SLOWER TITRATION OF LIRAGLUTIDE ACHIEVES BETTER TOLERABILITY IN SOME PATIENTS

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ABSTRACT

Objective: Liraglutide, when titrated according to the package insert, has a 20% incidence of nausea. More recently, liraglutide was studied in combination with insulin degludec. The titration schedule for the combination injection is considerably slower than that recommended for liraglutide alone, and has only a 9% incidence of nausea.

Methods: A slower titration of liraglutide was administered to 3 patients who were unable to tolerate a higher dose due to nausea.

Results: In all 3 patients, the slower titration allowed them to ultimately tolerate the higher dose.

Conclusion: Slower titration of liraglutide may improve tolerability and should be considered as an “off-label” means of achieving slower, but improved, tolerability for this drug in some patients. A larger study looking at different titration schedules to see which achieves optimal tolerability in the shortest amount of time should be encouraged. (AACE Clinical Case Rep. 2018;4:e7-e8)

INTRODUCTION

Liraglutide is available as a treatment for type 2 diabetes at a maximum dose of 1.8 mg/day, or as a weight-loss drug at a maximum dose of 3.0 mg/day. The most common side effect limiting its use is nausea, and the package insert warns of a 20% incidence of nausea at the 1.8 mg dose (1). The recommended titration schedule is to begin with 0.6 mg daily, and to increase weekly by 0.6 mg until the maximum dose is achieved. Liraglutide has been studied as a combination injection together with insulin degludec (2). In published trials, the titration schedule for the combination used an increase of 0.07 mg twice a week of liraglutide, which calculates to an increase of 0.14 mg/week. The published incidence of nausea was only 7.8 to 9.0%. In a head-to-head trial, the titration schedule for liraglutide resulted in a 20% incidence of nausea, compared to 9.0% in the combination titration schedule, where both arms achieved the same dose of 1.8 mg/day (3).

Patients were identified who failed to reach the maximum dose of liraglutide due to nausea and vomiting using the recommended titration schedule. After the combination studies were published, I reasoned that slower titration might improve tolerability for these patients.

CASE REPORTS

Three patients were started on liraglutide at 0.6 mg/day. After 1 week they were advised to increase their dose by only 2 or 3 clicks every 4 to 14 days (each click, though not marked, is 0.06 mg, resulting in a weekly increase of 0.09 to 0.18 mg), comparable to the titration schedule reported in the combination studies (see Table 1). Patients were told to dial to 1.2 mg and then add an additional 2 or 3 clicks during the first week followed by 4 or 6 clicks during the second, and so on, until they achieved the 1.8-mg dose. They were warned that there would not be markings on the pen at the intermediate doses.

So far, all 3 patients, previously intolerant of high doses of liraglutide due to severe nausea and/or vomiting, have been able to tolerate injections at doses of 1.8 mg for 6 months or longer.
DISCUSSION

Slower titration of liraglutide appears to enhance tolerability and should be considered as an “off-label” means of achieving slower, but improved, tolerability for this drug in some patients. A larger study looking at different titration schedules to see which achieves optimal tolerability in the shortest amount of time should be encouraged.

DISCLOSURE

Dr. Grajower is on the speakers’ bureau of Novo Nordisk Inc.

REFERENCES


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<th>Table 1</th>
<th>Slower Titration Schedules Used to Achieve Higher Doses of Liraglutide</th>
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<td>Patient</td>
<td>Recommended highest tolerated dose (mg/d)</td>
</tr>
<tr>
<td>1</td>
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<tr>
<td>2</td>
<td>1.2</td>
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