

# Low dose liraglutide in Indian patients with type 2 diabetes in the real world setting

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### ABSTRACT

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.

**Key words:** India, liraglutide, type 2 diabetes

## INTRODUCTION

Liraglutide is a human glucagon-like peptide-1 (GLP-1) analog and acts as a GLP-1 receptor agonist. Liraglutide is presently used in selected patients with type 2 diabetes mellitus (T2DM). We assessed the efficacy, safety and tolerability of low dose (0.6 mg) liraglutide in overweight or obese Indian patients with T2DM.

## MATERIALS AND METHODS

A single center, retrospective observational study conducted for 24 weeks in a real-world setting. Dose of liraglutide was 0.6 mg/day. All patients received liraglutide in addition to their existing antidiabetic therapy except dipeptidyl peptidase-4 inhibitors/insulin. All were evaluated at baseline and after 12 and 24 weeks of therapy. Physical examination and glycemic control (fasting plasma glucose and postprandial plasma glucose [FPG; PPG],

glycosylated hemoglobin [HbA1c]), were repeated and evaluated. Adverse events (AEs) were recorded. Safety and tolerability of liraglutide and the dropout rate was assessed continuously during the study.

## 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:  $5.8 \pm 3.97$  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  $8.03 \pm 1.49$ , at twelve weeks mean HbA1c (%) was  $7.69 \pm 1.64$  and at 24 weeks HbA1c was significantly ( $P < 0.05$ ) reduced at  $7.29 \pm 0.9419$ . Mean reduction in HbA1c was 0.74% with 7 (41.12%) of 17 patients reached HbA1c target of  $<7\%$  at 24 weeks.

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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  $168.3 \pm 21.5$  mg/dl and PPG of  $210.5 \pm 69.4$  mg/dl.

Baseline mean weight was  $85.71 \pm 14.47$  kg, with a mean body mass index (BMI) of  $34.6 \pm 5.08$  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/m<sup>2</sup>. 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/m<sup>2</sup>, 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  $83.9 \pm 11.71$ - $76.7 \pm 5.16$ . 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  $\beta$ -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.<sup>[1]</sup> Clinical trials have established that liraglutide decreases HbA1c singly or in combination and also results in weight loss.<sup>[2,3]</sup> 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.<sup>[4]</sup> However we could not escalate the dose due to prohibiting cost and adverse gastrointestinal effects.

Kesavadev *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.<sup>[5]</sup>

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/m<sup>2</sup>; mean HbA1c: 8.4%).<sup>[6]</sup> Mean change in HbA1c was  $-1.46 \pm 0.95$  with liraglutide 0.6 mg/day without causing major hypoglycaemia or weight gain or loss.<sup>[6]</sup> 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:  $1.8 \pm 0.2$ ,  $2.6 \pm 0.2$  and  $2.8 \pm 0.2$  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.

## REFERENCES

1. Tandon N, John M, Sharma SK, Kesavadev J, Ganapathi B. A clinician's perspective on liraglutide in clinical practice. *J Assoc Physicians India* 2010;58:29-30.
2. McGill JB. Insights from the liraglutide clinical development program – The liraglutide effect and action in diabetes (LEAD) studies. *Postgrad Med* 2009;121:16-25.
3. Madsbad S. Liraglutide effect and action in diabetes (LEAD) trial. *Expert Rev Endocrinol Metab* 2009;4:119-29.
4. Nauck M, Frid A, Hermansen K, Shah NS, Tankova T, Mitha IH, *et al.* Efficacy and safety comparison of liraglutide, glimepiride, and placebo, all in combination with metformin, in type 2 diabetes: The LEAD (liraglutide effect and action in diabetes)-2 study. *Diabetes Care* 2009;32:84-90.

5. Kesavadev J, Shankar A, Krishnan G, Jothydev S. Liraglutide therapy beyond glycemic control: An observational study in Indian patients with type 2 diabetes in real world setting. *Int J Gen Med* 2012;5:317-22.
6. Kaku K, Rasmussen MF, Clauson P, Seino Y. Improved glycaemic control with minimal hypoglycaemia and no weight change with the once-daily human glucagon-like peptide-1 analogue liraglutide as add-on to sulphonylurea in Japanese patients with type 2 diabetes. *Diabetes Obes Metab* 2010;12:341-7.

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