

Case Report

Liraglutide as an effective tool for obesity management in type 1 diabetes – case report

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Abstract

Glucagon-like peptide-1 receptor agonists (GLP-1-RA) are recommended for the management of type 2 diabetes as well as for obesity treatment. They have multiple effects, including stimulation of insulin secretion, inhibition of glucagon release, gastric emptying delay, and food intake suppression. Type I diabetes mellitus (DMT1) requires life-long insulin therapy. However, obesity is caused by overeating; thus, additional insulin injections pose a risk for cardiovascular events, osteoarthritis, and obstructive sleep apnea. In this case report, we inform about a patient with DT1 and binge-eating behavior who used liraglutide 3.0 mg for 3 months for obesity management with significant improvement in HbA1c level (7.5% vs. 6.9%), weight (82.6 vs. 75.2 kg), BMI (32.3 vs. 29.4 kg/m²), waist circumference (94 vs. 88 cm), and leptin level (24.5 vs. 10.3 ng/ml). Further studies of GLP-1-RA in DT1 management can help to reduce the risks of obesity-related conditions and decrease the daily insulin dose requirement.

Keywords: liraglutide, GLP-1-RA, obesity, DT1.

Introduction

GLP-1-RA has been approved for the management of type 2 diabetes mellitus [1, 2] as well as for obesity treatment [3]. GLP-1-RA have multiple metabolic effects: they stimulate glucose-dependent insulin secretion [4], decrease gastric emptying [5], and inhibit food intake [6]. Contraindications to the use of GLP-1-RA include hypersensitivity, pregnancy, gastroparesis, inflammatory bowel disease, a personal or family history of multiple endocrine neoplasia 2A, multiple endocrine neoplasias 2B, or medullary thyroid cancer [7–10]. DMT1 is a result of the autoimmune destruction of β -cells that leads to insulin deficiency and the requirement of life-long replacement insulin therapy [11]. Obesity is well-studied as a risk factor for type 2 diabetes and prediabetes. However, no specific guidelines exist for treating and preventing obesity in DMT1 [12]. The mechanisms that drive obesity in DT1 are likely to include genetics, epigenetics, enteroendocrine

hormones, microbiome, and effects on multiple tissues, organs, cells, and organelles [12]. In DT1, insulin sensitivity is initially reduced but normalizes after improved glycemic control, whereas glucose effectiveness remains impaired [13]. Intensive insulin therapy causes hypoglycemic episodes (62 incidents/100 patient-years) and weight gain of approximately 4.6 kg over a period of 10 years [14]. In addition, many patients fail to reach HbA1C goals despite aggressive treatment [15].

Liraglutide is the most widely studied GLP-1-RA in DMT1 patients as an add-on therapy to insulin. Studies consistently showed an approximate 0.2% to 0.5% HbA1c lowering when liraglutide was added to insulin therapy [16–18]. Liraglutide produced a statistically significant reduction in body weight, averaging 2.3 to 6.8 kg over a 4- to 24-week period, respectively [16–20].

In the LIRA-1 study [19], which included 100 patients aged 18 years or older with DT1, insufficient glycaemic control (HbA1c >8%), and overweight (BMI >25 kg/m²), the reduction in HbA1c did not differ between insulin



plus placebo and insulin plus liraglutide treatment. Liraglutide was associated with reduced hypoglycaemic events, bolus and total insulin dose, and body weight.

Some studies revealed that GLP-1-RA add-on to insulin therapy increased the level of C-peptide in C-peptide-positive individuals with DM1, but it remained undetectable in C-peptide-negative subjects [21, 22]. That indicates the stimulating effect of GLP-1-RA on β -cells, which induces endogenous insulin secretion.

Leptin is a hormone produced by adipocytes, and its level increases in obesity, especially with gaining subcutaneous fat [23, 24]. It is shown that leptin positively correlates with a level of insulin resistance (IR) [25, 26]. Typically, individuals with DM1 do not have IR, but during life-long insulin therapy and gaining weight, it develops and results in increased insulin requirement. GLP-1-RA is believed to improve IR and, thus, decrease total daily insulin dose [27, 28]. Leptin plays a major role in inhibiting food take by affecting the satiety center in the hypothalamus, which leads to negative food behavior [23, 29]. It is assumed that leptin levels increase in individuals with hyperphagic eating disorders such as binge eating or night-eating syndrome [30]. Some studies demonstrated that GLP-1-RA could affect the hypothalamic satiety center, which causes optimizing food intake and reducing binge episodes [31].

