NATIONAL HEMOPHILIA FOUNDATION
for all bleeding disorders

MASAC Document # 265
(Replaces Document #251)

MASAC Guidelines for Pregnancy and Perinatal Management of Women with Inherited Bleeding Disorders and Carriers of Hemophilia A or B

The document was approved by the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation (NHF) on February 20, 2021, and adopted by the NHF Board of Directors on March 4, 2021.

Women with bleeding disorders are at risk for bleeding in the peripartum period. Women with bleeding disorders and female carriers of hemophilia may also have affected newborns who are at risk for bleeding at birth and in the neonatal period. These guidelines provide recommendations for the diagnosis and management of women with bleeding disorders during pregnancy, labor and delivery, and in the postpartum period to minimize the risk of bleeding-related complications and facilitate early diagnosis of affected infants.

Preconception Diagnosis and Genetic Counseling

Adolescent females and women who may be carriers of hemophilia A or B, should be evaluated before they become pregnant. Factor assays should be completed during the non-pregnant state in a reference lab that specializes in coagulation testing. Normal factor activities do not exclude the diagnosis of genetic hemophilia carrier. Genetic testing should be done to establish hemophilia carrier status in potentially affected women. It is most effective to first test the male proband in the family and then test family members. (1)

It is also critically important to diagnose adolescent females and women with family history of von Willebrand disease and other inherited bleeding disorders prior as early as possible and to define risk of transmission to children prior to pregnancy.

Preconception genetic consultation should be offered to all women with bleeding disorders and possible carriers who plan to pursue a pregnancy. Women and their families should be acquainted with the various methods of diagnosing a potentially affected infant prior to delivery and the associated risks of each. Methods include preimplantation diagnosis, invasive prenatal diagnosis (chorionic villus sampling, amniocentesis, and cordocentesis), and ultrasound determination of fetal sex. (2-4) It regard to fetal sex, that female sex does not exclude potential for bleeding diathesis related to hemophilia carrier status especially in carriers with skewed x-inactivation or in females with compound heterozygosity for two factor gene variants.

7 Penn Plaza · Suite 1204
New York, NY · 10001
(800) 42.HANDI · (212) 328.3700 · fax (212) 328.3777
www.hemophilia.org · info@hemophilia.org

Pregnancy Management

Pregnancy should be managed by a multidisciplinary team of specialists, including a coagulation disorders specialist, an obstetrician/gynecologist and an anesthesiologist, all of whom are knowledgeable in the management of women with bleeding disorders. Early pregnancy care should include anticipatory guidance about bleeding because spontaneous early pregnancy loss is associated with need for interventions in approximately 50%. (5) Women with bleeding disorders are not generally believed to be at increased risk of miscarriage unless they have either fibrinogen or factor XIII deficiency. (4,6, 7) Women who have fibrinogen deficiency with a bleeding phenotype are at a high risk of miscarriage if their fibrinogen levels are below 100 mg/dL. They should receive replacement therapy during pregnancy to maintain their levels above 100 mg/dL. (6) Women with severe factor XIII deficiency are also at high risk of miscarriage and should also receive replacement therapy monthly during pregnancy. (4)

Any early pregnancy procedures should be performed in settings where hemorrhage could be managed, including uterine evacuation for early pregnancy loss and procedural abortion. Bleeding prophylaxis for uterine evacuation can include uterotonics and anti-fibrinolytics (e.g. tranexamic acid). Prophylaxis with VWF concentrate, desmopressin, and/or anti-fibrinolytics is indicated prior to uterine evacuation and other invasive procedures during pregnancy, such as chorionic villous sampling, amniocentesis, and cerclage.

Labor and Delivery Management

Women with bleeding disorders are at risk of bleeding complications during pregnancy and in the postpartum period. A plan for the management of childbirth should be in place well before delivery. Women should give birth in a facility that has available consultation with a bleeding disorders specialist, neonatology, and the appropriate laboratory, pharmacy and transfusion services support. Clotting factor replacement and other hemostatic agents and blood products must be available on-site.

Hemophilia A carriers may have congenitally low factor levels that increase their risk of bleeding. Even though their factor VIII levels rise during pregnancy, they may not rise to the levels achieved by women without a bleeding disorder. Similarly, women with von Willebrand disease have von Willebrand factor levels and factor VIII levels that rise during pregnancy, but possibly not to the levels achieved by women without a bleeding disorder. Factor IX levels do not rise during pregnancy. Factor VIII, IX, or VWF levels should be assessed once or twice in the third trimester of pregnancy in order to plan for possible administration of clotting factor concentrates or other clotting factor replacement therapy at the time of delivery.

Hemophilia carriers and women with VWD should receive factor replacement prophylaxis at the time of delivery if their factor levels are less than 50% (50 IU/dL). (2-4) When available, recombinant or virally inactivated clotting factor concentrate should be used as opposed to fresh frozen plasma or cryoprecipitate. (2-4) Women with factor levels above 50% (50 IU/dL) should be given the option of neuraxial anesthesia. (8) Targeting a VWF activity level of 0.50 to 1.50 IU/mL over targeting an activity level of 1.50 IU/mL is advisable. (9) VWF activity levels should be maintained at 0.50 IU/mL while the epidural is in place and for at least 6 hours after

removal. The assessment of whether neuraxial anesthesia is appropriate for an individual patient is a complex decision that includes assessment of factors outside the scope of these guidelines. The ultimate decision about whether it is appropriate for an individual patient to undergo these procedures lies with the obstetric anesthesiologist or other clinician performing the procedure. Decisions regarding anesthesia and delivery should be made in the context of a multidisciplinary discussion with input from anesthesia, hematology, and obstetrics and shared decision making with the patient. These discussions should take place well in advance of the patient's due date. Patients should also be assessed for thrombotic risk post-delivery, and prophylaxis (e.g., compression stockings or low-molecular-weight heparin) should be provided when needed. (See MASAC Document #250 for specific treatment product recommendations for each of these bleeding disorders.)

