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Regional anesthesia in a pregnant woman affected by obesity and hyperhomocysteinemia

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Abstract

Hyperhomocysteinemia is due to congenital and acquired changes in the metabolism of homocysteine. During pregnancy, women with MTHFR genetic disorders, which causes a key enzyme in the body to function at lower than normal rate, and hyperhomocysteinemia undergo antepartum anticoagulant treatment with low molecular weight heparin. Complications of pregnancy related to thrombosis and the fact that birth and the onset of labor is unpredictable, lead to unique challenges when it comes to choosing the type of anesthesia. This presentation focuses on the anesthetic implications arising in parturient women affected by thrombophilia.

Keywords: *thrombophilia, pregnancy, regional anesthesia*

Introduction

Hyperhomocysteinemia is a genetic disease, but it can also be induced by acquired factors (unhealthy lifestyle, with a low diet in folic acid and B-group vitamins, kidney diseases, thyroid diseases, neoplasms and so forth). Hyperhomocysteinemia is part of the hereditary thrombophilias and mainly associated with the homozygous state of the C677T mutation, being in a combined heterozygous state for the two methylene-tetrahydro-folate reductase (MTHFR) mutations: A1298C and C677T, less frequent.

The increase of the plasmatic level of homocysteine is associated with a higher risk of thromboembolic events, and this physio-pathological correlation is still intensely studied. Furthermore, the association of pregnancy with thrombophilia is highly correlated with the occurrence of severe feto-maternal complications. The pregnant state is characterized by physiological hypercoagulation caused by an increase in most coagulation factors (I, II, VII, VIII, IX, X) and a decrease in anticoagulant and fibrinolitic factors, changes that are essentially produced on hormonal basis[(1)]. For these reasons, the association of the thrombophilic state with the hypercoagulant context of the pregnancy leads to the recommendation the anticoagulant treatment.

The association of trombophilia with pregnancy creates a particular anesthetic context because the predisposition to hypercoagulation requires anticoagulant treatment to prevent thromboembolism on a continuous basis. However, in the specialty bibliographic sources, the cases of post-regional anesthesia hematomas are rather scarce (1/150,000-250,000), therefore there is the possibility that the risk may be overrated. General anesthesia with nitrous oxide inhibits the conversion of homocysteine in methionine, increasing the risk of postanesthetic hrombosis[(2-6)].

The originality of our paper consists in the unitar and detailed presentation of the anesthesiologic and obstetrical data and pregnancy outcome regarding the controversy of wich anesthesia general or regional is more suitable for the parturient women with hyperhomocysteinemia obesity and secondary feto-maternal complications.

Case report

We present a patient with preeclampsia and a history of hyperhomocysteinemia from the point of view of anesthesia and postpartum treatment, including the anticoagulant management and the theoretical risk of the use of nitrous oxide.

The patient aged 32, G5 P1, height 168 cm, weight 125 kg, high blood pressure, hyperhomocysteinemia (17,1 μm/l at 6 gestational weeks), genetically tested for MTHFR mutations, with homozygous A1298C mutation.

The patient was registered with 6 weeks pregnancy and included in the screening program for thrombophilia, having in the view the heredocollateral history (brother with thrombophlebitis of the inferior left limb, under treatment with Sintrom 4mg/day and father with thrombotic stroke) and the personal obstetrical history (high blood pressure 160/100 mm Hg at 6 weeks pregnancy, 2 molar pregnancies, 2 spontaneous abortions at 12 and 14 weeks of gestation). During the pregnancy, the patient follows low sodium and low calorie diet, folic acid 5 mg/day, B6 and B12 vitamins, antihypertensive treatment, anticoagulant treatment with enoxaparine prescribed in collaboration with the hematologist (enoxaparine 0.6 ml twice a day).

Results

At 34 weeks pregnant, the patient was admitted to the hospital for high blood pressure values (160/120 mm Hg) and for the reevaluation of the antihypertensive treatment (750 mg alpha-methyldopa, three times a day and 10 mg amlodipine, in a unique dose). While monitoring the pregnancy under the treatment, at 36 weeks of gestation, the patient has a blood pressure of 180/100 mmHg, intrauterine growth restriction (estimated fetal weight below the 10th centile of the normal expected at the respective gestational age) (Figures 1 and 2).

