

Case Report

Exposure to High-Dose Liraglutide in a Pregnant Woman With Obesity

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BACKGROUND: Animal studies indicate that liraglutide is not recommended for managing gestational diabetes mellitus and obesity during pregnancy due to potential developmental toxicity. We report a case of liraglutide exposure during the first trimester in a woman with obesity taking the maximum dose (3 mg subcutaneously daily), along with a neurodevelopmental assessment of the child conducted 14 months postpartum. Additionally, this report includes a literature review on the teratogenic effects of anti-obesity medications.

CASE: A 29-year-old woman, gravida 9 para 6, with obesity and no history of chronic diseases was admitted at 7 weeks of gestation after taking liraglutide 3 mg/d subcutaneously for weight loss for 8 months. Liraglutide was immediately discontinued, and routine antenatal man-

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Teaching Points

1. Clinicians should counsel women on the risks and benefits of anti-obesity medications such as liraglutide, emphasizing the importance of informing health care professionals if pregnancy occurs during treatment.
2. Ongoing assessments of women and their children after inadvertent liraglutide exposure during pregnancy will be critical to monitor for any potential adverse effects.

agement was initiated. The patient underwent cesarean delivery at 37 weeks of gestation; the neonate had low birth weight but was otherwise healthy. Follow-up during 14 months postpartum indicated appropriate childhood weight gain and normal neurodevelopmental assessment for age.

CONCLUSION: This case report demonstrates a normal pregnancy outcome after exposure to a high dose of liraglutide during the first 7 weeks of pregnancy, apart from a low birth weight. These findings enhance the limited understanding of liraglutide exposure during pregnancy. More studies are required to establish a causal relationship between neonatal weight and liraglutide exposure. Longitudinal follow-up of children beyond 14 months is essential to evaluate growth and neurodevelopmental outcomes and assess any long-term teratogenic effects from anti-obesity drugs.

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Glucagon-like peptide-1 (GLP-1) agonists have been introduced as a new pharmacotherapy for weight management. Semaglutide¹ and tirzepatide² have shown potential for greater than 10% weight loss in people with and without type 2 diabetes. Other drugs, such as a combination of naltrexone and bupropion, have achieved approximately 5–6% weight reduction.^{3–6} Liraglutide, a GLP-1 analogue, is approved for treatment of type 2 diabetes at doses up to 1.8 mg subcutaneously daily.⁶ At a 3-mg dose, liraglutide can reduce body weight by 5–15% and is also approved for use in patients without diabetes.^{6–9} Given that reproductive-aged females are using these medications, it is important to better understand their safety in pregnancy.

Although there are concerns regarding the teratogenic effects of anti-obesity medications broadly,^{10–13} exposure to orlistat in early pregnancy did not show an increased risk of major malformations.¹⁰ However, other medications, such as amphetamines and

topiramate, have been associated with oral clefts.^{14,15} Although sibutramine has been withdrawn in the United States and Europe, cardiovascular defects were observed in exposed pregnant women.¹⁰ Available data related to GLP-1 agonists and congenital malformations and other offspring outcomes are limited.

We present a case of a woman with obesity who was exposed to liraglutide at the maximum subcutaneous dose of 3 mg daily during the first trimester, along with a comprehensive systematic literature review (see Appendix 1, <http://links.lww.com/AOG/E68>, for search strategy) on the teratogenic effects of anti-obesity drugs.

CASE

A 29-year-old woman, gravida 9 para 6, with obesity (body mass index [BMI, calculated as weight in kilograms divided by height in meters squared] 36.03) presented to the emergency department of a tertiary care facility in Qatar with headache, diarrhea, and abdominal pain. She was found to have a pregnancy at 7 weeks of gestation. She had a 2-year history of obesity, no other chronic medical conditions, and a history of two previous stillbirths at 27 and 28 weeks of gestation. Additionally, she had anxiety and depression for which she had been taking sertraline 50 mg daily, but discontinued before pregnancy.