DDAVP (1-desamino-8-D-arginine vasopressin) is a synthetic vasopressin that can be used to raise both von Willebrand factor levels and factor VIII levels in patients who respond and can be used during pregnancy for prophylaxis prior to invasive procedures such as amniocentesis. (2-4,10) Sánchez-Luceros et al noted no adverse events in 34 women with VWD who received a single dose of DDAVP immediately prior to epidural catheter placement. (11) However, the use of DDAVP at the time of childbirth can cause fluid retention. The United Kingdom guidelines for the management of women with bleeding disorders recommend that fluids be restricted to 1000 mL for the 24-hour period after DDAVP administration.(5) Since women routinely receive two to three times that amount of fluid at the time of delivery, routinely receive oxytocin which also causes fluid retention, and invariably undergo redistribution of fluid from the extravascular to the intravascular space after delivery, DDAVP must be used with caution, and electrolytes and urine output must be monitored closely for 24 hours.(3)

Method of Delivery

As of December 2008, the Centers for Disease Control (CDC) Uniform Data Collection (UDC) database contained data on 580 male infants with hemophilia A or B. In 569 out of the 580 infants, the mode of delivery and the outcome were known. 385 infants with hemophilia (68%) were delivered vaginally and 184 by caesarean delivery. There were 16 intracranial hemorrhages among the 385 infants delivered vaginally (twelve were delivered by vacuum extraction and four by forceps), giving a rate of intracranial hemorrhage of 4 percent among infants delivered vaginally. In contrast, there was one intracranial hemorrhage among 184 infants delivered by caesarean section, giving a rate of 0.5%. Among the 236 mothers who were known to be carriers, delivery plans were modified somewhat: 156 infants (66%) were delivered vaginally with 1 operative vaginal delivery and 2 intracranial hemorrhages (1.3%), while among the 80 infants who were delivered by caesarean section there were no intracranial hemorrhages. (12)

In 2019 the PedNET Haemophilia Research Foundation published results from the PedNET multicenter study including 926 neonates (786 with severe and 140 with moderate hemophilia). Six hundred thirty-three were delivered by vaginal delivery and 293 by Cesarean section. Fifteen (2.4%) of vaginal deliveries were complicated by intracranial hemorrhage compared to 5 (1.7%) of Cesarean sections (P=not significant). As demonstrated in other studies vaginal delivery with instrumentation was associated with high risk of intracranial and other major bleeds. (13).

While most infants of hemophilia carriers can be safely delivered vaginally, the outcome of labor cannot be predicted, and a spontaneous (non-operative) vaginal delivery cannot be guaranteed. A vaginal delivery may be associated with abnormal labor. Therefore, obstetricians caring for women who are carriers of hemophilia should discuss with the woman the maternal and fetal risks of a vaginal delivery versus a planned caesarean delivery; the option of a planned caesarean delivery should be considered when an affected or potentially affected infant is anticipated. (12) In women who elect vaginal delivery, forceps and vacuum extraction, interventions that triple the risk of intracranial hemorrhage in affected infants, should be avoided, as should fetal scalp electrode monitoring during labor.

Umbilical Cord Blood Sampling

Umbilical cord blood should be obtained through proper technique at the time of delivery in order to avoid venipuncture of the infant and to ensure that the neonate is tested early for hemophilia. (4, 6, 7, 14) Instructions should be provided to the obstetrical team prior to delivery and plan should be confirmed in regards to exactly which test should be sent and which laboratory the test should be test to. Confirm that lab will run factor assays on cord blood.

(See Appendix A for the Indiana Hemophilia & Thrombosis Center Procedure for Collecting, processing & Shipping the Cord Blood Sample.)

Postpartum Management to Prevent Bleeding

Obstetricians and midwives routinely take precautions to prevent postpartum hemorrhage, and this is especially important in women with bleeding disorders. The third stage of labor should be actively managed to reduce blood loss and reduce the incidence of postpartum hemorrhage. (7, 15) Anti-fibrinolytics can be used to prevent or treat postpartum hemorrhage. (4, 7) Specifically, tranexamic acid is advised in women with type 1 VWD or low VWF levels (and this may also apply to types 2 and 3 VWD) during the postpartum period.(9) Tranexamic acid may be given systemically via the oral or IV route. The oral dose is 25 mg/kg (typically 1000-1300 mg) 3 times per day for 10 to 14 days or longer if blood loss remains heavy. (9)

Factor levels may drop precipitously postpartum and should be monitored. In women who require clotting factor replacement therapy, prophylaxis should be continued for at least five days postpartum or longer, since delayed postpartum hemorrhage is not uncommon and may occur more than two weeks after delivery.(3, 7, 12) Clotting factor replacement initially should be targeted closer to the physiological level of 150% then 50%. (9)

Recommendations

1. Multidiscplinary approach to pregnancy and delivery should be supported and women should only deliver at hospitals that have the essential resources.

2. NHF should work with NHLBI, the American Thrombosis and Hemostasis Network (ATHN), the Foundation for Women and Girls with Blood Disorders, the International Society of Hemostasis and Thrombosis and CDC to develop a national research agenda on pregnancy and perinatal management of women with inherited bleeding disorders and carriers of hemophilia A or B.

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