ARTÍCULO ORIGINAL

Sickle cell disease and pregnancy. Experience at the Instituto de Hematologia e Inmunología, Cuba

Anemia drepanocítica y embarazo: experiencia en el Instituto de Hematología e Inmunología, Cuba

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ABSTRACT

Pregnancy in women with sickle cell disease (SCD) is a high-risk situation associated with increased incidence of maternal and fetal morbidity and mortality. In Cuba, the maternal care program includes the primary level and the gestational age at booking is before the 12 week of gestation and all deliveries are institutional. All pregnant women with SCD in La Habana are attended at the *Institute of Hematology and Immunology* (IHI) by a multidisciplinary team and labor takes place at the obstetrics service of the *General Hospital next* to the IHI. From January 2000 to December 2009, 68 pregnant women with SCD were attended in labor; the frequency of the visits is every two weeks from gestational age at booking until week 32 of pregnancy and weekly until week 36 when they are hospitalized, in week 38 induction of labor is made. Patients were hospitalized upon the appearance of any event and in such cases induction of labor was made in week 36, if fetus was mature. The fetal well-being was evaluated starting from week 28 and every two weeks until childbirth. Non prophylactic blood transfusion or prophylactic exchange transfusions were indicated as this depends on the criteria of attending team; only 16 patients presented alert signs of requiring blood transfusion, 4 requiring blood exchange transfusions. All these procedures were carried out in the third trimester of pregnancy; 47 patients required caesarea indicated by the obstetrician; 17 newborns were underweight but only one with low apgar score. Two fetal deaths occurred and one new born had early neonatal death. Only one maternal death was reported.

Key words: sickle cell disease, pregnancy and labor.

RESUMEN

El embarazo en la anemia drepanocítica (AD) es considerado una situación de alto riesgo por la alta incidencia de la morbimortalidad materno-fetal. En Cuba, el programa de atención integral a las embarazadas se incluye desde el nivel primario de salud y la captación se realiza antes de las 12 semanas de gestación y los partos son institucionales. Todas las embarazadas con AD en La Habana son atendidas en el Instituto de Hematología e Inmunología (IHI) por un equipo multidisciplinario y los partos se realizan en el Servicio de Obstetricia del Hospital General Docente "Enrique Cabrera". Desde enero del año 2000 hasta diciembre del 2009, 68 embarazadas con AD fueron atendidas por un equipo multidisciplinario. La frecuencia de las consultas fue quincenal hasta las 32 semanas de la gestación y posteriormente semanal hasta la semana 36 en que fueron ingresadas; el embarazo se interrumpió en la semana 38. Las pacientes que presentaron algún evento fueron hospitalizadas y en ellas la interrupción se realizó en la semana 36 si el feto era viable. El bienestar fetal fue evaluado desde la semana 28 cada 2 semanas hasta el nacimiento. No se realizaron transfusiones ni exanguinotransfusiones profilácticas y solo fueron indicadas según los criterios del equipo médico tratante; 16 pacientes recibieron transfusiones de glóbulos y la exanguinotransfusión se realizo en 4, todas en el tercer trimestre del embarazo. En 47 pacientes se realizó cesárea y siempre por indicación obstétrica; 17 recién nacidos tuvieron bajo peso pero solo uno tuvo un conteo de Apgar bajo. Ocurrieron 2 muertes fetales y una neonatal; se reportó una muerte materna.

Palabras clave: anemia drepanocítica, embarazo, parto.

INTRODUCTION

Pregnancy in women with sickle cell disease (SCD) is a high-risk situation associated with increased incidence of maternal and fetal morbidity and mortality.[1-3] The incidence of complications increases mainly in late pregnancy, during delivery and in postpartum periods and anemia also increases, as well as painful vaso-occlusive crisis (VOC), acute chest syndrome (ACS), placental thrombosis, infections, toxemia and spontaneous abortion(4-6). Maternal death is more frequent than in healthy women.[4,5] However, according to *Serjeant GR* et al.[6] no difference in pregnancy-induced hypertension and preeclampsia was found between SCD and Hb AA pregnant women. This observation has also been pointed out by other authors.[7]

Pregnant women with SCD have high risk of intra-uterine growth retardation, preterm delivery, intra-uterine fetal death and perinatal mortality related to hypoxemia[4,8] and placental thrombosis.[3,4] Newborns with low birth weight are frequent.[9]

The incidence of SCD (Hb SS and Hb SC) is frequent in Cuba due to the incidence of hemoglobin S and hemoglobin C trait in the whole country and particularly in La Habana, of 3 and 0,7 %, respectively.[10-12]

Following the Cuban guidelines for maternal care program which includes the primary level (family doctor and nurse care), gestational age at booking is before

the 12 weeks of gestation; on average, a woman is examined 15 times during her pregnancy and all deliveries are institutional.[13]

All pregnant women with SCD in La Habana, are attended at the *Instituto de Hematología e Inmunología* - Institute of Hematology and Immunology - (IHI) by a multidisciplinary team of hematologists and obstetricians and if necessary, by a nutritionist, and labor takes place at the obstetrics service of the Hospital General Docente "Enrique Cabrera" - "*Enrique Cabrera" Teaching and General Hospital* - (HEC), next to the IHI.

METHODS

From January 2000 to December 2009, 68 pregnant woman with SCD were attended in labor: 42 with Hb SS, 19 with Hb SC and 7 with S/? thalassemia; average age was 27,1 years old (15-39 years). In 43 women it was her first birth and 25 already had one child. Of these 68 patients, 3 came from other provinces in critical state due to serious complications at the end of their pregnancy who unfortunately died early in postpartum. None of these 3 women had previously been attended at the IHI for which reason they cannot be included for the analysis of the results of the period.

