication set up by treating physicians. To be included in this study, patients must have received insulin by MDI that included long acting analogue insulin during the previous 3 months. They must have been under the same physician for at least 6 months, have history of using SMBG on average of four or more times per day, will be doing carbohydrate counting and were psychologically stable.

Devices and protocols

Thirty patients used Medtronic veo pump from March 2013, 2 patients used Dana pump from May 2013 and 5 patients used Roche pump on November 2013. All patients

were followed up in the Pediatric Diabetes Clinic at the National Centre for Diabetes and Endocrinology, Tripoli, Libya. Guide lines for initial pump setting recommended by the Medtronic pump protocol were used for all pumps (i.e. using rapid-acting analogue and a total daily dose reduction by 25%). Durations for observation was 12 months for the Medtronic group, 10 months for Dana group and 5 months for Roche group.

Outcome measures

The primary outcome measure was the change HbA1c from baseline. Secondary outcome: Occurrence of acute complication (DKA and severe hypoglycemia). We also wished to monitor the difference in score results of health quality questionnaire between the two visits.

Data collection

Data were collected in a predesigned case sheet in terms of demographic characters of patients, duration of DM, indication for pump wearing, height, weight at the start and at completion of the observation; HbA1c: before pump therapy, after 3 months& at completion of observation on March 2014 also occurrences of severe hypoglycemia that requires hospital management or DKA episodes were documented.

Customized "Health Quality Patient Questionnaire" (19) was used on two separate visits for patients; (visit-1) to collect baseline patient's data and characteristics prior to pump use; (visit 2) to evaluate and compare with patient's data belongs to pump use and knowledge about diabetes care including patient's attitude towards pump after one year of therapy. Responses are made on a 5-point scale from 1="never" to 5="always"; It was ten measures. We considered 50 as the highest score.

Data analysis and statistics

SPSS software version 20, used to analyze the collected data; mean, standard deviation and percentages used for descriptive statistics and paired samples test, because the collected data follow normal distribution (Kolmogorov-Smirnov Test), p value <0.05 considered significant.

Results

Patients' characteristics

32 patients (86.5%) were between 2 - 22 years old with mean age 15 years and 5 patients (13.5%) were between 23-52 years (Table 1). 34 patients (94.4%) had had diabetes for 1 to 14 years with mean 6.9 years; 5.61% of patients have diabetes for more than 14 years.

Table 1. The baseline, demographic, clinical and biochemical characteristics the first Libyan cohort of patients with T1DM to use insulin pump therapy.

Characteristics	Details	Frequency	Percentage
Age	2-22 years	32	86.5%
	23-52 years	5	13.5%
Sex	Males	19	51.4%
	Females	18	48.^%
Duration of diabetes	1-14 years	35	94.5%
	15-35 years	2	5.6%
Indications for insulin pump	High HbA1c	11	29.7%
	MDI is cumbersome	10	27.0%
	Wide variation of blood glucose	4	10.8%
	Severe hypoglycemia	4	10.8%
	Hypoglycemic unawareness	3	8.1%
	Diabetic ketoacidosis	2	5.4%
	Toddler	1	2.7%
	Pregnancy (1st trimester)	1	2.7%
	Pregnancy (Pre-conception)	1	2.7%

