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Anesthetic Considerations for the Parturient with Immune Thrombocytopenic Purpura

Leah A. Davis

ANESTHETIC CONSIDERATIONS FOR THE PARTURIENT WITH IMMUNE THROMBOCYTOPENIC PURPURA

by

Leah A. Davis

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Abstract

Title: Anesthetic Considerations for the Parturient with Immune Thrombocytopenic Purpura

Background: Immune thrombocytopenic purpura (ITP) is an autoimmune disease that accounts for 5% of pregnancy-associated thrombocytopenia. The condition in the parturient is associated with complications that include maternal hemorrhage and fetal intracranial hemorrhage. Furthermore, it places the parturient at increased risk of developing neurologic complications following administration of neuraxial anesthesia. Although the incidence of ITP is low, anesthetists should be informed of the condition to prevent potentially fatal complications.

Purpose: The purpose of this independent project is to present a case report and provide anesthesia providers with evidence-based research regarding the anesthetic considerations for parturients with ITP.

Process: A review of the literature was performed using PubMed and CINAHL databases from the University of North Dakota's Harley E. French Library of the Health Sciences. Each reference utilized was carefully scrutinized for inclusion within the review.

Results: ITP is an autoimmune disorder that accelerates the rate of platelet destruction and leads to persistent thrombocytopenia. Frequent monitoring of maternal and fetal wellbeing as well as collaboration among the obstetrician, hematologist, anesthetist, and neonatologist is required to mitigate complications. Antepartum management may include administration of oral corticosteroids or intravenous immunoglobulins (IVIg) depending on clinical manifestations and maternal platelet counts. Additionally, life-threatening bleeding or emergent delivery may necessitate platelet transfusion in conjunction with IVIg infusion. The mode of delivery is dependent on the maternal condition and obstetrical indicators with the primary goal of maintaining a platelet count greater than 50,000 per microliter (mcL) to minimize the risk of

maternal hemorrhage during both vaginal and cesarean delivery. Controversy exists regarding the lowest safe platelet count required for administration of neuraxial anesthesia in the parturient with thrombocytopenia. Several studies have proposed utilizing thromboelastography (TEG) and rotational thromboelastometry (ROTEM) to help guide safe anesthetic practices. Due to inadequate evidence and conflicting reports, the use of TEG/ROTEM as well as a minimally safe platelet count cannot be supported at this time. Current evidence suggests that the provision of neuraxial anesthesia in thrombocytopenic parturients be considered on an individual basis after conducting a careful risk-benefit analysis.

Implications: By understanding the pathophysiology, potential complications, and anesthetic considerations associated with ITP in the parturient, maternal and neonatal morbidity and mortality may be reduced.

Keywords: Immune thrombocytopenia, thrombocytopenia, pregnancy, obstetrical anesthesia, spinal anesthesia, and cesarean section.

Anesthetic Considerations for the Parturient with Immune Thrombocytopenic Purpura

Thrombocytopenia is a clinical condition in which there is a decreased number of circulating platelets (Berkley & Kilpatrick, 2009). It complicates approximately 7% of all pregnancies and may result from a number of causes (Berkley & Kilpatrick, 2009). No matter the etiology, all forms of thrombocytopenia can be attributed to either increased platelet destruction or decreased platelet production (Berkley & Kilpatrick, 2009). Immune thrombocytopenic purpura (ITP) is an autoimmune disease that accounts for 5% of pregnancy-associated thrombocytopenia (Stavroe & McCrae, 2009). Hallmark features of the condition include platelet destruction resulting in platelet counts less than 100,000 per microliter (mcL) with no clinically apparent cause (Berkley & Kilpatrick, 2009). The major complications associated with ITP are maternal hemorrhage and fetal thrombocytopenia with potential fetal intracranial hemorrhage (Hindley, 2016).