The patient reported using subcutaneous liraglutide 3 mg/d for weight loss for the previous 8 months, confirming exposure throughout the first 7 weeks of pregnancy. Liraglutide was then discontinued. She did not take anti-obesity medications during the remainder of her pregnancy.

On the first day of prenatal care, 2 weeks after the patient's emergency department visit, her BMI had increased to 36.12. Her examination was unremarkable, with normal blood pressure (116/64 mm Hg) and laboratory results. She showed no signs of renal or liver disorders, and urine microalbumin test results were negative. Her initial glycosylated hemoglobin A_{1C} concentration was 32 mmol/mol (5.1%). Starting at 80 kg, her weight reached 131 kg by the end of her pregnancy. Results of genetic testing and all ultrasonograms were normal. During her pregnancy, the patient experienced chronic anemia, with hemoglobin and ferritin improving to 11.8 g/dL and 38.2 micrograms/L, respectively, before delivery. She was prescribed both oral and intravenous supplementation in the third trimester.

The neonate was delivered by elective cesarean at 37 3/7 weeks of gestation. A pediatrician attended the delivery, and the vigorous newborn had Apgar scores of 9 and 10 at 1 and 5 minutes, respectively; birth weight was 2.330 kg (low birth weight), but length and head circumference were normal. A comprehensive examination revealed no congenital anomalies or dysmorphic features. The newborn remained in the hospital for 2 days.

At age 3 months, the infant presented to the pediatric emergency department due to bronchiolitis from respiratory

syncytial virus. The condition was managed symptomatically on an outpatient basis, requiring no hospitalization. The child was examined at 9 months, 11 months, 12 months, and, most recently, at 14 months for routine growth and neurodevelopmental assessment. All growth parameters, such as weight, length, head circumference, and neurodevelopment, have been noted to be appropriate for age during these visits. Despite having birth weight below the 3rd percentile, the child was noted to be thriving by her first birthday. Her weight was 8.4 kg, placing her in the 27th percentile (−0.6 SD) for age and sex, with a height of 73.5 cm (34th percentile, −0.39 SD) and head circumference of 44.5 cm (35th percentile, −0.38 SD). Assessment of gross motor, fine motor, social, speech, and hearing skills revealed normal development.

DISCUSSION

This case involves administration of the maximum dose of liraglutide (3 mg daily) in a woman with obesity through 7 weeks of gestation, with follow-up of the child through age 14 months. Neonatal neurodevelopmental assessment was normal, suggesting that liraglutide did not negatively affect early fetal development. This case report adds to the limited data on GLP-1 agonists during pregnancy and provides some reassurance about liraglutide's safety in the event of inadvertent early-pregnancy exposure.

The teratogenic effects of U.S. Food and Drug Administration–approved anti-obesity medications that have been noted in the literature are summarized in Table 1. Animal studies suggest that GLP-1 agonists should be avoided during pregnancy due to an association with reduced fetal weight, delayed ossification, and skeletal variants.⁹ Human studies on liraglutide are limited but indicate more favorable outcomes. A recent multicenter cohort study by Dao et al,¹⁶ involving 487 pregnancies, found no increased risk of major birth defects associated with GLP-1 agonist use in the first trimester. The major birth defect rates were 2.6% in the GLP-1 agonist group compared with 2.3% in the diabetes group (adjusted odds ratio 0.98, 95% CI, 0.16–5.82) and 3.9% in the overweight/obese group (adjusted odds ratio 0.54, 95% CI, 0.11–2.75). The GLP-1 agonist group showed a cumulative incidence of 59% live births, 23% pregnancy losses, and 18% terminations. Although the diabetes reference group had a lower termination rate (6%), the higher number of elective terminations in the GLP-1 group may reflect unplanned pregnancies and concerns about potential risks.¹⁷ The study's limitations include early discontinuation of GLP-1 agonist (median exposure of only 5 weeks); grouping of all GLP-1 agonists together, with limited exposure to specific drugs such

