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Anesthesia implications of coagulation and anticoagulation during pregnancy

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ARTICLE INFO

Keywords:
Thrombophilias
Neuraxial anesthesia
Thrombocytopenia
Anticoagulation
Epidural/Spinal hematoma
Hemophilia
Bleeding disorders

ABSTRACT

Coagulation is an organized and well-orchestrated process that depends on the intrinsic balance between procoagulants, anticoagulants, and fibrinolytic systems. During pregnancy, this balance is affected in various ways and becomes more critical due to the physiologic changes and obligate hemorrhage after delivery. In some instances, this equilibrium will be disrupted. In this article, we describe the anesthetic implications of bleeding disorders, thrombophilias, and anticoagulation for the safe management of the parturient, with an emphasis on how this impacts decision-making by the anesthesiologist.

Alterations in the procoagulant, anticoagulant, and fibrinolytic system during pregnancy, along with the physiologic and anatomic changes in pregnancy, result in a hypercoagulable state during pregnancy.[1] These physiologic changes increase the incidence of venous thromboembolism (VTE) during pregnancy, occurring with an incidence of 1 in 1000–2000 pregnancies, four to five times the rate in non-pregnant women of the same age.[2] In contrast to, but in some ways related to, this hypercoagulability, hemorrhage is also a well-known complication during pregnancy, especially postpartum. According to Berg et al.,[2] hemorrhage was responsible for 12% of the maternal deaths reported in the United States from 1998 to 2005. Hemorrhage is more likely to occur in the parturient who is anticoagulated or with an inherited or acquired bleeding diathesis, although the major cause of postpartum hemorrhage remains uterine atony, which may not be associated with disorders of coagulation. Obstetric anesthesiologists are well aware of these changes, and the anesthetic/analgesic plan for the parturient will be dictated, to some extent, by the parturient's hematologic state (e.g., hypercoagulable, anticoagulated, and thrombocytopenic). In addition, the obstetric anesthesiologist may be directly or indirectly involved with other situations besides the provision of anesthesia/analgesia during the puerperium, including managing any imbalance in the coagulation cascade (hemorrhage or embolism).

Normal changes in the coagulation system during pregnancy

Changes in the coagulation system are an adaptation for the expected hemostatic challenge during delivery of the newborn and placenta.[1,3,4] Teleologically, this might explain why the majority of hemostatic changes transpire closer to the third trimester of pregnancy.[4,5] These changes include an increase in the procoagulant factors V, VII, VIII, IX, X, XII, and fibrinogen.[3,6,7] Levels of von Willebrand factor increase throughout pregnancy as well. Similarly, levels of the endogenous anticoagulant protein S decline throughout pregnancy, which is felt to convey much of the thrombotic risk of pregnancy. The gravid uterus compresses the inferior vena cava,[8] causing stasis. In general, pregnancy contributes to Virchow's triad (stasis, trauma/anatomic alteration of vasculature, and hypercoagulability) that promotes thrombosis.[4] The presence of the "normal"

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http://dx.doi.org/10.1053/j.semperi.2014.07.003
0146-0005/

hypercoagulability of pregnancy has few anesthetic implications and may actually make neuraxial procedures and other invasive interventions safer in parturients than other patients; however, the frequent necessity for anticoagulation and thromboprophylaxis may have important implications for obstetric and anesthetic and analgesic management and procedures.

Bleeding disorders

von Willebrand disease (vWD)

von Willebrand disease (VWD) is the most common of the inherited bleeding disorders with an incidence of 1–3% in the general population and has a worldwide distribution.[9–12] von Willebrand factor (vWF) is a plasma protein that promotes platelet adhesion at sites of vascular injury and protects factor VIII from intravascular proteolysis.[11] The most common form of von Willebrand disease, type 1, is characterized by decreased vWF synthesis. The less common type 2 VWD, divided into subtypes 2A, 2B, 2M, and 2N, is caused by mutations that lead to decreased vWF activity or decreased factor VIII, while vWF antigen levels remain normal. Type 3 VWD, whose hallmark is severe deficiency of vWF, is quite rare.

