Diabetes & Metabolic Syndrome: Clinical Research & Reviews 9 (2015) 30–33

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Efficacy and safety of liraglutide therapy in 195 Indian patients with type 2 diabetes in real world setting

Jothydev Kesavadev *, Arun Shankar, Gopikakrishnan Gopalakrishnan, Sunitha Jothydev

Jothydev's Diabetes Research Centre, Trivandrum, Kerala, India[1]

ARTICLE INFO

Keywords:
Liraglutide
Type 2 Diabetes
India

ABSTRACT

Background: GLP-1 analogues has established role in the management of type 2 diabetes mellitus (T2DM). Liraglutide, a human GLP-1 analogue is used as an adjunct to diet and exercise in adults with T2DM for improvement of glycemic control.

Objective: To assess the efficacy and safety of liraglutide in Indian patients with T2DM in real-world setting.

Methods: A prospective, open label, single arm, single centre, observational study of 24 weeks duration in a real-world setting. Subjects with T2DM with impaired glucose control despite of antidiabetic therapy and clinically suitable for liraglutide therapy were enrolled and managed. All subjects received liraglutide therapy in addition to their existing anti-diabetic therapy. Starting dose of liraglutide (Victoza) was 0.6 mg/day for 7 days followed by 1.2 mg/day for next 7 days and finally 1.8 mg/day for 22 weeks. Subjects were evaluated at baseline and at 24 weeks. Adverse events (AE) noted during course of therapy were recorded. Student *t* test (two tailed, dependent) was performed for assessment of statistical significance.

Results: Total 195 subjects were studied over 24 weeks. Mean fasting plasma glucose (FPG) was decreased from 163.81 mg/dL to 111.6 ($P < 0.001$); similarly HbA1c was reduced from 8.14% to 6.96% ($P = 0.006$) at 24 weeks. At week 24, 49.23% and 41.03% subjects treated with liraglutide reached an HbA1c $< 7.0\%$ and $\leq 6.5\%$, respectively. Mean weight was reduced from 86.41 kg to 82.37 kg ($P < 0.001$). Additionally mean systolic and diastolic blood pressure was reduced from 129.31 and 76.18 mm of Hg to 119.59 ($P = 0.90$) and 70.88 ($P < 0.001$) mm of Hg, respectively. Serum cholesterol was reduced from 166.68 mg/dL to 124.86 mg/dL ($P < 0.001$). Twenty-two (11.28%) subjects reported adverse events (AE), the most common AEs being vomiting, tiredness, loose motion and nausea. All AEs were mild to moderate in nature without any serious AE.

Conclusion: In 195 Indian patients with T2DM receiving anti-diabetic drugs, addition of liraglutide resulted in significant improvement in glycemic parameters and was well tolerated. Clinically significant reduction in weight, blood pressure and serum cholesterol were also noted.

1. Introduction

Presently type 2 diabetes mellitus (T2DM) is one of the most common chronic diseases affecting almost all countries across the world. The prevalence of T2DM is increasing continuously with decreased physical activity, change in dietary habits and increased obesity. In India, T2DM is an important public health problem with estimated number of adults with diabetes 61.3 million in 2011; estimated number is expected to reach 101.2 million by 2030 [1]. Growing prevalence with very high number of patients with diabetes and pre-diabetes is a huge burden on health care systems in India [2].

The ADA/EASD position statement recommends a patient centred approach for attaining good glycaemic control [3]. The UKPDS has shown that a mean difference of 1% HbA1c may also be able to lower the risk of mortality and morbidity (21% deaths related to diabetes, 14% chances of myocardial infarction and 37% chances of microvascular complications) [4]. This clearly highlights importance of optimal glycemic control. However management of T2DM is often challenging for treating physician due to progressive nature of the disease and multiple pathophysiological

* Corresponding author. Tel.: +91 471 2356200; fax: +91 471 2356666.
E-mail address: jothydev@gmail.com (J. Kesavadev).
[1] www.jothydev.net.

http://dx.doi.org/10.1016/j.dsx.2014.04.034
1871-4021/

processes. In many situations complex treatment regimens are required to achieve optimal glycemic control [3]. This is often associated with an increased risk of hypoglycaemia and weight gain.

Incretin based therapies like GLP-1 analogues and DPP-4 inhibitors are recent addition in management of T2DM. Liraglutide (Victoza®; Novo Nordisk A/s) is a GLP-1 receptor agonist which has 97% analogy to native GLP-1 and increased resistance to DPP-4 action [5]. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM [5]. Liraglutide is available in India since July 2010. We evaluated efficacy and safety of liraglutide in 195 Indian patients with T2DM in real-world situation at a Diabetes Research Centre in South India.