In this situation, we decided to finalize the pregnancy through a cesarean section and to stop the administration of enoxaparine.

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At 4 hours after the ending of the anticoagulant administration, we determined the level of heparin (residual activity of the Xa factor) which was 0.6U/mL; after another 4 hours, we evaluated the level of the heparinemy, in which the value was 0.1U/mL. During this time, the values of the blood pressure tended to rise even under antihypertensive treatment (189/105 mm Hg). Our final decision was to perform an emergency surgical intervention.

During the pre-anesthetic exam we discovered grade IV Mallampatti, in which body mass index was 44.29 (grade III obesity) and 189/105mm Hg blood pressure. The lab exams showed: Quick-test time 12.6 seconds, prothrombin index 108.6%, international normalized ratio 0.92, activated partial thromboplastin time 27.4 s, hemoglobin 13.7g/dl, hematocrit 42%, number of thrombocytes 172.000/mm^3, negative products of fibrin degradation, positive (+) malaria F-test, heparinemy (residual activity of the Xa factor) 0.1U/mL (8 hours after the interruption of anticoagulant), homocysteine 5.17micromoles/l.

We performed general anesthesia, more specifically rachianesthesia using a 26G Spinocan needle, L3-L4 level, bupivacaine 0.5% 3ml. Metoclopramide 10 mg, clonidine 150 micrograms we administrated before surgery. The rachianesthesia was performed under asepsis conditions, without incidents, difficulties or complications.

A segmental transverse cesarean section was also performed with extraction of a live male baby, 2500 g, 8 Apgar score after 1 minute, 9 Apgar score after 5 min. The blood pressure during surgery was 140/90 mmHg.

No excessive intra-operatory bleeding or other incident was noted. The anticoagulant treatment is resumed 12 hours after the surgery, with enoxaparine 0.6 ml at 12 hours. Postoperative lab exams showed hemoglobin 12.3g/dl, hematocrit 37%, Quick-test time 12.3 seconds, activated partial thromboplastin time 23.5 seconds, international normalized ratio 0.90, prothrombin index 100%, positive (+) fibrin degradation product, and positive (+) malaria F-test.

Discussion

Hyperhomocysteinemia has a prevalence of almost 5-16% on the general population[7-10]. Since hyperhomocysteinemia is a well known risk factor for arterial and venous thromboses, and also for abortion, it is recommended that the levels of homocysteine be normalized through adequate vitamin substitution, as we have done in our case once the diagnosis of thrombophilia with homozygous A1298C mutation and hyperhomocysteinemia to be established. The conventional treatment for hyperhomocysteinemia includes the use of B vitamins supplements: folic acid, B6, B12 and anticoagulant treatment to prevent vascular thromboses[11].

Genetic anomalies of MTHFR affect the synthesis of N5-methyltetrahydrofolate (MTHF). Genetic defects of MTHFR determine important increases of homocysteine (100 μm/l); however, compared to the B6 and B12 vitamin deficiency, MTHFR anomalies are less frequent. A decrease in the level and activity of MTHFR induces hyperhomocysteinemia, which represents a risk factor for thrombotic events[12-16].

In the present case, the patient was tested for both forms of polymorphism of the MTHFR gene, thus we found a homozygous A1298C genotype and hyperhomocysteinemia (17.1 μm/l at 6 weeks of pregnancy). Our results, in contrast with other similar data in which the A1298C form was associated with hyperhomocysteinemia and a low level of folic acid, determined to find that the major causes for hyperhomocysteinemia is the vitamin deficiency. As expected, following the administration of daily supplements of folic acid, B6 and B12 vitamins, the plasma values of homocysteinemia dropped to 5.17 μm/l.

The higher 10 μm/l plasma levels are associated with a doubling of the vascular risk. The increase in the thrombotic risk results from the atherogenic activity of homocysteine, which increases the pro-coagulant activity of plasma. The higher 12 μm/l plasma levels should be treated in an aggressive manner with folic acid and B vitamins[17-20].

Hyperhomocysteinemia determined by mutations of the MTHFR gene or by folate deficiency is associated with major complications of the pregnancy in the 3rd trimester (preeclampsia, uteroplacental apoplexy, normally inserted placenta detachment), because hyperhomocysteinemia impacts on the function of endothelial cells, determining intervillous thromboses and impairment in placental perfusion[20]. This was also reflected in the case presented, through the occurrence of preeclampsia with high blood pressure values (189/105 mmHg), and as well intrauterine growth restriction.

