



MASAC GUIDELINES FOR PERINATAL MANAGEMENT OF WOMEN WITH BLEEDING DISORDERS AND CARRIERS OF HEMOPHILIA A AND B

The following recommendation was approved by the Medical and Scientific Advisory Council (MASAC) on October 31, 2009, and adopted by the NHF Board of Directors on November 1, 2009.

Bleeding in the peripartum period is a major issue for women with bleeding disorders. Now that more women with bleeding disorders are being identified, it is important that guidelines be established for the management of these women during pregnancy, labor and delivery, and in the postpartum period to minimize the risk of bleeding-related complications.

Preconception Genetic Counseling

Girls and women who are at risk for being carriers of hemophilia A and B, severe von Willebrand disease (vWD), and other severe bleeding disorders should have their bleeding disorder status determined before they become pregnant. If clotting factor levels are inconclusive and an affected individual is available, genetic mutation analysis should be done to establish a definitive diagnosis of carrier state for hemophilia A or B. Preconception genetic consultation should be offered to all women with bleeding disorders or who are carriers and 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 gender. (1-3) (Grade C, Level IV)*

Pregnancy Management

Pregnancy should be managed by a multidisciplinary team of specialists including a coagulation disorders specialist, an obstetrician and an anesthesiologist, all of whom are knowledgeable in the management of women with bleeding disorders. Women with bleeding disorders are not generally believed to be at increased risk of miscarriage unless they have either fibrinogen or factor XIII deficiency.(3-5) 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 and should receive replacement therapy during pregnancy to maintain their levels above 100 mg/dL.(4) (Grade C, Level IV) Women with severe factor XIII deficiency are also at high risk of miscarriage and should also receive replacement therapy monthly during pregnancy.(3) (Grade C, Level IV)

Labor and Delivery Management

Women with bleeding disorders are at risk of bleeding complications during pregnancy and the postpartum period. Women should give birth in a facility that has the appropriate laboratory, pharmacy and blood bank support. A plan for the management of childbirth should be in place well before delivery.

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 perhaps not to the levels achieved by women without a bleeding disorder. Factor IX levels do not rise during pregnancy. Factor levels should be assessed one 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).(1-3) (Grade C, Level IV) When available, recombinant or virally inactivated clotting factor concentrate should be used as opposed to fresh frozen plasma or cryoprecipitate.(1-3) (Grade C, Level IV) Women with factor levels above 50% (50 IU/dL) should be given the option of regional anesthesia.(6) (See MASAC Document #190 for specific treatment product recommendations for each bleeding disorder.)

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 responders and can be used during pregnancy for prophylaxis prior to invasive procedures such as amniocentesis.(1-3,7) (Grade C, Level IV) 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.(8) 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.(2) (Grade C, Level IV)

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 likely 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. (9) (Grade B, Level III)

While the majority of 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 recommended when an affected or potentially affected infant is anticipated.(9) (Grade B, Level III) In those 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 electrodes 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.(3-5, 10) (Grade C, Level IV) (See Appendix A for the Indiana Hemophilia & Thrombosis Center Procedure for Collecting, processing & Shipping the Cord Blood Sample.)

Postpartum Management of the Mother 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. (5, 11) (Grade A, Level Ib) Anti-fibrinolytics can be used to prevent or treat postpartum hemorrhage. (3, 5) (Grade C, Level IV) 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 three to five days postpartum or longer, since delayed postpartum hemorrhage is not uncommon and may occur more than two weeks after delivery.(2,5,9) (Grade C, Level IV)

Grade	Level	Evidence obtained from:
A	Ia	Meta-analysis of randomized-controlled trials
	Ib	At least one randomized-controlled trial
B	IIa	At least one well-designed controlled study without randomization
	IIb	At least one other type of well-designed quasi-experimental study
	III	Well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies
C	IV	Expert committee reports or opinions and/or clinical experiences of respected authorities

*Recommendations in these guidelines were assigned a grade and level of evidence using the United States (U.S.) Agency for Health Care Policy and Research Criteria below:

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