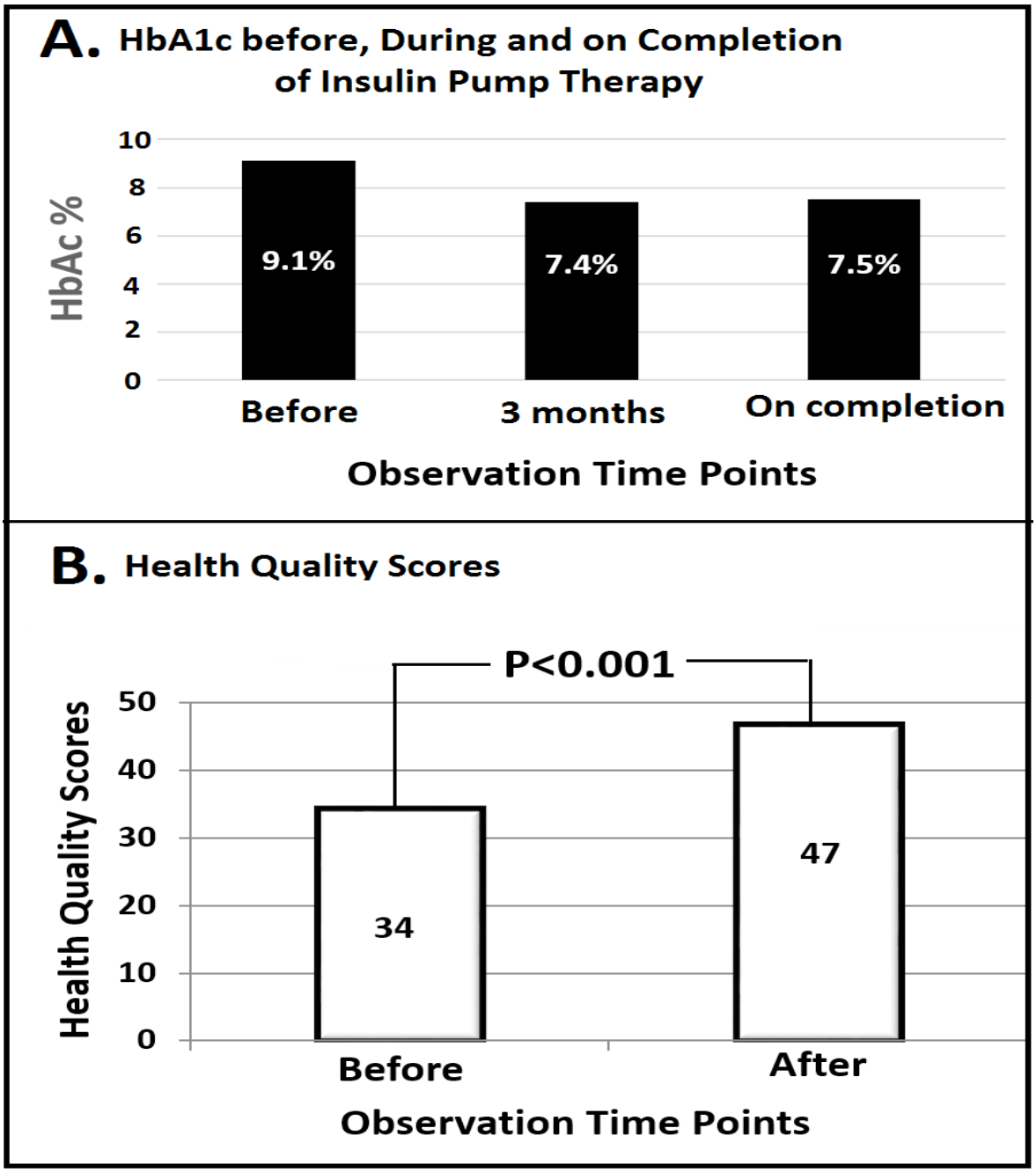

Figure 1. The change in the mean HbA1c (A) and score of health quality questionnaire (B) before, during and end of the observation period.

Indications for insulin pump therapy

The indications of insulin pump use by the treating physicians were high HbA1cin nearly one third of the new patients. Wide variation of blood glucose, severe hypoglycemia and/or hypoglycemic unawareness, recurrent DKA were reported by the treating physicians. However, 27.0% of the patients had a good metabolic control but multiple daily insulin was reportedly were cumbersome and "compromising" the quality of life (Table 1).

Impact of insulin pump therapy

The mean HbA1c decreased from 1.6on the HbA1c scale after the first three months of insulin pump use. This was maintained till during observations at 6-12 months (P<

0.001; ANOVA for repeated measures) (Figure 1A). BMI increase 21.2 to 22.0; with p=0.026 independent of the age (r=0.180; P=0.295). The health quality improved as reflected in improved of scores (Figure 1B). Two episodes of DKA in one patient who had severe contact dermatitis at the site of cannula and sensor. One severe hypoglycemia required hospital management due to unmatched CHO intake to insulin dose due to incorrect carbohydrate counting.

