Clinical Characteristics and Satisfaction of Liraglutide Treatment among Patients with Type 2 Diabetes: A Prospective Study

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ABSTRACT:

BACKGROUND: Evaluation of patient-reported results, treatment satisfaction, in particular, is popularly gaining recognition as crucial to the assessment of the efficiency of new therapies. The aim of this study is to examine the clinical features and treatment satisfaction with liraglutide in insulin-dependent obese patients having uncontrolled diabetes.

METHODS: A prospective study was performed for 12 weeks using 64 type 2 diabetes (T2D) patients, 30 to 70 years of age, who came in for treatment to the Diabetes Treatment Center in Prince Sultan Military Medical City, Riyadh, Saudi Arabia, from November 2017 to July 2018. All the patients enrolled in this study were given liraglutide in addition to their existing treatment. For the first week, they were subcutaneously administered 0.6 mg once per day, which was gradually raised to 1.2 mg after 1 week, and the final given dose went up to 1.8 mg per day until the study period was completed. Purposive and suitable selection of the respondents was performed at their convenience. They were interviewed adopting the Diabetes Treatment Satisfaction Questionnaire (Arabic version) at baseline and after 12 weeks. Besides, the clinical variables like hemoglobin A_{1c} (HbA_{1c}), fasting blood sugar (FBS), total daily insulin dose (TDD), number of injections, and hypoglycemia/weeks were also recorded at baseline and at the end of the study.

RESULTS: In comparison with the baseline values, notable positive differences were identified in the domains of treatment satisfaction, namely, satisfied with current treatment ($P = .0001$), frequency of perceived hyperglycemia ($P = .0001$), frequency of perceived hypoglycemia ($P = .0001$), convenience of current treatment ($P = .0001$), understanding diabetes ($P = .0001$), recommend the current treatment ($P = .018$), and continue the present treatment ($P = .0001$) when the study is completed. After 12 weeks, the addition of liraglutide to the existing treatment showed significant positive changes on FBS ($P = .0001$), HbA_{1c} ($P = .001$), TDD ($P = .0001$), number of injections ($P = .0001$), documented hypoglycemia/weeks ($P = .0005$), and body weight ($P = .0001$) in comparison with the baseline values.

CONCLUSIONS: The addition of liraglutide to the existing treatment raised the level of treatment satisfaction and minimized the frequency of hypoglycemic/hyperglycemic events apart from the other clinical variables.

KEYWORDS: diabetes treatment, type 2 diabetes, treatment satisfaction, liraglutide

Introduction

The most recent reports from World Health Organization (WHO) and from the International Diabetes Federation (IDF) revealed that over the past 30 years there has been a dramatic increase in the prevalence of type 2 diabetes (T2D) worldwide.[1,2] Furthermore, an estimate indicated that diabetes directly accounted for nearly 1.6 million deaths. In fact, the WHO predicts that diabetes will rank seventh as the cause of death by 2030.[1]

Diabetes is a disease that is eminently treatable, and its repercussions too can be easily prevented or blocked by incorporating amendments in the diet, physical activity, and medication, and obtaining regular screening and treatment for the T2D-related complications.[3–6] Several medications are available for diabetes which can pose difficulties for the selection of the ones more suited for specific patients. Evaluation of patient-reported results, treatment satisfaction, in particular, is popularly gaining recognition as crucial to the assessment of the efficiency of new therapies.[7,8] Treatment compliance, glycemic control, and treatment preference are all found to be related to treatment satisfaction.[8]

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) or incretin mimetics are injectable hormones that raise the glucose-dependent insulin secretion and lower the glucagon secretion by inciting the beta cells.[9,10] One of the approved GLP-1 RAs to treat diabetes is liraglutide (Victoza).[11] Besides, from prior studies, it is evident that Victoza (liraglutide) 1.2 mg or 1.8 mg is an injectable prescription medication for T2D adults which together with diet and exercise may raise the blood glucose and glycated hemoglobin levels with low risk for hypoglycemia, hyperglycemia, and weight loss.[12–14] From the research, it is clear that, when insulin therapy is started, patients initially undergo some degree of diabetes-related distress, meaning that they may consider the injection regimen as highly

demanding, and more often than not they feel quite unsatisfied with their diabetes treatment than do their normal counterparts.[15] In fact, patient satisfaction has become an acceptable indicator of health care quality, very significant in chronic diseases such as T2D.[15]

