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High-risk thrombophilias and pregnancy: use of pravastatin, low molecular weight heparin and aspirin, report of 2 cases

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Objective

Venous thromboembolism is an important cause of mortality and morbidity during pregnancy, with pulmonary thromboembolism being the leading cause of maternal death in developed countries. The incidence ranges from 0. 5 - 1. 8%, with a 6 to 10 times higher risk than in the non-pregnant state. The presence of acquired or hereditary thrombophilias during pregnancy shifts the balance in favor of venous thromboembolism and secondary complications due to uteroplacental vascular insufficiency. These adverse outcomes include: recurrent gestational loss, intrauterine death, intrauterine growth restriction, preeclampsia and placental abruption. Patients with high-risk thrombophilias incorporate a high risk of presenting pathologies associated with uteroplacental insufficiency, such as preeclampsia, a multisystemic disorder that complicates 3-5% of pregnancies and is the main cause of maternal, fetal and neonatal morbidity and mortality. Patients with antiphospholipid antibody syndrome have a RR of 9. 72; 95% CI (4. 34-21-75) for developing preeclampsia. Preeclampsia has a worldwide incidence of 10 million each year, of which 76, 000 women and 500, 000 newborns die., For this reason it is imperative to have preventive measures that act directly on the cause of these pathologies, as is the case of aspirin. Currently under study is the benefit of using pravastatin in women with high risk thrombophilias. In this report we demonstrate the adequate perinatal results when using pravastatin in conjunction with low molecular weight heparin and aspirin in patients with high-risk thrombophilias.

Methods

Review of two patient´s files in the National Institute of Perinatology; and latest literature review on the use of pravastatin in combination with low molecular weight heparin and aspirin in the prevention of adverse perinatal outcomes in women with high-risk thrombophilias.

Results

Clinical case 1 Background: Antiphospholipid antibody syndrome, history of four events of pulmonary thromboembolism, homozygous for the MTHFR CG77T mutation, antecedent of deep vein thrombosis, chronic systemic hypertension, hypothyroidism. Obstetric history: First pregnancy delivered by Caesarean section at 34-35 weeks, second pregnancy management with LMWH 60 mg daily and Aspirin 100 mg resulted in fetal death at 36 weeks. Interventions: Aspirin 100 mg daily was started at 12 weeks, pravastatin 40 mg daily at 22 weeks, echocardiogram was performed at 24 weeks with normal results. After 25 weeks, a vena cava filter was proposed, however, the patient did not accept it. Results: Female newborn was delivered via Caesarean section, without complications, weighing 2830 grams, size 48 cm, Apgar 8/9, Silverman 2, Capurro 37. 1 for joint accommodation. Clinical case 2 Background: Antiphospholipid antibody syndrome, history of preeclampsia with severe features, marginal deficiency of plasma antithrombin, mild factor XII deficiency, moderate hyperhomocysteinemia, heterozygous status for C677T mutation of the MTHFR gene, Type 2 platelet hyperactivity. Obstetric history: During the first pregnancy, a diagnosis of preeclampsia was made with severe features, so delivery was induced at 25. 6 weeks. Interventions: management during pregnancy with prednisone 5 mg daily, hydroxychloroquine 200 mg daily, enoxaparin 60 mg sc daily, aspirin 100 mg daily from 12 weeks and pravastatin 40 mg daily from 22 weeks. Results: Caesarean delivery of DCDA twins at 32. 3 weeks. Twin 1 male, 1942 grams, size 44 cm, Apgar 7/9, SA 1, Capurro 33. 1 destined to UCIREN 1. Twin 2 female, 1892 grams, size 45. 5, Apgar 8/9, SA 3, Capurro 33. 1, UCIREN 1.

Conclusion

In the two documented cases, there was a normal evolution of pregnancy, without preeclampsia and with adequate

birthweights. Preeclampsia is one of the most serious complications of pregnancy where both fetal and maternal wellbeing is compromised, there is no treatment other than the birth of the fetus and placenta. If it occurs severely in early pregnancy (<34 weeks), delivery at early gestational age results in adverse outcomes associated with prematurity (cerebral palsy, and neonatal death). On the other hand, if the disease comes to term, the mother can suffer adverse outcomes and even death. The current drugs are mainly symptomatic and have no effect on the direct cause, and although the birth may be beneficial for the mother, it is often not optimal for the fetus especially in the case of extreme prematurity. Efforts to reduce the risk of placental insufficiency are very important. The development of effective pharmacological strategies such as the added use of pravastatin to aspirin and heparin to stop the progression of preeclampsia and restriction of uterine growth, has a significant impact in reducing perinatal morbidity and mortality, since its administration significantly reduces the release of sFlt-1, blood pressure, proteinuria, placental insufficiency and incidence of intrauterine growth restriction. It is complicated to carry out drug trials during pregnancy since the potential risks to the fetus and the alteration in the maternal physiology are involved. Therefore a broad and specific knowledge is needed on the part of a multidisciplinary team that involves pharmacists and maternal-fetal doctors; as well as carrying out clinical trials or series of cases to implement these measures in high-risk patients and in developing countries like Mexico, in which preeclampsia remains one of the leading causes of maternal death.