Discussion

This is the first experience with insulin pump therapy from Libya. Diabetes care including advanced therapies are provided by the public sector. When insulin pumps were procured, their distribution and supervision was conducted through the National Center for Diabetes and Endocrinology in Tripoli giving a golden opportunity for us to learn from this experience and share it with others. The exercise was conducted as a quality assurance

Results showed most of our patient's age between 2- 22 years mean age 15 years; which age insulin pump therapy has been started, no sex difference with 94.39% have diabetes for 1 to 14 years (mean 6.9 years); if we compare these results with study which was done at Germany on large group, In which they analyzed age-specific differences for starting CSII of total of 1567 children and adolescents mean age 12.4 years, mean diabetes duration 5.2 years (20). This means no great difference between mean ages at starting CSII and mean for diabetes duration at different centers for pump therapy.

Indications for pump therapy almost the same in all T1DM as our study mostly either due to high HbA1c or due to perception of MDI being cumbersome to a major extent that is compromising quality of life despite good metabolic control. However, wide variation of blood sugar, severe hypoglycemia and hypoglycemic unawareness were other indications for use of pumps therapy in our center. A smaller proportions included recurrent DKA and pregnancy. Our results are comparable to a recent German study in which dawn phenomenon (27.4%), reduction of hypoglycemia (20%) and improvement of hyperglycemia (18.1%) were the commonest indications for starting CSII (20).

The mean HbA1c reduction occurred by 1.7 points on the scale after such a short time of 3 months is very meaningful and more so as it was maintained till last observation over a period of 6-12 months, without hypoglycemic events. This prompt good glycemic control achieved by insulin pump therapy is in line of evidence provided by the star 3 study group who demonstrated effectiveness of sensor-augmented insulin-pump therapy in T1DM (21). The reduction of HbA1c in the star 3 study was even less than our own (from 8.3% to 7.5% (p<0.001) (21).

Poorly controlled diabetes is well known to be associated with poor nutrition. In our study, BMI improved albeit slightly from 21.2 to 22 kg/m^2. In the very young, lack of correlation with age is also important. Also this increment was not related to any increase in the insulin dose since the total daily dose was reduced by protocol by 25% at initiation of insulin pump therapy. In the Star 3 study, there was no weight gain in pump group perhaps suggesting a worse initial glycemic control in our patients (21).

Two episodes of DKA occurred in a single patient who has severe contact dermatitis at the site of cannula and sensor. The uniqueness of the characteristics of the case is in line with the modern pump literature. With good compliance and adequate family support, the risk of DKA is lower that was originally thought. Many short-term studies reported no DKA at all, possibly due to the increased support provided to participants. Indeed, the use of CSII has been shown to decrease the DKA risk in patients who suffered recurrent DKA before initiation of insulin pump (22). One episode of severe hypoglycemia that required hospital management was clearly due to mismatching of CHO intake to insulin dose. This rate of severe hypoglycemia is fairly low taking the achieved mean HbA1c of 7.4% in consideration. Adolescents who underwent intensive insulin therapy in the diabetes control and complications trial (DCCT) had higher rates of hypoglycemia for similar HbA1c values (1).

The health-related quality showed a marked numerical improvement with high statistical significance (34 to 47; P =0.001). Such findings are consistent with previous studies reporting greater improvement in overall patients' satisfaction for pump therapy compared to MDI (19,23).

In conclusion, our experience indicated that insulin pump therapy is very effective tool in our hands to achieve and maintain good glycemic control in patients with T1DM. It was very good tool to engage patients and families and to enhance communication between patients/families and health care providers giving more opportunities for education and support for diabetes self- management. Further studies are needed on a larger scale for more.

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Authors' Contributions
All authors contributed significantly to the study. Specifically, FBR and NA planned the study, WH and NA collected all the data and NBG conducted all the statistical analysis. They all contributed to the manuscript and approved its final version.

Compliance with Ethical Standards
1. Funding: This study received no funding whatsoever. However, training and technical support was provided by the pump vendors as part of their commitment to patients' care.

2. Conflict of Interest: None of the authors declared any conflict of interest.

3. Ethical approval: The study was approved by the National Center for Diabetes and Endocrinology as an audit/quality assurance exercise. All participants and/or their families provided verbal informed consent for their data to be included in the assessment as an observational exercise and any resulting publication anonymously.

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