Table 1. Teratogenic Effects of U.S. Food and Drug Administration–Approved Medications for Weight Management

Medication	Type of Study	Gestational Age at Which Pregnancy Was Detected	Teratogenic Effects on Humans
Bupropion	Retrospective case–control study	Between 1 mo before and 3 mo after becoming pregnant	Left ventricular outflow tract heart defects ²⁴
Liraglutide	Case report	24 6/7 wk	Fetal arrhythmia ^{13,19}
Orlistat	Case report	13 wk	None
Phentermine	Retrospective observational		No increase in birth defects ¹⁰
Semaglutide	Case report	26–28 wk	Bilateral porencephalic cysts ¹¹
Tirzepatide	None	None	None
Topiramate	None	None	None
	Cochrane	1st trimester	Cleft lip or palate or both ¹²

as exenatide; and a sample size that may have been insufficient to draw definitive conclusions.

Two case reports^{18,19} provide insights into women exposed to liraglutide during early pregnancy. The first, by Greco in 2015,¹⁸ describes a woman with type 2 diabetes and polycystic ovarian syndrome who took liraglutide 1.8 mg daily until pregnancy was detected at 13 weeks of gestation. After discontinuing liraglutide and starting insulin therapy, she gave birth to a healthy child, with no developmental abnormalities noted at 3 months postpartum. The second case, from 2018, involved a 28-year-old woman with poorly controlled type 2 diabetes who continued liraglutide and metformin throughout her pregnancy. Her glycemia normalized, and she delivered a healthy male neonate by elective cesarean at 39 weeks of gestation. Liraglutide levels measured in maternal and umbilical vein serum showed no significant transfer to the fetus.¹⁹

A case series reported a woman who had two unplanned pregnancies while receiving exenatide. In the first pregnancy, exenatide was discontinued and she delivered a neonate with an atrial septal defect that closed spontaneously by age 3 years, with normal development. In the second pregnancy, exenatide was continued until the pregnancy was detected at 13 weeks of gestation, after which insulin was used for diabetes management. Notably, both siblings are healthy, at age 7 years and 5 years.²⁰ Another case report involved a 35-year-old woman with type 2 diabetes who discontinued liraglutide on an incidental pregnancy diagnosis at 14 weeks of gestation, resulting in a child without congenital anomalies.²¹

A systematic review²² investigated the effects of GLP-1 agonists on offspring outcomes during pregnancy and lactation. A key finding was that exenatide showed a fetal/maternal peptide concentration ratio of 0.017 or lower in ex vivo human placental perfusion, indicating negligible placental passage. Animal studies

have shown that GLP-1 agonists are excreted in breast milk, which may reduce fetal growth during breast-feeding. However, no human safety data on GLP-1 agonists during lactation are available.²²

Our case is one of the few available to clarify the effects of liraglutide exposure during the first trimester and examines high-dose liraglutide in a woman, with neurodevelopmental follow-up of her child through 14 months of age. Previous reports have predominantly focused on lower doses, limiting their applicability to women considering higher doses for weight management or glycemic control. Additionally, many existing case reports lack long-term follow-up, leaving developmental outcomes unclear. Although the absence of developmental concerns at a 14-month follow-up is noteworthy, it does not eliminate the possibility of long-term effects.

Women should stop taking anti-obesity medications 2 months before becoming pregnant.^{17,23} If they become pregnant while taking liraglutide, they should notify their health care professional to discuss risks and management strategies. Regular monitoring and follow-up are recommended to ensure proper counseling and support during treatment, especially if pregnancy is possible. Nutritional counseling should also be emphasized during the prepregnancy period to improve outcomes and address potential side effects, such as iron deficiency, associated with weight loss. Future studies should report detailed fetal outcomes and include long-term follow-up for child outcomes after in utero exposure to GLP-1 agonists.

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