Much research has been performed on the factors linked to diabetes treatment satisfaction.[16,17] Patients with T2D showing higher levels of glycosylated hemoglobin (HbA_{1c}) and increased weight expressed a lower degree of satisfaction, as did patients with diabetes-related complications.[17] However, only limited studies are available for the use of liraglutide and treatment satisfaction among the patients on insulin therapy. Therefore, this study aimed at identifying the clinical features and treatment satisfaction in obese insulin-dependent patients with uncontrolled diabetes, after adding liraglutide along with the existing treatment.

Methods

Study design and setting

A 12-week prospective study was performed using 71 T2D patients who visited the Diabetes Clinic at Diabetes Treatment Center, Prince Sultan Military Medical City (PSMMC), Saudi Arabia from November 2017 to July 2018, adopting the protocol drawn up by the Declaration of Helsinki and approved by the PSMMC Research Ethics Committee. Out of 71 patients, 7 did not continue the study for reasons that violated the inclusion criteria, failed to tolerate, not willing to continue the medication, or for personal reasons. It should be mentioned here that those who failed to show up at 12 weeks after the baseline visit were also completely excluded from the study. A total of 64 patients continued until the end of the study.

Inclusion and exclusion criteria

The study involved 30- to 70-year-old obese patients (body mass index [BMI] $\geqslant 30\,kg/m^2$)[18] with uncontrolled T2D ($HbA_{1c} > 7\%$),[19] undergoing insulin treatment and naïve to liraglutide therapy and being followed up for a minimum of 1 year. Patients who were excluded were those with a history of psychopathology, pregnant or intending to become pregnant, breast-feeding, as well as those having a history of medullary thyroid carcinoma or multiple endocrine neoplasia type 2, active (during the past 12 months) disease of the gastrointestinal, pulmonary, neurological, genitourinary, or hematological system, medical instability, and impairments of the visual, hearing, or cognitive aspects.

Patient selection criteria and treatment

For this study, each patient was carefully selected keeping in mind their convenience and availability during their scheduled routine outpatient clinic visits. Informed consent for participation in the study, both verbal and written, was obtained from
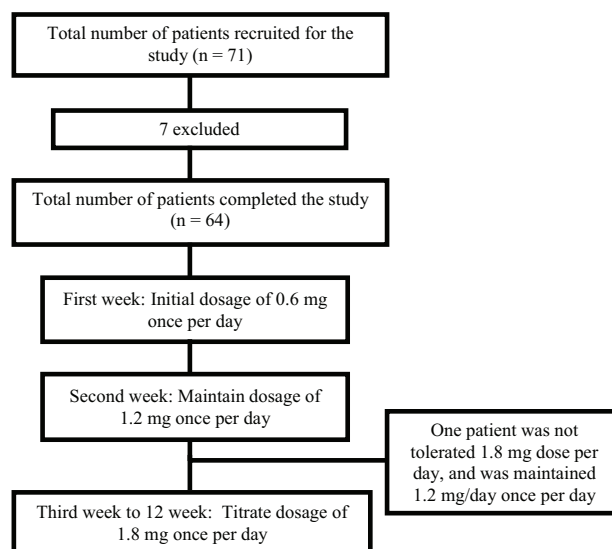

Figure 1. Patient description and liraglutide treatment.

the patients regarding aim and methodology prior to completion of the study. Participants were free to opt out of the research at will, and no explanations were required. In this study, all the patients included were administered liraglutide subcutaneously, with an initial dosage of 0.6 mg once per day for the first week and then increased after 1 week to 1.2 mg and the dose given being raised to 1.8 mg per day until the study completion. Those who failed to tolerate the 1.2 mg/1.8 mg dose were excluded from the study, whereas those intolerant to the 1.8 mg dose were advised to continue with the 1.2 mg dose per day (Figure 1).