Providing anesthesia to a parturient is challenging due to the anatomic and physiologic changes that occur during healthy pregnancies (Nagelhout & Plaus, 2014). When pregnancy is complicated by ITP, anesthesia providers are presented with a unique situation that requires careful consideration and planning. Currently, neuraxial anesthesia is considered the favorable method of anesthesia for labor and delivery (Nagelhout & Plaus, 2014). It has significant advantages over general anesthesia as a primary anesthetic including decreased risk of maternal mortality and more favorable neonatal outcomes (Nagelhout & Plaus, 2014). Unfortunately, the presence of thrombocytopenia places the parturient at risk for developing spinal-epidural hematomas that may result in permanent neurologic injury (Bernstein et al., 2016). Controversy exists regarding the lowest safe platelet count required for administration of neuraxial anesthesia.

Ultimately, it is the anesthesia providers responsibility to weigh the risks and benefits of anesthesia modalities in this unique population (Myers, 2012; Provan et al., 2010).

Obviously, the combination of pregnancy and ITP would be considered a low occurrence, high stakes situation that requires thorough anesthetic planning and vigilant monitoring. In the following pages, a case report of a parturient with chronic ITP who underwent a planned cesarean section is presented. A literature review that covers the pathophysiology, diagnosis, clinical presentation and anesthetic considerations for ITP will follow.

Purpose

The purpose of this independent project is to present a case report and provide anesthesia providers with evidence-based research regarding the anesthetic management of a parturient with ITP. By understanding the pathophysiology, potential complications, and anesthetic considerations associated with this condition, maternal and neonatal morbidity and mortality may be reduced.

Case Report

A 23-year-old, 90 kg, 155 cm, Native American female presented for a planned repeat cesarean section for intrauterine pregnancy at 36-weeks gestation with incomplete uterine rupture. She denied having any allergies. Her medical history included chronic ITP, anxiety, depression, and iron deficiency anemia. Obstetric history included gravida four and para three. She received late prenatal care in her third trimester of pregnancy, and her ITP was not medically managed. Surgical history included three previous cesarean sections and laparoscopic cholecystectomy. There was no history of anesthetic complications. Current medications included cyanocobalamin, vitamin B6, prenatal multivitamin, and iron supplement. Pertinent labs included hemoglobin 12.4 g/dL, hematocrit 37.2%, and a stable platelet count of 87,000 per

mcL. Additionally, she was type and screened for two units of packed red blood cells (PRBCs), which were retrieved from lab prior to the start of the case.

The patient was considered an American Society of Anesthesiologists (ASA) physical status level two with a Mallampati class II airway. Bilateral breath sounds were clear to auscultation. Normal S1 and S2 heart sounds with regular rate and rhythm were noted upon cardiovascular exam. Preoperative vital signs were: heart rate 72/min, blood pressure 122/70 mmHg, respirations 12/min, oxygen saturation (SpO2) 99% on room air, and temperature 36.1° Celsius. Fetal heart monitoring showed 140-150 beats per minute, moderate variability, reactive accelerations, and absent decelerations.

Prior to transport to the operating room, an intravenous (IV) lactated ringers bolus of 1000 mL was administered via a 20-gauge IV catheter by obstetric nursing staff. A new bag of lactated ringers was initiated, and the infusion was maintained continuously. The patient was transferred to the operating room where she was assisted into a sitting position on the operating table. Non-invasive monitors were applied which included: a finger pulse oximeter, a five-lead electrocardiogram (EKG), and a blood pressure cuff.

The patient was instructed to arch her back into a flexed position with assistance from nursing staff. Vital signs were: heart rate 91/min with normal sinus rhythm, blood pressure 134/76 mmHg, and SpO2 99% on room air. The patient's back was cleansed, utilizing sterile technique, with betadine solution, and a sterile drape was applied. Three milliliters (mL) of 1% lidocaine without epinephrine was administered for local infiltration in a fan-like pattern at the L3-L4 inter-spinous space. A blunt bevel 20-gauge introducer needle was advanced into the Ligamentum Flavum via a midline approach. A 25-gauge, 3.5-inch pencil point spinal needle was then inserted through the introducer. After a positive loss of resistance, the stylet was

withdrawn, and clear, free-flowing cerebrospinal fluid (CSF) return was confirmed. A syringe containing 1.6 mL 0.75% bupivacaine/8.25% dextrose, 20 mcg fentanyl, and 0.2 mg Duramorph was attached to the spinal needle. The syringe was gently aspirated for positive CSF return followed by slow injection of the entire volume into the intrathecal space. The spinal needle and introducer were removed simultaneously without incident.

