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Case Report

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Positive Pregnancy Outcome following First Trimester Dulaglutide Exposure in a Women with Type 2 Diabetes and PCOS: A Case Report

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ABSTRACT

Background: Insulin has been the gold standard treatment for T2DM during pregnancy. However, emerging studies indicate that GLP-1 agonists have shown significant improvement in insulin resistance. Despite promising results, research conducted on pregnant animal models has shown fetal developmental defects associated with GLP-1 agonists. There is scarcity of research conducted on the use of GLP-1 agonists in human pregnancies. This case report describes the exposure to dulaglutide (GLP-1 agonist) during first trimester of pregnancy.

Case: A 41-year-old female with type 2 diabetes mellitus and polycystic ovarian syndrome had been taking dulaglutide until 15 weeks of gestation. She delivered a healthy baby boy via cesarean delivery at 36 weeks' gestation.

Conclusion: In our case, exposure to dulaglutide during the first trimester showed no significant developmental effects on the baby. However, current research is insufficient to categorize GLP-1 agonists as safe during pregnancy.

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Teaching Points

1. Preconception counseling about medications that patients are currently taking.
2. Awareness that GLP1 agonists in their promotion of weight reduction can lead to ovulation, thus increasing fertility.
3. Medications without safety evidence in pregnancy should be stopped.

Introduction

Diabetes mellitus and polycystic ovarian syndrome (PCOS) are two of the most prevalent endocrine disorders, contributing to complications during pregnancy. The CDC has estimated that 37.3 million adults have diabetes, of which 12.6 million were women of reproductive age [1,2]. Poorly controlled pregestational diabetes throughout pregnancy links to substantial birth defects in 5-10% of all pregnancies, along with spontaneous abortion occurring in 15-20% of cases. These complications encompass various issues, including pre-eclampsia, preterm delivery, and fetal growth abnormalities. Both type 2 diabetes mellitus (T2DM) and PCOS share associations with insulin resistance and obesity. Notably, experiments with animal models reveal that hyperglycemia induces increased oxidative stress, which occurs through the generation of reactive oxygen species (ROS) in cells and tissues of developing embryos and fetuses. ROS damages cell membrane, leading to dysregulated programmed cell death contributing to abnormal organogenesis. While traditional insulin treatment has served as the standard approach for T2DM during pregnancy, recent studies advocate for the safe usage of glucagon like peptide-1 agonists (GLP-1) as an alternative. Recent findings indicate that GLP-1 agonists show promising results in improving both body weight and insulin resistance [3,4]. This is particularly relevant considering that weight gain and obesity significantly impact the clinical outcomes of patients with PCOS [5]. However, there remains a scarcity of research addressing the efficacy of GLP-1 agonists in improving pregnancy outcomes for women with T2DM and PCOS. Within this context, this is a report of a case involving exposure to dulaglutide, a GLP-1 agonist, during the first trimester of pregnancy.

Case

A 41-year-old female with a past medical history of T2DM and PCOS presents to the emergency room with abdominal cramping following a positive pregnancy test at home. She wanted to make sure everything was okay since she had a history of a previous miscarriage. She endorsed an episode of vaginal bleeding a week prior to this visit. A transvaginal ultrasound showed a single, live intrauterine pregnancy estimated to be 12 weeks' gestation and a serum quantitative human chorionic gonadotropin (hCG) level of

41,701mIU/mL). These findings were consistent with diagnosis of pregnancy (G2P0T0A1). No medication changes were made at the time of diagnosis, patient was taking dulaglutide 0.75mg weekly and metformin 1000 mg tablet twice a day.

The patient had an initial prenatal appointment at 12 weeks 5 days and was advised to stop smoking, start prenatal vitamin, start 162mg of aspirin at 14 weeks and labs were drawn. She was also provided guidelines for blood pressure monitoring. She presented to the endocrine clinic for follow-up of T2DM at 16 weeks' gestation. The patient reported she stopped dulaglutide at 15 weeks' gestation, but she was still taking metformin. Other notable findings included a hemoglobin A1c of 8.4% and BMI of 45kg/m2. Other vital signs were unremarkable.

The patient continued metformin 1,000mg twice a day and was advised check her blood sugar 4-6 times daily and was referred to diabetes education for lifestyle counseling. Two weeks later, she started taking insulin lispro before meals and insulin detemir once a day. Despite insulin use and frequent dose increases throughout the pregnancy, patient's blood sugar readings remained elevated throughout pregnancy and her hemoglobin A1c lowered to 8.1%. She did not experience any episodes of hypoglycemia that required glucagon administration. The patient was diagnosed with chronic hypertension with superimposed preeclampsia and started on labetalol 200mg BID at 26 weeks' gestation. Patient was monitored regularly with fetal ultrasound, at 25 weeks mild polyhydramnios was noted that improved by 32 weeks. At 36 weeks' gestation, the patient delivered a healthy baby boy via Cesarean delivery.

Discussion

In our case, the exposure to dulaglutide during the first trimester did not exhibit any notable developmental effects on the baby. However, it is imperative to emphasize that dulaglutide is contraindicated during pregnancy, primarily based on research conducted on animal models, which has shown birth defects [4].

GLP-1 agonists continue to become more widely used for glucose control especially in patients with T2DM. Current evidence indicates that there may be a pathophysiological connection between obesity, changes in GLP-1 kinetics and the development of PCOS. Research has shown that PCOS and obesity have many effects on ovulation, fertility treatment response, pregnancy rates, and overall outcome of the pregnancy. Studies have shown a global decline in fertility rates, which has been associated with the rising prevalence of obesity. The use of medications like GLP-1 agonists has been a significant advancement in promoting weight loss and enhancing fertility rates. One study showed a strong connection between weight reduction and fertility, revealing that 90% of women regained ovulatory function following a 6-month weight loss program [6,7].

In our case, it is crucial to highlight that the patient had a high-risk pregnancy due to factors such as advanced maternal age, smoking, obesity, uncontrolled T2DM, and PCOS. Given the complexity of her condition with multiple co-morbidities, first trimester fetal exposure to dulaglutide did not appear to be a contributing factor for a poor birth outcome or cause additional complications.

Apart from our case, there have been a few other cases reported that has shown that the use of GLP-1 agonists during pregnancy did not cause any harm to the fetus.

In one specific case, a 37-year-old woman with T2DM and PCOS was exposed to liraglutide during her first trimester of pregnancy. The medication was discontinued at 13 weeks of gestation, and the patient delivered a healthy female infant at 37 weeks' gestation via prior Cesarean delivery. Apart from a transient neonatal hypoglycemia that resolved within 24 hours, no other complications were observed in the infant. In another case, a 38-year-old woman with T2DM was exposed to dulaglutide until 15 weeks' gestation. She was treated for gestational hypertension at 35 weeks and delivered a male infant who developed jaundice, which resolved shortly after birth. Despite our case and these others, caution must be exercised when considering the use of GLP-1 agonists in pregnant women. The current research on this topic is insufficient to categorize GLP-1 agonist as safe during pregnancy [8,9].

Furthermore, recently GLP-1 agonists have gained significant attention as weight loss medications, particularly among young adults including women of reproductive age. This growing interest emphasizes the need for additional research to assess the potential risks and benefits of GLP-1 agonists in human pregnancies. Clearer guidelines are essential for physicians and patients to effectively manage these complex medical conditions during pregnancy.

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