Data collection

The standardized questionnaire was used and patient age, weight, height, and length in time of diabetes were recorded. Clinical variables such as HbA_{1c} and diabetes treatment satisfaction were collected at baseline and at the 12th week. Hypoglycemia: All the patients in the study were requested to record finger stick blood glucose readings in a standard self-monitoring blood glucose diary that was reviewed and documented to identify any hypoglycemic or hyperglycemic events. The hypoglycemic events were defined to standardized concepts: an event indicated a measured glucose concentration of $\leqslant 70\,mg/dL$ (documented hypoglycemia).

Diabetes treatment satisfaction

The Diabetes Treatment Satisfaction Questionnaire (DTSQ) was developed to determine the degree of patient satisfaction with the treatment offered. Being translated and used widely in several countries, DTSQ is now extensively used in more than 100 languages, because it is quite easy to answer and usable for both patients undergoing medical therapy as well as those lacking it.[20] The DTSQ is internationally validated and officially

approved by WHO and the IDF for both type 1 and type 2 diabetes (T2D).[21] This study used a specifically designed and validated Arabic version of the DTSQ to measure satisfaction with the diabetes treatment. The goal of this tool is to estimate the changes in the level of patient satisfaction regarding therapy modifications, as well as to compare the degree of satisfaction among those employing different treatment strategies. The DTSQ provides a high degree of accuracy in measuring treatment satisfaction in T2D patients.[21,22] The DTSQ includes 8 health concepts: 6 questions deal with general satisfaction with scores from 0 (very dissatisfied) to 6 (very satisfied). Scores were calculated as the total of 6 satisfaction items: "current treatment," "convenience," "flexibility," "understanding," "recommend," and "continue," yielding a total score between 0 and 36. The other 2 items, namely, events of "perceived frequency of hyperglycemia" and "perceived frequency of hypoglycemia," were independently estimated. Both questions were calculated with a score from 0 (never experienced) to 6 (most of the time).[21,22]

Statistical analysis

Data analysis was performed employing the Microsoft Excel 2010 (Microsoft Corporation, Seattle, WA, USA) and Statistical Package for Social Sciences version 22.0 (SPSS Inc, Chicago, IL, USA). Apart from the descriptive analysis, the differences present in the group were identified using the paired "t" test. Pearson's correlation coefficient was used to find the statistical association between treatment satisfaction score and clinical parameters. Data are expressed as mean ± standard deviation. A P value of <.05 was accepted as statistically significant.

Results

The traits of the study population and treatment procedure are shown in Table 1 and Figure 1. Most of the patient population in the study falls within the 30- to 50-year age group (58%), are female (53.1%), and have had diabetes for >7 years (60.9%).

In Table 2, the differences in the treatment satisfaction assessments performed at baseline and after 12 weeks of the study are evident in the following categories: satisfied with current treatment, frequency of hyperglycemia, frequency of hypoglycemia, convenience, flexibility, understanding, and recommend current treatment. When compared with the baseline level, significant positive differences are distinct in the categories: (1) satisfied with current treatment (P=.0001), (2) frequency of hyperglycemia (P=.0001), (3) frequency of hypoglycemia (P=.0001), (4) convenience of current treatment (P=.0001), (5) understanding diabetes (P=.0001), (6) recommend the current treatment (P=.018), and (7) continue the current treatment (P=.0001) after the study completion. Compared with baseline (14.5 ± 2.4), a significant improvement was found in the overall diabetes treatment satisfaction at the end of the study (19.6 ± 3.6; P=.0001).

Table 1. Baseline characteristics of the study population (n=64).

VARIABLE(S)	FREQUENCY	PERCENTAGE
Age (years)		
30-50	37	57.8
51-70	27	42.2
Sex		
Male	30	46.9
Female	34	53.1
Smoking status, n (%)		
Current	11	17.2
Former	6	9.4
Never	47	73.4
Duration of diabetes (years)		
≤7	25	39.1
>7	39	60.9
Insulin treatment modality		
Basal	17	27
Basal-bolus	15	23
Premix insulin	32	50
HbA$_{1c}$ level (%)		
7-8.5	18	28.1
8.6-10	27	42.2
>10	19	29.7
Baseline comorbidities		
Dyslipidemia	21	32.8
Hypertension	43	67.2

From Table 3, the differences in clinical characteristics with current treatment on fasting blood sugar (FBS), HbA$_{1c}$, total daily insulin dose (TDD), number of injections, and documented hypoglycemia/weeks are clearly seen in the study population at baseline and after 12 weeks of the study. When compared with the baseline level, significant positive differences are evident in the domains: satisfied with FBS (P=.0001), TDD (P=.0001), number of injections (P=.0001), and hypoglycemia/weeks (P=.0005).