The patient was repositioned in the supine position with left uterine displacement. Bilateral arms were secured on arm boards and abducted less than 90 degrees. Oxygen was applied via nasal cannula at 3 L/minute with end-tidal carbon dioxide (ETCO2) monitoring present. A skin probe was placed in the left axillary fold for temperature monitoring. Vital signs were reassessed and found to be: heart rate 114/min, blood pressure 86/62 mmHg, SpO2 100%, and temperature 36.2° Celsius. A phenylephrine 100 mcg bolus was administered IV for hypotension. Three minutes later, vital signs were reassessed and found to be: heart rate 95/min, blood pressure 106/64 mmHg, SpO2 100%, and temperature 36.2° Celsius. Due to the patient's increased risk of hemorrhage, an 18-gauge IV catheter was placed in addition to the pre-existing 20-gauge IV catheter. An IV infusion of normal saline via blood tubing was connected to the 18-gauge catheter and infused continuously. Two grams of cefazolin IV was administered for a preoperative antibiotic. The abdomen was prepped to the level of the xiphoid process, and Foley catheter placed by nursing staff. The patient denied sensation to the T6 dermatome distribution during application of antiseptic prep solution. Prior to incision, the surgeon utilized forceps to assess the height of the intrathecal blockade. Once again, the patient denied sensation below the T6 dermatome level.

The surgical incision was made ten minutes after intrathecal injection. Prior to uterine incision, the surgeon noted an intact uterus with a uterine window. The 2.55 kg neonate was

delivered nine minutes after surgical incision, and an IV infusion of 20 units oxytocin in a 1000 mL bag of lactated ringers was initiated. Neonatal Apgar scores were assessed by neonatal intensive care unit (NICU) nursing staff and noted to be nine (60 seconds after delivery) and nine (5 minutes after delivery). Seven minutes after delivery of the neonate, the patient complained of nausea. Vital signs noted to be: heart rate 86/min, blood pressure 128/72 mmHg, SpO2 100%, and temperature 36.3° Celsius. Four mg of ondansetron was administered with relief of nausea. The abdominal wound was closed by the surgeon. The neonate was transferred to the NICU, and the patient was transferred to the post-anesthesia care unit (PACU). The patient was administered diphenhydramine 25 mg IV in PACU for itching, but had an otherwise uneventful recovery.

During the 1-hour 25-minute surgical procedure, the patient received a total of 1000 mL of normal saline, 1400 mL of lactated ringers, and 500 mL of lactated ringers with 20 units oxytocin. Estimated blood loss was 500 mL, and urine output was 400 mL. The patient and neonate had an uneventful hospital stay and were discharged home on postoperative day four.

Literature Search

According to Stillwell, Fineout-Overholt, Melnyk, & Williamson (2010), a literature search using the Cochrane Library, PubMed, and CINAHL will result in the strongest level of evidence. For this literature search, PubMed and CINAHL databases were accessed via the Harley E. French Health Sciences Library. PubMed and CINAHL were utilized because they contain medical, scientific, nursing, and allied health literature that applies to the clinical inquiry presented (Stillwell et al., 2010).

Keywords and Limits

A total of four searches were conducted using Medical Subject Heading (MeSH) terms within the PubMed database. Using MeSH terms results in a comprehensive literature search by

finding all articles related to the keywords. The first search utilized the MeSH terms “anesthesia, obstetrical” and “thrombocytopenia” in all fields. This resulted in 66 articles. To make the number of articles more manageable, the limits “within ten years,” “humans,” and “full text” were applied. This decreased the search results to 19, with four articles specifically pertinent to the topic of interest.

