

Effect of Two Supplements on Gestational Hypertriglyceridemia: Report of Two Cases

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Abstract

Introduction: Hypertriglyceridemia (HTG) is a physiological condition of pregnancy. However, in some patients, it could be harmful due to possible complications such as pancreatitis. Treating this clinical condition during pregnancy is controversial as many drugs are not allowed in different trimesters. The current report discussed 2 cases of HTG and their outcomes during pregnancy.

Case Presentation: The 1st patient had twin pregnancy and a "milky" blood sample raised suspicion on abnormal lipid profile (LP) during the pregnancy screening tests. There was a positive history of HTG and the available laboratory results showed triglyceride (TG) 3920 mg/dL, cholesterol (Chol) 1370 mg/dL, and normal amylase and lipase serum levels. The patient received daily LP and blood glucose monitoring as well as insulin, gemfibrozil, and fish oil prescription. In the 30th week of gestation, one of the fetuses was lost and a cesarean section, because of preterm uterine contractures, was performed. Mother and baby were discharged in good conditions. The 2nd patient presented with nausea, vomiting, and abdominal pain in the 22nd week of gestation. The patient had gestational diabetes without the history of HTG. Laboratory results were as follows: TG 878 mg/dL, Chol 249 mg/dL, amylase 251 U/L, and lipase 29 U/L. The patient was treated as pancreatitis induced by HTG. Therefore, gemfibrozil and fish oil were prescribed in addition to hydration and low fat diet. A healthy term baby was the result of pregnancy.

Conclusions: Establishing prompt medical treatment and controlling comorbid conditions are essential in gestational HTG. Although there are controversial reports about using medications such as fibrates and fish oil, gemfibrozil and fish oil were recommended as an effective treatment for the patients with gestational HTG.

Keywords: Fish Oil, Gemfibrozil, Gestational Hypertriglyceridemia

1. Introduction

Hypertriglyceridemia (HTG) during pregnancy is a well-known condition as an indirect result of physiologic changes in sexual hormones. Increase in TG level is caused by 2 major reasons. First, increase in liver lipase enzyme activity, which results in increase of TG synthesis in liver; second, reduction in lipoprotein lipase activity, which by itself results in the reduction of fat tissue catabolism (1). High concentration of TG in mother provides enough substrate for fetus metabolism, when the blood glucose level is low. In addition, high concentration of low-density lipoprotein (LDL) helps steroidogenesis of placenta (2). HTG could be hereditary or acquired. Obesity, diabetes, pregnancy, nephrotic syndrome, and hypothyroidism can induce acquired HTG (2, 3). This metabolic disturbance has an important role in atherosclerosis (2). Moreover, it can increase cardiovascular events as well as increase in insulin resistance, coagulopathy, and endothelial damage. Acute pancreatitis is a complication of HTG (2, 4). Pregnant females with the history of metabolic disorders are more

prone to develop acute pancreatitis during pregnancy because of HTG (1, 5). Proper management of HTG during pregnancy is still under consideration (6). The management of 2 patients with gestational HTG in the 28th and 22nd weeks of gestation and their pregnancy outcomes were discussed here. The first clue in the diagnosis of the first case was the milky appearance of blood sample, obtained for the gestational diabetes screening test. In the 2nd case nausea, vomiting, and epigastric pain were the signs.

2. Case Presentation

The 1st patient is a 29-year-old pregnant female G2L1 at the 28th week of gestation with a monochorionic-diamniotic twin pregnancy. The patient was referred to the clinic because of impaired glucose tolerance test (GTT) and abnormal lipid profile. During pregnancy screening, a milky blood sample raised suspicion on abnormal lipid profile. The patient had a history of HTG (400 mg/dL), diagnosed 2 years ago. Nevertheless, the patient was not

taking any medications for HTG and only had low triglyceride (TG) diet recently. There was no positive family history for the abnormal lipid profile. Laboratory results after referral were as follows: TG 3920 mg/dL, cholesterol (Chol) 1370 mg/dL, aspartate aminotransferase (AST) 160 U/L, alanine aminotransferase (ALT) 188 U/L, lactate dehydrogenase (LDH) 1050 IU/L, and normal levels of amylase and lipase. The abdominal ultrasonography showed monochorionic-diamniotic twin pregnancy (gestational ages of 28 week + 4 days and 26 weeks + 2 days) with anterior placenta, and adequate amniotic fluid. After ruling out pancreatitis and preeclampsia, the patient underwent daily lipid profile and blood glucose monitoring. Insulin (day time: 7 units of regular and 14 units of neutral protamine Hagedorn (NPH) insulin - afternoon time: 5 units of regular and equal units of NPH insulin), gemfibrozil (2 tablets twice a day), and fish oil (one 360 mg pearl of omega-3 every 6 hours) were prescribed. Low-fat, diabetic diet was also started. In the 30th week of gestation, preterm contractions began. Due to breech presentation of the 1st fetus in active phase of labor, caesarian section was decided. During which, 1 of the fetuses was lost due to respiratory distress syndrome. The patient was discharged in good conditions with prescription of gemfibrozil twice daily. The laboratory results on the day of discharge were as follows: TG 1886 mg/dL, Chol 899 mg/dL, AST 28 U/L, ALT 34 U/L, and LDH 485 IU/L. During the monthly follow-up, serum lipid profile was checked and the patient did not have any specific symptoms.