From Figures 2 and 3, a notable difference was observed in the study population regarding perceived hyperglycemia, hypoglycemia, HbA$_{1c}$, and body weight. The liraglutide treatment showed improvements in perceived hyperglycemia (P=.0001) and hypoglycemia (P=.0001). Furthermore, body weight (P=.0001) and HbA$_{1c}$ (P=.0001) of the study population also showed a remarkable decrease.

Table 2. Effectiveness of liraglutide on DTSQ scores.

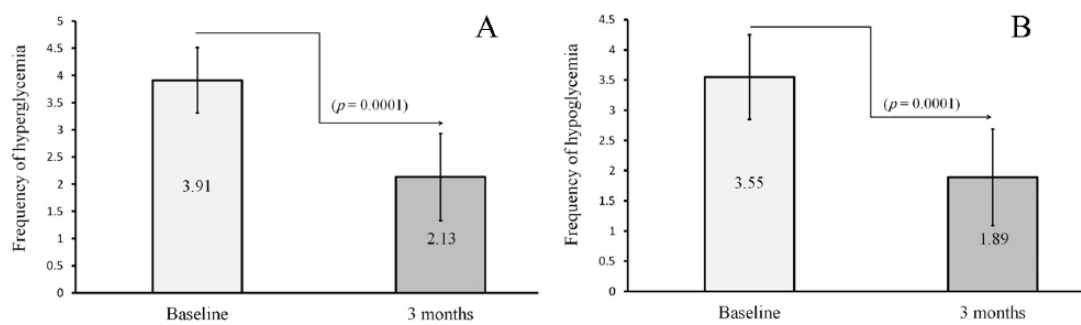| DIABETES TREATMENT SATISFACTION	BASELINE (MEAN±SD)	12WEEKS (MEAN±SD)	CHANGES	PAIRED "*T*" TEST	*P* VALUE
Satisfied with current treatment	2.11±1.2	3.61±0.6	1.5	−8.7	.0001
Convenience of current treatment	2.11±1.4	2.94±0.8	0.83	−3.8	.0001
Flexibility of current treatment	2.31±1.4	2.70±1.0	0.39	−1.6	.108
Understanding diabetes	2.20±1.6	3.16±0.8	0.96	−4.0	.0001
Recommend the current treatment	2.73±1.3	3.42±1.4	0.69	−2.4	.018
Continue the present treatment	2.67±1.6	3.80±1.0	1.13	−4.2	.0001
Total satisfaction score (Q 1, 4, 5, 6, 7, 8)	14.5±2.4	19.6±3.6	5.10	−9.7	.0001

DTSQ, Diabetes Treatment Satisfaction Questionnaire.
Baseline versus 12 weeks compared by paired *t* test; data are expressed as mean±standard deviation.

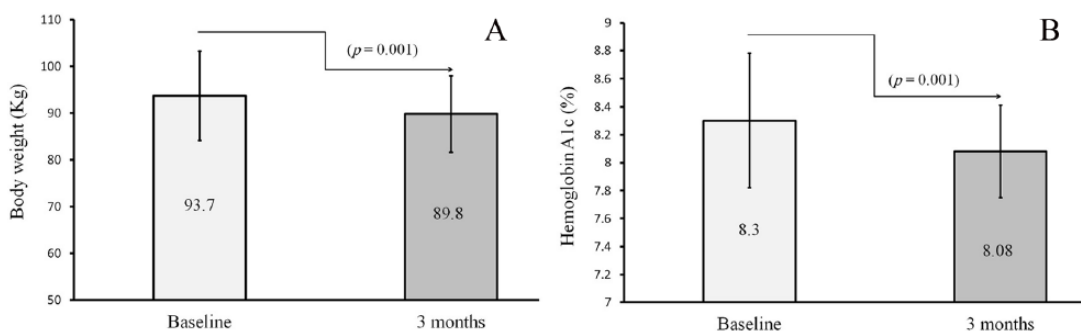**Table 3.** Effectiveness of liraglutide on clinical outcomes.