The second search using PubMed was performed using the MeSH terms “cesarean section” and “thrombocytopenia” in all fields. This search produced 273 results. The search was further refined by adding the search filters “within ten years,” “humans,” and “free full text.” This decreased the search results to 15 articles, with one article specifically pertinent to the topic of interest.

The third search performed with PubMed used the MeSH terms “thrombocytopenia” and “spinal anesthesia.” Nineteen articles resulted from this search. The limits “within ten years,” “humans,” and “full text” were applied. This exploration reduced the results to 10 with one pertinent article saved for the review.

CINAHL was the next database chosen for the literature search. A total of three searches were conducted using the CINAHL database. First, the search words “idiopathic thrombocytopenia” and “pregnancy” were used with the all text option. This yielded 14 results. The search was further refined by using the limits “published dates between 2008 and 2017”, “peer-reviewed,” “academic journals,” and “English language.” The application of these limits resulted in six articles, three of which were saved for review.

The second search within the CINAHL database utilized the search words “thrombocytopenia” and “cesarean section” with the all text option. This resulted in 27 articles. After applying the limits “published dates between 2007 and 2018”, “peer-reviewed,” “academic

journals," and "English language," the results were further reduced to 11 articles. One article was a duplicate, and two articles were saved.

The third search within the CINAHL database utilized the search words "spinal anesthesia" and "thrombocytopenia" with the all text option. This resulted in seven articles. After applying the limits "published dates between 2007 and 2018", "peer-reviewed," "academic journals," and "English language," the results were further reduced to three articles. One article was a duplicate, and two articles were saved.

Additionally, four applicable articles were found by reviewing the reference list of evidence-based research articles that had already been evaluated. The identification of key search terms as well as the use of controlled vocabulary within credible healthcare focused databases proved to be an effective and efficient literature search strategy. After searches within PubMed and CINAHL databases had been completed, a total of seventeen articles were saved and reviewed. A detailed review of the literature will be discussed in the following section.

Review of Literature

Pathophysiology and Diagnosis

The normal platelet count in women ranges from 150,000 to 400,000 per mcL (Berkley & Kilpatrick, 2009; Hindley, 2016). However, this value is often lower in parturients due to the expansion of plasma volume, hemodilution, and increased platelet activation and clearance that occurs with healthy pregnancies (Berkley & Kilpatrick, 2009; Provan et al., 2010). Thrombocytopenia is clinically defined as a platelet count less than 150,000 per mcL and is a relatively common syndrome that affects approximately 7% of all pregnancies (Stavroe & McCrae, 2009). Thrombocytopenia during pregnancy is associated with many etiologies including infections, folic acid deficiency, hematologic disorders, immunologic destruction, and

excess bleeding (Berkley & Kilpatrick, 2009). No matter the etiology, all forms of thrombocytopenia can be attributed to either increased platelet destruction or decreased platelet production (Berkley & Kilpatrick, 2009; Hindley, 2016; Stavroe & McCrae, 2009).

ITP is a thrombocytopenic syndrome that accounts for 5% of pregnancy-associated thrombocytopenia (Stavroe & McCrae, 2009). ITP is an autoimmune disorder that involves the formation of IgG antiplatelet antibodies that recognize specific antigens on platelet membranes (Stavroe & McCrae, 2009; Wyszynski et al., 2016). The binding of the IgG antibodies to the platelet membrane marks the platelet for destruction by the reticuloendothelial system in the spleen (Stavroe & McCrae, 2009; Wyszynski et al., 2016). This accelerates the rate of platelet destruction and leads to persistent thrombocytopenia (Stavroe & McCrae, 2009; Wyszynski et al., 2016). The clinical presentation of ITP can be variable and can occur in both pregnant and non-pregnant individuals (Stavroe & McCrae, 2009). It more commonly presents as an asymptomatic disorder that is detected with routine laboratory testing (Stavroe & McCrae, 2009). However, some patients may present with a history of gingival bleeding, epistaxis, easy bruising, and petechiae (Berkley & Kilpatrick, 2009).