The 2nd patient was a 25-year-old primigravida at the 22nd week of gestation presented with nausea, vomiting, and epigastric pain. The patient had gestational diabetes and was taking insulin injections. There was no notable finding in her medical history. Similar to the previous patient, a milky blood sample was an alarming signal for the lipid profile disturbance. While the pain was mild and patient's vital signs were stable, an abdominal ultrasonography was performed and there was no remarkable sign in the abdomen and uterine. Laboratory results were as follows: TG 878 mg/dL, Chol 249 mg/dL, amylase 251 U/L, and lipase 29 U/L. Also, serum calcium was within the normal range. The patient was treated as an HTG induced pancreatitis and underwent serum therapy. She was not allowed to feed orally until regaining her appetite. During admission, in addition to hydration and low-fat and diabetic diet, gemfibrozil (2 tablets twice a day) and fish oil (one 360 mg pearl of omega-3 every 6 hours) were prescribed. Also, blood glucose was controlled by the insulin administration (day time: 8 units of regular and 16 units of NPH insulin - afternoon time: 6 units of regular and equal units of NPH insulin). The patient was discharged with the following laboratory results and advised to consult a doctor if

the symptoms reoccurred: TG 540 mg/dL, Chol 242 mg/dL, amylase 63 U/L, and lipase 17 U/L. A healthy term baby was the result of her pregnancy. After delivery, medications were stopped, and the patient received medical follow-ups every 2 months.

3. Discussion

Hyperlipidemia is a common condition resulted from changes in lipids metabolism in late pregnancy. Pregnancy is a unique cause of acquired HTG (1-3), because serum TG, Chol, very low-density lipoprotein (VLDL), and high-density lipoprotein (HDL) levels are higher in the 3rd trimester of gestation in comparison to non-pregnant females (3). The relative deficiency of lipoprotein lipase (LPL) and dysbetalipoproteinemia can cause severe gestational hyperlipidemia. Deficiency of LPL also results in hyperlipidemia. However, patients with relative LPL deficiency have normal lipid profile. Their disease remains undiagnosed until a major stress, such as pregnancy (7).

Dyslipidemia usually occurs during the 3rd trimester of pregnancy and TG concentrations higher than 1000 mg/dL is observed in the cases with sever hyperlipidemia (1, 2). Pancreatitis may also develop in patients with lower TG levels, such as the current study cases who developed pancreatitis with TG levels lower than 1000 mg/dL. Diabetes is a secondary cause of disturbances in lipid metabolism and is usually accompanied by rises in VLDL and TG levels (8). In the current report, both patients had gestational or overt diabetes. Increased concentration of plasma TG is related to blood glucose level in diabetes. Therefore, control and appropriate adjustment of blood glucose in diabetic patients is reported as a goal for HTG treatment (2, 5).

There are various treatment options available to treat HTG (2). Fibrate compounds such as gemfibrozil (300 mg twice daily) are used in sever HTG cases and can lower TG levels (2, 8, 9). Daily fish oil can decrease both TG and VLDL levels and can also be used as a supplement during pregnancy (2, 10, 11). Daily therapeutic dosage of omega-3 fatty acid varies from 2.7 to 18 g/d during pregnancy (11). However, it is believed that excessive amount of omega-3 fatty acid does not affect the progressive gestational HTG (11). Takaishi et al., concluded that omega-3 fatty acids and diet therapy may play a protective role in the cases with HTG in pregnancy (11). Tracer kinetic studies showed that omega-3 fatty acids reduces the production of VLDL-TG and increases TG clearance. In addition, fish oil increases β -oxidation in adipose tissue and also increases fatty acid uptake, and reduces VLDL synthesis (12). Some studies expressed doubts about advantages of using fibrate compounds in pregnancy, due to the scarcity of available evidence regarding the safety of fibrate administration in

pregnancy (7, 13, 14). However, both cases in the current study were informed about the possible complications; they agreed to take the medication and successfully responded it.

Colelitis is a common predisposing factor of HTG condition in pregnancy and occurs in 1:3300 cases (5). Pancreatitis is not a common medical condition in pregnancy. Although mortality from pancreatitis in pregnancy has dropped in recent years, it is still a concern both for mother and fetus' health (1, 4). Pancreatitis symptoms are non-specific during pregnancy, but epigastric pain, nausea, and vomiting are observed in most cases (1). Lotfalizadeh et al., reported a case of hypertriglyceridemic pancreatitis in a pregnant female presented with hypertension and hyperlipidemia. Their patient took gemfibrozil (300 mg 3 times daily) before admission. During hospitalization, gemfibrozil was replaced by fish oil. They successfully controlled pancreatitis and HTG; however, the intrauterine fetal death occurred. Later, they started fish oil and gemfibrozil to decrease serum TG level and the patient was discharged in good condition with TG level lower than 200 mg/dL (15).

Pancreatitis is diagnosed by the detection of increased serum amylase and/or lipase activity. Imaging modalities, such as abdominal ultrasonography, do not confirm the diagnosis, but can be useful to detect some causes of pancreatitis such as gallstones (1). Although the current study cases had normal serum calcium level and normal abdominal sonography without gallstones, abnormal lipid profile was considered as the reason of pancreatitis (1). Treatment was similar to non-pregnant females, based on pain relief, adequate hydration, restriction of oral intake, and low fat diet (1).

3.1. Conclusion

In the pregnant females with abnormal lipid profile, the 1st step is to consider severe conditions such as pancreatitis. After ruling out such important differential diagnoses, establishing prompt medical treatment and adequate control of comorbid conditions including diabetes is essential. Although different pharmaceutical therapies of HTG in pregnant females are controversial, in the present report the patients with gestational HTG successfully responded to treatment with gemfibrozil and fish oil. It is recommended to prescribe these supplements as an adjuvant to diet therapy in such patients.

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