CLINICAL VARIABLES	BASELINE (MEAN±SD)	12WEEKS (MEAN±SD)	CHANGES	PAIRED "*T*" TEST	*P* VALUE
Fasting blood sugar (mg/dL)	182±20.8	160±27.8	22	5.5	.0001
Total daily insulin dose (U/kg/day)	1.1±0.04	0.66±0.47	0.44	5.7	.0001
Number of injections/day	2.56±0.83	1.47±0.50	1.0	9.0	.0001
Documented hypoglycemia/week	2.22±0.8	1.92±0.94	29	2.9	.0005

Baseline versus 12 weeks compared by paired *t* test; data are expressed as mean±standard deviation.

Figure 2. Effectiveness of liraglutide treatment on perceived hyperglycemia (A) and hypoglycemia (B) (DTSQ scores; Q 2, 3).
DTSQ, Diabetes Treatment Satisfaction Questionnaire.
Baseline versus 12 weeks compared by paired *t* test; data are expressed as mean±standard deviation.

Figure 3. Effectiveness of liraglutide treatment on body weight (A) and hemoglobin A$_{1c}$ (B).
Baseline versus 12 weeks compared by paired *t* test; data are expressed as mean±standard deviation.

Table 4. Age and sex differences in diabetes treatment satisfaction scores and hemoglobin A_{1c}.

DIABETES TREATMENT SATISFACTION AND HEMOGLOBIN A_{1C}	SEX (MEAN±SD)		P VALUE	AGE (MEAN±SD)		P VALUE
	FEMALE	MALE		30-50 YEARS	51-70 YEARS	
Satisfied with current treatment	3.8±0.71	3.4±1.5	.25	3.76±1.18	3.41±1.3	.27
Perceived hyperglycemia	2.17±0.59	2.09±0.66	.62	2.22±0.63	2.0±0.62	.17
Perceived hypoglycemia	2.13±1.04	1.68±0.76	.04	1.97±0.83	1.78±1.05	.41
Convenience of current treatment	2.7±1.36	3.15±1.52	.22	2.78±1.47	3.15±1.43	.32
Flexibility of current treatment	2.4±1.32	2. 97±1.6	.12	2.46±1.4	3.04±1.58	.12
Understanding diabetes	3.17±1.72	3.15±1.61	.96	3.08±1.7	3.26±1.6	.67
Recommend the current treatment	3.83±1.57	3.06±1.62	.06	3.35±1.68	3.52±1.60	.69
Continue the present treatment	3.93±1.63	3.68±1.64	.53	4.03±1.59	3.48±1.67	.19
Total satisfaction score	19.8±1.63	19.4±4.1	.66	19.4±3.7	19.8±3.4	.67
Hemoglobin A_{1c}	8.0±0.21	8.03±0.38	.68	8.0±0.12	8.04±0.43	.60

Baseline versus 12 weeks compared by paired *t* test; data are expressed as mean±standard deviation.

Table 4 demonstrates the sex and age differences in treatment satisfaction and HbA_{1c}. No significant differences were observed between the different sex and age groups regarding the HbA_{1c} and diabetes treatment satisfaction scores except the perceived hyperglycemia subdomain among the different sexes ($P = .04$). Pearson's correlation coefficients analysis showed no statistically significant association between treatment satisfaction and clinical parameters expect HbA_{1c} ($P = .042$).