Most studies show that thrombophilia is involved especially in recurrent abortion, preeclampsia and intrauterine growth restriction[3,5,8,19].

The American Society for Regional Anesthesia and Pain Medication decided, in the second consensus of the Conference for Regional Anesthesia and Anticoagulation in 2002, that the use of subcutaneous mini-doses of non-fractionated heparin for thromboprophylaxis does not contraindicate the use of some anesthesia techniques at the level of the rachidian canal. However, the number of thrombocytes must be evaluated before we administer rachianesthesia[18,19].

The safest solution would be general anesthesia, but one that does not involve the use of nitrous oxide[4,7,14]. Nitrous oxide

Figure 1. Types of anesthesia used in obese and hyperhomocysteineminic parturients (disharmonic intrauterine growth restriction, own collection)

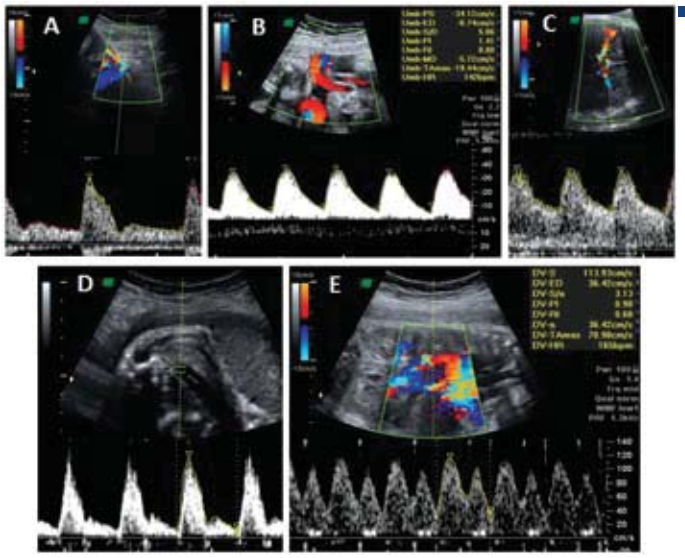

Figure 2. Types of anesthesia used in obese and hyperhomocysteineminic parturients (pulsed Doppler investigation of the feto-maternal vascular sites. A: high specters of the uterine arteries, notch present. B: High resistances at the level of the umbilical artery. C: Low vasodilatation and resistances at the level of the middle cerebral artery. D, E: Normal vecilocimetries at the level of the arterial and venous duct, own collection)

oxidizes the cobalt atom of vitamin B12, thus inactivating the methionine synthase and determining a dose-dependent increase of the plasma concentrations of homocysteine 4 days after the surgery[12,18].

We did not administer nitrous oxide general anesthesia to our patient because nitrous oxide promotes procoagulant activity, increases platelet adhesivity, affects endothelial functions and factor V, inhibits the C-protein and antithrombin III.

Severe neurological deficiencies were observed and reported in children who underwent general anesthesia with nitrous oxide[15]. In our case, we have used the technique of regional anesthesia, more precisely rachianesthesia, after we stopped the administration of enoxaparine 8 hours before surgery. Later evolution was favorable, and the anticoagulant treatment was started again 12 hours after surgery, with enoxaparine 0.6 ml every 12 hours.

Conclusions

Anticoagulant and antithrombotic therapy are increasingly recommended for thromboprophylaxis and the treatment of thrombotic complications during pregnancy, as well as for the prophylaxis of high-risk pregnancy loss, such as pregnancy associated with thrombophilia. Many antithrombotic and anticoagulant agents are available nowadays. New anticoagulants appear and clinical applications in pregnant patients continue to evolve and to represent unique challenges for the anesthesiologist.

The decision to use rachianesthesia, epidural anesthesia or general anesthesia in parturient women who also receive this type of medication should be individualized and should be based on a careful evaluation of the risk-benefit ratio.

Regional anesthesia can be performed in safe conditions if the anticoagulant therapy is interrupted 8-12 hours before the surgery and if the number of thrombocytes, activated partial thromboplastin time, international normalized ratio levels and the activated X factor activity (heparinemy) are within normal limits. Therefore, general anesthesia that involves the exposure of this type of patients to nitrous oxide should be avoided. ■

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