Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS II

Primary Hyperparathyroidism With Severe Hypercalcemia During Pregnancy: A Challenging Diagnosis and Management

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Background:Primary Hyperparathyroidism (PHPT) is rare in pregnancy and the physiological adaptations in mineral and skeletal homeostasis that occur during gestation need to be taken into consideration for the diagnosis and management. **Clinical case**:A 30-year-old primgravid woman with history of kidney stones presented at our institution during the 13th week of twin gestation with severe nausea and vomiting. She had previously been hospitalized at 9 weeks for hypercalcemia and acute kidney injury, and treated with steroids for presumed granulomatous disease without improvement. She was on prenatal vitamins and family history was significant for kidney stones, but not hypercalcemia. At admission, calcium was 14.4 mg/dl, ionized calcium 1.89 mmol/L (1.16-1.32), PTH 15.2 pg/ml (12-88), albumin 3.4 g/dl, phosphorus 2.1 mg/dl, and creatinine 1.8 mg/dl. PTHrP was <2 pmol/L (<4.2) and 1, 25-dihydroxyvitamin D was 191 pg/mL (2nd trimester range 72-160 pg/ml). She was treated with IV hydration, but her calcium remained elevated and severe hypercalcemia recurred after stopping hydration. She underwent neck exploration and right upper parathyroidectomy in the second trimester. The other parathyroid glands were noted to be normal. Intraoperative PTH dropped from 25.2 pg/mL to 4.4 pg/mL. Final pathology showed a hypercellular parathyroid. Her calcium dropped to normal levels in the early postoperative period. Calcitonin was initiated by another provider two weeks postoperatively for persistent mild hypercalcemia. Her calcium levels remained at the upper limit of normal during her 2nd and 3rd trimesters. PTH remained suppressed at 3.2 pg/ml. She had a C-section at 34 weeks for premature rupture of membranes. Her twins did not develop hypocalcemia or hypoparathyroidism. The most recent postpartum calcium was 9.2 mg/dl with PTH 3.3 pg/ml.**Conclusions:**Our case highlights the challenge in the diagnosis and management of PHPT in pregnancy. During pregnancy, PHPT is diagnosed by elevated ionized or albumin corrected calcium and non-suppressed PTH level. It is important to note that 1,25-dihydroxyvitamin D levels physiologically increase in the second and third trimester. Since both PHPT and pregnancy cause intestinal calcium absorption and bone resorption, PHPT during pregnancy has increased risk of severe hypercalcemia, pancreatitis and renal stones. During the third trimester the transfer of calcium through the placenta and the uptake of calcium by the fetal skeleton can protect against severe hypercalcemia. However, hypercalcemic crisis can occur because of the peak release of PTHrP by the placenta and breasts, or after delivery due to loss of calcium transfer to the placenta. Parathyroidectomy is preferably performed in the second trimester to reduce fetal and maternal complications. After delivery neonatal hypocalcemia can have a delayed onset, a prolonged course and could be permanent.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL STUDIES IN DIABETES

Ready-To-Use Glucagon for the Prevention of Exercise-Induced Hypoglycemia in a Clinical Research Setting

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OBJECTIVE: A mini-dose of a novel ready-to-use liquid stable glucagon (RTUG; Xeris Pharmaceuticals) was evaluated for the prevention of exercise-induced hypoglycemia (EIH) during and after moderate-to-high intensity aerobic exercise, in both a clinical research center (CRC) and outpatient setting. The observations from the CRC setting are reported here.

METHOD: A Phase 2 randomized, placebo-controlled, double-blind, two-treatment, crossover study enrolled 48 adults with Type 1 diabetes (T1D) treated with continuous subcutaneous insulin infusion, to evaluate the efficacy of pre-exercise RTUG in addition to standard of care basal insulin rate reduction. The CRC setting included 2 separate daytime exercise sessions 2 to 28 days apart. At 5 minutes prior to each exercise session, subjects reduced their basal rate of insulin infusion by 50% and self-administered placebo or RTUG 150 micrograms (μg) before performing 45 minutes of moderate-to-high intensity, aerobic exercise with a target of 80% maximum heart rate. Blood glucose was measured before, during, and after exercise to evaluate the incidence and severity of hypoglycemia.

RESULT: Of the 45 subjects (93.8%) that completed both exercise sessions in the CRC, EIH occurred more in placebo (n=8) compared to RTUG (n=1). More subjects used glucose tablets to treat EIH in placebo (n=4) compared to RTUG (n=1). Placebo-treated participants consumed 7-fold greater glucose tablets during and after exercise, and experienced more episodes of post-exercise hyperglycemia (blood glucose >250 mg/dL), compared to RTUG. Treatment emergent adverse events with RTUG were comparable to placebo. RTUG 150 μg caused no edema, erythema, nor injection site reactions. RTUG was safe and well tolerated and no serious adverse events occurred.

CONCLUSION:RTUG 150 μg adequately maintained euglycemia during and following prolonged, continuous, moderate-to-high intense aerobic exercise in the controlled CRC setting. When used prior to moderate-to-high intensity aerobic exercise, RTUG may reduce exercise-induced hypoglycemia in adults with T1D. These findings support the continued evaluation in the outpatient setting.