2. Materials and methods

This was a prospective, open label, single arm, single centre, observational study of 24 weeks duration in a real-world setting at Jothydev's Diabetes and Research Center (JDC) at Trivandrum, Kerala, India. Subjects with T2DM clinically suitable for liraglutide therapy were enrolled in the study and were managed with Diabetes Tele Management System (DTMS®) [6]. DTMS® is a unique telemedicine tool in vogue since 1998 at JDC. This consists of special software, networked computers and a multidisciplinary team following up subjects via telephone or Internet providing continuous education, modification of dosages and lifestyles and ensuring compliance with therapeutic instructions. The team at Jothydev's Diabetes Research Center comprised of more than 30 members; which includes trained doctors, dietitians, nurses, pharmacists, educators and a psychologist.

All subjects received liraglutide therapy in addition to their existing anti-diabetic therapy except DPP-4 inhibitors. The starting dose of liraglutide injection was 0.6 mg/day for 7 days which was escalated to 1.2 mg/day for next 7 days and finally 1.8 mg/day for 22 weeks. There was no washout period for the drugs previously used in these patients and the duration of therapy was 24 weeks (6 months). Individualized diet modification and exercise plan was discussed and prescribed.

Subjects with known contraindications for liraglutide therapy based on prescribing information of Victoza® injection were excluded from the study [5]. Formal written informed consent for participation in the study was obtained from each patient.

All subjects were evaluated at baseline and after 24 weeks of therapy. Physical examination, glycemic control (fasting plasma glucose [FPG], glycosylated haemoglobin [HbA1c]), and serum cholesterol were performed.

The doses of other anti-diabetic drugs were modified as and when required via DTMS®. After 24 weeks of therapy, liraglutide therapy was continued in select patients depending on clinical requirement.

The safety and tolerability of liraglutide was assessed continuously during the study and any adverse event (AE) noted during course of therapy was recorded.

3. Statistical methods

Statistical methods: Descriptive and inferential statistical analysis has been carried out in this study. Results on continuous measurements are presented on Mean ± SD (Min–Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. The following assumption on data is made, *Assumptions*: (1) dependent variables should be normally distributed, (2) samples drawn from the population should be random, and (3) cases of the samples should be independent.

Table 1
Baseline demographic data.

S. No.	Parameter	Observed value
1	Number of patients	195
2	Male:female	108:87
3	Age (years, Mean ± SD)	45.87 ± 10.71
4	Duration of T2DM (years, Mean ± SD)	6.48 ± 6.35
5	Weight (kg, Mean ± SD)	86.40 ± 12.82
6	Systolic blood pressure (mm of Hg, Mean ± SD)	129.32 ± 14.43
7	Diastolic blood pressure (mm of Hg, Mean ± SD)	70.88 ± 8.05

SD, standard deviation.

Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale with in each group. *P* value less than <0.05 was considered statistically significant.

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs and tables.

4. Results

A total 195 (male: 108 and female: 87) subjects received liraglutide for 24 weeks. Mean age was 45.87 (Min: 20 years; Max: 72 years) years. Mean duration of T2DM was 6.48 years and mean weight was 86.40 kg (Table 1). 58 patients were receiving insulin (Table 4).

4.1. Improvement in glycemic parameters

At baseline, all the subjects were receiving clinically relevant anti-diabetic and other therapy for management of T2DM and associated co-morbidity. At baseline subjects were not well controlled and mean FPG of 163.81 mg/dL and HbA1c of 8.14% were observed. After initiation with liraglutide the mean FPG decreased by 52.21 mg/dL ($t = 11.38$; $P < 0.001$) at week 24. Similarly significant reduction of 1.18% ($t = 2.80$; $P = 0.006$) was noticed in HbA1c at week 24 (Table 2 and Fig. 1).

At week 24, 49.23% and 41.03% subjects treated with liraglutide reached an HbA1c < 7.0% (ADA target) and ≤6.5% (AACE and IDF target), respectively.

4.2. Improvement in non-glycemic parameters

A weight reduction of 4 kg ($t = 13.79$; $P < 0.001$) was noticed at week 24. Similarly at week 24, clinically significant reduction of 9.72 mm of Hg in systolic blood pressure (SBP) and 5.3 mm of Hg ($t = 7.75$; $P = <0.001$) in diastolic blood pressure (DBP) was noticed. At week 24, reduction of 41.82 mg/dL ($t = 8.15$; $P < 0.001$) in serum cholesterol was noticed (Table 3 and Fig. 1).

Table 2
Improvement in glycemic control.

	Baseline	After 24 weeks	Significance
FPG (mg/dl, Mean ± SD)	163.81 ± 67.47	111.60 ± 30.61	$t = 11.38$; $P < 0.001$**
HbA1c (%Mean ± SD)	8.14 ± 1.89	6.96 ± 1.16	$t = 2.80$; $P = 0.006$**

FBG, fasting blood glucose; HbA1c, glycosylated haemoglobin; $P < 0.05$ – suggestive significance;* moderately significant; ** strongly significant.