**INTRODUCTION**

Liraglutide, a human glucagon-like peptide-1 receptor agonist, decreases glycosylated hemoglobin and causes weight loss. However, the cost of therapy and gastrointestinal side-effects such as nausea and diarrhea are important impediments to adherence and long-term compliance. We assessed the efficacy, safety and tolerability of low dose (0.6 mg) liraglutide in obese uncontrolled longstanding type 2 diabetes in Indian patients. Low dose liraglutide improved glycemic control and decreased weight. However, there was a significant drop out because of gastrointestinal intolerance and financial constraints.

**RESULTS**

A total of 30 patients with 23 (76.7%) females, 7 (23.3%) males, overweight and obese patients with T2DM received liraglutide injections. Median age of patients was 50.5 years (range: 31-72 years). Duration of diabetes was mean: 5.8 ± 3.97 years, median: 5.3 years (range: 0.1-11.7).

A total of 17 patients were studied for 24 weeks. One patient discontinued after 2 weeks because of gastrointestinal intolerance. Seven patients were lost to follow-up after 12 weeks probably because of financial constraints. Five patients refused to continue liraglutide after 12 weeks because of gastrointestinal intolerance, mainly vomiting and diarrhea. Three more patients refused to continue liraglutide after 24 weeks follow-up because of gastrointestinal intolerance.

Baseline mean HbA1c (%) was 8.03 ± 1.49, at twelve weeks mean HbA1c (%) was 7.69 ± 1.64 and at 24 weeks HbA1c was significantly ($P < 0.05$) reduced at 7.29 ± 0.9419. Mean reduction in HbA1c was 0.74% with 7 (41.12%) of 17 patients reached HbA1c target of <7% at 24 weeks.

**Key words:** India, liraglutide, type 2 diabetes
After 24 weeks of liraglutide therapy, mean fasting and postprandial plasma glucose decreased significantly ($P < 0.05$) by 38.5 mg/dL and 50.71 mg/dL, respectively from a mean baseline FPG of 168.3 ± 21.5 mg/dL and PPG of 210.5 ± 69.4 mg/dL.

Baseline mean weight was 85.71 ± 14.47 kg, with a mean body mass index (BMI) of 34.6 ± 5.08 kg. At twelve weeks, 19 of 29 patients who continued liraglutide had a non-significant mean weight loss of 2.73 kg and non-significant decrease in BMI of 1.15 kg/m². At 24 weeks follow-up, 15 of 17 patients who continued liraglutide, had a mean weight loss of 6.03 kg and decrease in BMI of 2.67 kg/m², which were significant ($P < 0.05$).

There was no significant change in systolic blood pressure, but diastolic was reduced by 7.2 mm of Hg ($P = 0.004$) from baseline of 83.9 ± 11.71-76.7 ± 5.16. Eight patients reported AEs leading to treatment refusal. AEs were nausea ($n = 6$), feeling of satiety ($n = 7$) and vomiting ($n = 5$), loose stools ($n = 2$). However, no serious AE or hypoglycemic episodes were observed.

**DISCUSSION**

There is a progressive decline in β-cell function in T2DM requiring treatment adjustment. Co-morbidities such as obesity, cardiovascular diseases and patient factors like financial capabilities, compliance needs to be taken into consideration while individualizing therapy.

First-line therapy includes metformin; however, there is a lack of consensus with regard to add-on agents. Clinical trials have established that liraglutide decreases HbA1c singly or in combination and also results in weight loss. But cost of therapy, is an important impediment to adherence and long-term compliance. Liraglutide is associated with gastrointestinal side-effects such as nausea and diarrhea, which are usually transient and may be alleviated by gradual dose escalation of liraglutide. LEAD trials, recommended starting at 0.6 mg daily for at least 1 week to establish tolerability and then escalating to 1.2-1.8 mg daily. In LEAD-2 study mean HbA1C decrease was 1.0% for 1.2-1.8 mg liraglutide and 0.7% for 0.6 mg liraglutide. However we could not escalate the dose due to prohibiting cost and adverse gastrointestinal effects.

Kesavade et al. evaluated the efficacy and safety of 1.8 mg/day of liraglutide in 14 overweight and obese Indian T2DM patients (diabetes for <12 weeks). Mean HbA1c (2.26%) and weight reduction was 8.65 kg at 24 weeks, greater than LEAD studies. Significant reduction in SBP of 15.15 mm of Hg was noted. There was no episode of hypoglycemia or any other serious AE.

A 24-week double-blind trial Kaku et al. evaluated the efficacy and safety of 0.6 mg and 0.9 mg/day liraglutide added to sulphonylurea in 264 Japanese subjects (mean BMI: 24.9 kg/m²; mean HbA1c: 8.4%). Mean change in HbA1c was -1.46 ± 0.95 with liraglutide 0.6 mg/day without causing major hypoglycaemia or weight gain or loss. In our retrospective study in a real-life setting low dose liraglutide (0.6 mg/day) reduced HbA1c by 0.74% in obese uncontrolled type 2 diabetes of mean 5.8 years, with 41% achieving target HbA1c of <7%. However, a significant proportion of our patients dropped out or refused to continue even low dose liraglutide because of gastrointestinal intolerance (which was much more than LEAD study) and financial constraints. We noticed a significant reduction in body weight even with low dose liraglutide therapy probably due to gastrointestinal effects; these observations were at variance with previous studies. In LEAD-2, weight loss was dose dependent: 1.8 ± 0.2, 2.6 ± 0.2 and 2.8 ± 0.2 kg for 0.6 mg, 1.2 mg and 1.8 mg liraglutide, respectively while, gastrointestinal AE (nausea, vomiting and diarrhea) in 35%, 40% and 44% with 0.6, 1.2 and 1.8 mg liraglutide, respectively. Gastrointestinal events led to withdrawal 5% of all liraglutide treated subjects in a dose-dependent manner.

**CONCLUSION**

Low dose liraglutide (0.6 mg/dl) once a day improved glycemic control and decrease in weight, in obese uncontrolled longstanding type 2 diabetes. However, a significant proportion of patients dropped out because of gastrointestinal intolerance and financial constraints. In the real world setting, especially in developing countries like India, these factors have a major impact on GLP-1 based therapies like liraglutide.

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