Discussion

The HbA_{1c} levels should not be the only method of assessing the effectiveness of the diabetes treatment, but attention must also be paid to patient-reported outcomes, including patient satisfaction, well-being, and quality of life (QoL). This is crucial because any enhancement in treatment satisfaction levels may raise patient self-efficacy and commitment to therapy, resulting in attaining long-term stable glycemic control and minimized risk of diabetic complications.[20] This prospective study revealed notable positive differences in the treatment satisfaction levels post the addition of liraglutide together with the existing treatment, in most of the subdomains of DTSQ, namely, satisfied with current treatment ($P = .0001$), convenience of current treatment ($P = .0001$), understanding diabetes ($P = .0001$), recommend the current treatment ($P = .018$), and continue the present treatment ($P = .0001$) in comparison with the baseline level at the completion of the study (12 weeks). The results from this study correspond with the findings of earlier studies which reported that greater treatment satisfaction could be achieved using injectable liraglutide, as it had the potential to ensure better glycemic control, fewer hypoglycemic and hyperglycemic events, weight loss, and perception of higher treatment efficacy.[10,23,24] Significantly, in this study, we also identified that the subdomains of frequency of hyperglycemia ($P = .0001$) and frequency of hypoglycemia ($P = .0001$) were definitely fewer in frequency from the baseline compared with the final point of assessment. Hypoglycemia and hyperglycemia have been well recognized simply as infrequent adverse effects in T2D patients on hypoglycemic agents and are related to reduced health-related QoL and treatment satisfaction.[25,26] Some recent studies further reported that patients with moderate or severe hypoglycemic symptoms showed lower satisfaction levels with their treatment and reduced commitment to medication than those lacking or having the symptoms.[27,28] It is noteworthy that the current treatment algorithm in this study was not related to any severe adverse events, neither to severe hypoglycemia nor to hyperglycemia; overall, during the trial the number of events of non-severe hypoglycemia and hyperglycemia was low, and higher satisfaction scores were reported among those in this study population.

With respect to the clinical variables, this study observed that the addition of liraglutide to the existing treatment produced positive differences in the FBS ($P = .0001$), HbA_{1c} ($P = .001$), TDD ($P = .0001$), number of injections ($P = .0001$), and documented hypoglycemia/week ($P = .0005$). Several studies indicate that liraglutide is a GLP-1 RA because the GLP-1 RAs encourage insulin secretion according to the blood glucose levels, by reducing the hypoglycemic episodes, glycemic control, fasting plasma glucose, and total insulin need.[29–35] Concurring with our results, earlier research also showed that liraglutide lowers the FBS and glycated hemoglobin, with a low risk of hypoglycemia.[12–14] From the recent studies, liraglutide was noted to appreciably heighten the glycemic control and lower the body weight without adversely affecting the QoL in T2D patients with obesity.[21,36]

Among the comorbid conditions in most T2D patients, obesity ranks high and the increase in the basal insulin

treatment has been found to be linked to further weight gain and heightened risk of hypoglycemia. In fact, multiple insulin injections administered daily normally induce even greater weight gain. Therefore, several individuals on multiple daily insulin injections end up having even higher insulin resistance and obesity, and frequently fail to achieve adequate glycemic control.[23,29,36,37] From the findings of recent studies, liraglutide was observed to clearly improve glycemic control and decrease body weight in obese patients.[23,29,36,37] The findings from this study also showed beyond doubt that the additional 12-week treatment of liraglutide plus the existing treatment caused a greater loss in body weight in the population under study. In a recent study, the weight loss and improved glycemic control induced by the added liraglutide were both linked to high levels of patient satisfaction.[36]

This study was mainly limited by the relatively small sample size, short-term duration, and the fact that the study was performed at only 1 center. Furthermore, the absence of a control group against which the study group could be compared limited the results, to the extent that they cannot be generalizable to real-world situations. Therefore, more research works, larger in scale and over longer time periods, are required to overcome these limitations. In conclusion, the addition of liraglutide to the existing treatment was proven to be an effective option for obese T2D patients, as it facilitated a decrease in body weight, better glycemic control, and lower frequency of hypoglycemia/hyperglycemia apart from the clinical variables. The liraglutide treatment also boosted the treatment satisfaction levels among the obese patients with T2D.

Author Contributions
AAAH and MAAD conceived and designed the study and contributed to the writing of the manuscript. AAAH and AAR wrote the first draft of the manuscript and agreed with manuscript results and conclusions. MAAD made critical revisions and approved the final version of the manuscript. All authors reviewed and approved the final manuscript.

Data Sharing Statement
There is no data sharing as this manuscript and the data were not published elsewhere.

Ethical Approval
The study protocol was approved by the Research and Ethics committee of Prince Sultan Military Medical City, Riyadh, Saudi Arabia.

Informed Consent
During the informed consent process, the study participants were assured that the data collected will be used only for stated purposes and will not be disclosed or released to others without the consent of the participants.

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