Clinical case

The patient, 43 y.o., has had DM1 for 14 years. She has been using an insulin pump with a total daily

insulin dose of 50 IU. Her initial weight was 82.6 kg, her BMI was 32.3 kg/m², and her waist circumference was 94 cm. The patient reported episodes of overeating caused by stress conditions such as air-raid warnings or electricity blackouts. She was tested for eating disorders with Binge-eating screener-7 (BES-7), which revealed positive results for binge-eating disorder. She was undergone biochemical testing, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol, and low and high-density cholesterol (LDL and HDL). Both liver aminotransferases exceeded reference ranges. High LDL, triglycerides, and low HDL indicated atherogenic dyslipidemia. HbA1c level before the liraglutide add-on was 7.5%, demonstrating poor glycemic control (target level was <7.0%). The leptin level was 24,5 ng/ml, two times higher than the reference range. C-peptide was undetectable due to the autoimmune destruction of β -cells and the absence of endogenous insulin secretion.

Before liraglutide initiation, the patient was carefully examined regarding possible contraindications to GLP-1-RA use. Liraglutide was initiated at 0.6 mg subcutaneously once daily and titrated up to 3.0 mg once daily over 5 weeks. After 3 months, the same anthropometric and laboratory tests were done, as well as testing with BES-7. Initial and post-interventional results are presented in Table 1.

After 3 months of liraglutide injections weight of the patient reduced by 7.4 kg (82.6 kg vs. 75.2 kg), BMI by 2.9 kg/m² (32.3 kg/m² vs. 29.4 kg/m²), waist circumference by 6 cm (94 cm vs. 88 cm). ALT and AST decreased by 13 and 11 U/L, respectively. LDL and triglycerides

Table 1: Initial and post-interventional levels of studied characteristics.

Characteristics	Initial levels	After intervention	Differences	Reference ranges
Weight, kg	82.6	75.2	-7.4	
BMI, kg/m ²	32.3	29.4	-2.9	18.5–24.9
Waist circumference, cm	94	88	-6	<80
ALT, U/L	39	26	-13	<35
AST, U/L	34	23	-11	<35
Total cholesterol, mmol/l	5.6	3.54	-2.06	<5.2
LDL, mmol/l	2.78	1.81	-0.97	<2.59
HDL, mmol/l	1.32	1.75	+0.43	>1.68
Triglycerids mmol/l	2.24	1.4	-0.84	<1.7
HbA1c, %	7.5	6.9	-0.6	<7.0
C-peptide, ng/ml	Undetectable	Undetectable	-	0.9–7.10
Leptin, ng/ml	24.5	10.3	-14.2	3.7–11.1

normalized, whereas HDL increased by 0.43 mmol/l. HbA1c level reached a target level (7.5% vs. 6.9%). Leptin level decreased by 14.2 ng/ml. C-peptide remained immeasurable. Total daily insulin dose reduced to 42 IU. BES-7 result demonstrated non-binge eating behavior. The patient did not report hypoglycemic events and continues to take liraglutide 3.0 mg/day.

Conclusion

DMT1 patients often suffer from obesity, posing a risk for cardio-vascular events, osteoarthritis and obstructive sleep apnea. There are no specific guidelines for obesity management in DT1. GLP-1-RA can be an option to reduce weight, BMI and waist circumference. Besides, they normalize liver functioning and lipid profile which helps to avoid long-term complications of obesity. Liraglutide as add-on therapy to insulin helps to reach the target level of HbA1c in those who require high total daily insulin doses. Unfortunately, the C-peptide level remains negative after liraglutide use, demonstrating absolute destruction of β -cells and no possibility of restoring their functioning. It also has a low risk of hypoglycemia that is perhaps decreased compared to insulin monotherapy, likely because of a decrease in total daily insulin dose.

Furthermore, liraglutide suppresses the hunger center in the hypothalamus, which results in optimizing binge eating behavior. GLP-1-RA, specifically liraglutide, can be used as a safe and effective tool for managing obesity in DT1. Further studies with other GLP-1-RA are needed.

Conflict of interest

The authors declare no conflict of interest.

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