Anesthetic implications of vWD

Aside from the obvious and serious risk of hemorrhage (usually postpartum) in any woman with a coagulation disorder, the major specific obstetric anesthetic concern with women who have or may have disorders of the coagulation system is the risk of epidural or spinal hematoma formation during or after neuraxial (spinal or epidural) procedures. The incidence of this complication is low, even in the presence of coagulation disorders, but the complication is difficult to detect and treat, and the morbidity (spinal cord injury) is exceptionally high.[13] The anesthetic management of these patients will be dependent on the type of vWD and the degree of deficiency of vWF and factor VIII. It is of utmost importance to include a hematologist as part of the multidisciplinary management of the parturient with vWD. Type 1 vWD is the most common of the three types (70–75% of patients with vWD)[9]; parturients suffering this type of vWD tend to benefit from the hematologic changes of pregnancy with increased levels of vWF and factor VIII, most of them reaching normal levels during the third trimester, and therefore do not require any pharmacologic intervention or alterations in care.[5]

Neuraxial anesthesia is not contraindicated for these patients as long as the coagulation factors are within normal limits, in particular vWF and factor VIII. Although there is no formal consensus, neuraxial anesthesia technique is generally considered to be safe when vWF:Rco (ristocetin cofactor activity) and factor VIII levels are 50 IU/dl or higher.[11] Varughese and Cohen[14] reported their experience providing epidural anesthesia (EA) in 15 women with vWD (93% of them with type 1 vWD) without any complications related to the neuraxial technique, but postpartum hemorrhage was reported in eight patients. Despite the relative safety (given normal coagulation factors) of administering epidural anesthesia to patients suffering this disease, it is important to remember that although there is an increase of vWF and factor VIII during the third trimester, these levels should be closely monitored.

There are three main strategies to treat patients with VWD, when necessary. The first involves stimulating endogenous endothelial release of vWF by using desmopressin. The second consists of using human-derived plasma concentrates (e.g., Humate P). The third strategy utilizes agents to promote hemostasis and wound healing but not necessarily increasing vWF (e.g., antifibrinolytics). One or a combination of these strategies may be used.[11] Since desmopressin acts by stimulating the endogenous release of vWF, a qualitative defect or lack of production of the protein could limit the use of this drug. Hence, patients with some forms of type 2 vWD (type 2B) may not benefit from the use of desmopressin as much as patients with vWD type 1. Desmopressin has no role in the treatment of type 3 vWD. If factor levels are normalized (naturally due to pregnancy, or with DDAVP or transfusion), Dunkley et al.[5] suggest maintaining normal levels for a period of 3 days after vaginal delivery and up to 7 days after cesarean delivery. The level of vigilance for the development of an epidural hematoma and postpartum hemorrhage after neuraxial procedures may perhaps be raised, but in the presence of normal factors, risk is not felt to be increased. Some suggestions for management of neuraxial anesthesia in patients with vWD are outlined in Table 1.

Hemophilia A (factor VIII deficiency), Hemophilia B (factor IX deficiency and Christmas disease), and other rare factor deficiencies

Both types of hemophilia disease are X-linked recessive disorders.[15] Despite being an X-linked disorder, female

Table 1 – Neuraxial procedures in patients with vWD

(1) Hematology consult and recommendations should be obtained to clarify the type of disease and appropriate intervention (if any). A facility with specialists in high-risk obstetrics, hematologists, a laboratory equipped to measure vWF:RCo and factors of coagulation, pharmacy, and blood bank with capabilities to provide the concentrates and blood products needed are crucial for the care of these patients.
(2) Early anesthesiology consultation.
(3) If the patient is appropriate for a neuraxial procedure (vWF and factor VIII $\geq$ 50 IU/dl):
  (a) A neurologic exam should be performed and documented by the anesthesiologist.
  (b) If the patient is having a vaginal delivery, a low-concentration epidural infusion (e.g., 0.0625–0.1% bupivacaine) should be used so as not to mask signs of neurologic compromise. (This recommendation probably could apply to ALL parturients as it reflects contemporary practice).
  (c) The patient should be closely monitored seeking for signs or symptoms of postpartum hemorrhage as well as neurologic changes.