The frequency of the visits is every two weeks from gestational age at booking until week 32 of pregnancy and weekly until week 36, when they are hospitalized. In week 38 induction of labor is made.

Patients are hospitalized upon the appearance of any event. All patients were hospitalized at 37 week of pregnancy and induction of labor was done at 38 week of pregnancy. In patients suffering VOC, ACS or hepatic crisis during pregnancy, induction of labor is made in week 36, if fetus is mature.

In the initial visit the following analysis are indicated: hemoglobin level, reticulocyte count, hemoglobin electrophoresis, serum iron and total iron binding capacity, liver function test, creatinine, blood group typing, red cell antibody screen and antibodies to hepatitis B, C, as well as to HIV. In the subsequent visits, hemoglobin level, reticulocyte count, weight, heart rate and uterine size are checked every two weeks. Shortness of breath, weariness and fatigue are also checked in each visit. The fetal well-being is evaluated starting from week 28 and every two weeks until childbirth; fetal growing, amniotic fluid index and placenta are evaluated by ultrasound; flowmetry and cardiotocography are evaluated weekly starting from week 29.

Prophylactic blood transfusions or exchange transfusions are indicated depending on the criteria of attending team and is related to strictly restricted maternal, obstetrical and hematologic indications:[1,14] no weight gain between two visits, hemoglobin drop (1g/dL or more of baseline hemoglobin), heart rate, shortness of breath, weariness, fatigue, stationary uterine size between two visits, oligohydramnios, etc. Women are given folic acid 5 mg daily until week 32 of pregnancy and 10 mg daily until labor. Iron is only given if there is evidence of iron deficiency. The treatment of sickle cell crisis in pregnancy is the same as the rest of normal pregnant patients.[15]

During labor it is necessary to maintain the room temperature between 76 - 80º F, hydration IV 1500 mL/24 hours and intermittent nasal oxygen therapy is needed. Vaginal delivery is preferred reserving cesarean for obstetric indications. If a cesarean section is planned in an untransfused patient with Hb SS, transfusion should be considered first, if possible, to avoid perioperative sickle cell

complications.

RESULTS

Of the 65 patients attended by our team, only 16 (24,6 %) presented alert signs of requiring blood transfusion. Indications of transfusion were caused by lack of weight gained or stationary uterine size between two visits, hemoglobin drop, and oligohydramnios.

Four blood exchange transfusions were necessary: 2 for widespread painful VOC, one for ACS and another for hepatic failure. All these procedures were carried out in the third trimester of pregnancy.

From the total of patients, 47 (72,3 %) required caesarea indicated by the obstetrician; 17 (26,1 %) newborns were underweight but only one with low apgar score and it was normal after 5 minutes.

Two (3,07 %) fetal deaths occurred and one new born (1,53 %) had early neonatal death. One maternal death of a patient with Hb SC (1,53 %) due to pulmonar tromboembolism was reported.

DISCUSSION

Pregnancy in women with SCD is a high-risk situation associated to increased incidence of maternal and fetal morbidity and mortality.[1-3]

In the multidisciplinary outpatient service of the IHI, 65 pregnant women with sickle cell disease were attended from January, 2000 to December, 2009; these pregnant women were seen and treated since gestational age at booking, during pregnancy and on delivery up to postpartum period.

During pregnancy patients had different hematological events due to SCD, all identified by other authors: the most frequent complication was painful VOC4,5,16 followed by low baseline hemoglobin;[3,4,17] 2 patients with ACS4 and another one had hepatic failure.[18] All of them were hospitalized according to our program of SCD and pregnancy.

Seventeen newborn were underweight (26,1 %), this outcome is similar to reports from other authors,[6,19,20] and only one with low apgar score. We had two (3,07 %) fetal deaths, which is inferior to the reports from Taylor MY et al., who in this retrospective study of 131 patients with sickle cell trait, showed 10 (8,13 %) intrauterine fetal deaths.[21] One new born (1,53 %) had early neonatal death.

Hypertension in the third trimester was reported which coincides with other authors: Al *Jama* et al,3 *Leborgne-Samuel* Y et al4 and *Yu CK* et al;17 oligohydramnios appeared in two patients (3,07 %) and missed abortion in one woman (1,53 %) were also reported.

Sixteen patients who presented alert signs required blood transfusion, the most frequent sign being not weight gain between two visits and low baseline hemoglobin. One patient required blood transfusion due to oligohydramnios at 32 weeks of pregnancy. Four exchange transfusions (6,15 %) were necessary: two for widespread painful VOC, one for ACS and another one for hepatic failure.

According to our experience,[14] pregnant patients received prophylactic transfusion

or prophylactic exchange transfusions since blood transfusion may cause a higher risk for delayed transfusion reaction, hyperhemolysis syndrome and possible death, and there was no significant reduction in obstetric complications or improvement in the fetal birth weight or incidence of intrauterine growth retardation. In this point several colleagues agree with us,[4,22-24] and others disagree.[25]

The index of caesarea was higher than the experience reported by other authors;[4,5,17,19,22] it was necessary in 47 (72,3 %) SCD pregnant woman, all indicated by the obstetrician and the main causes being fetal hypoxia, prolonged labor and delivery and widespread painful VOC.

Before and during postpartum the patient received counseling from the medical team explaining next pregnancy risks and information about the use of different contraceptives.

In summary, with a suitable follow-up by a multidisciplinary team every two weeks, hospitalization if any complication arises, supply of a supplement of folic acid, vitamins and minerals, with a careful serial fetal assessment, monitoring of fetal well-being from week 28 every 15 days, not administering prophylactic transfusions or exchange transfusions, hospitalization at 36 week of pregnancy and induction of labor at 38 weeks, good results in pregnant woman with SCD will surely be accomplished.

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