ITP is considered a diagnosis of exclusion because no specific platelet count threshold has been identified and platelet antibody tests do not help to differentiate between thrombocytopenic disorders (Stavroe & McCrae, 2009). A diagnosis of ITP is often made when a platelet count of less than 100,000 per mcL is present with an otherwise normal complete blood count and no clinically apparent causes of thrombocytopenia (Berkley & Kilpatrick, 2009; Stavroe & McCrae, 2009; Wyszynski et al., 2016). However, the diagnosis of ITP is more likely if the patient presents with a prior history of thrombocytopenia, severe thrombocytopenia (platelet count less than 50,000 per mcL), and/or underlying autoimmune disease (Stavroe &

McCrae, 2009). ITP can be diagnosed as an acute or chronic condition and is considered chronic when the thrombocytopenia persists for more than six months (Wyszynski et al., 2016). Interestingly, women with previously diagnosed ITP or chronic ITP can experience an exacerbation or relapse of the condition during pregnancy (Provan et al., 2010; Stavroe & McCrae, 2009).

Complications

Most pregnancies complicated by ITP are uneventful and result in good outcomes for both the mother and the neonate (Provan et al., 2010). However, frequent prenatal monitoring of maternal and fetal wellbeing is required to mitigate complications (Hindley, 2016; Myers 2012). The major complication associated with ITP in the parturient is excessive or spontaneous hemorrhage during the intrapartum and postpartum periods (Berkley & Kilpatrick, 2009; Hindley, 2016). The risk of hemorrhage is directly linked to the maternal platelet count, but rarely occurs with platelet counts greater than 20,000 per mcL (Berkley & Kilpatrick, 2009). According to Provan et al. (2010), current literature indicates that women with ITP have a low risk of maternal and fetal hemorrhage and can safely tolerate pregnancy.

The major complication associated with ITP in the fetus is the development of fetal thrombocytopenia and subsequent fetal intracranial hemorrhage (Hindley 2016; Stavroe & McCrae, 2009). The maternal IgG antibodies are actively transported into fetal circulation through the placenta (Hindley 2016; Stavroe & McCrae, 2009). These IgG antibodies can bind to the fetal platelet antigens and cause thrombocytopenia in the fetus (Hindley 2016; Stavroe & McCrae, 2009). The major concern associated with fetal thrombocytopenia is intracranial hemorrhage, which can occur during delivery (Hindley 2016; Stavroe & McCrae, 2009). Clinical manifestations of intracranial hemorrhage may not appear until 2-5 days postpartum, which

necessitates frequent neurological monitoring with platelet counts less than 50,000 per mcL (Berkley & Kilpatrick, 2009; Hindley 2016; Stavroe & McCrae, 2009). However, retrospective studies have shown that although 15% of neonates born to mothers with ITP will present with a platelet count less than 50,000 per mcL, the rate of intracranial hemorrhage is less than 1% (Berkley & Kilpatrick, 2009).

Prenatal Medical Management of ITP

Although anesthesia providers are not directly involved in the medical management of ITP, a general understanding is required to safely deliver care during the intrapartum period. Management of ITP during the prenatal period depends on the patient's clinical manifestations and platelet counts (Myers, 2012). A complete blood count (CBC) is typically drawn monthly in the first and second trimester, bimonthly in the third trimester, and weekly as the anticipated delivery date approaches (Myers, 2012; Provan et al., 2010). If severe thrombocytopenia or a rapid rate of platelet decline is noted, then more frequent CBC testing is required to assist in making decisions regarding the mode of delivery (Myers, 2012; Provan et al., 2010).

If there is no evidence of excessive or spontaneous bleeding and platelet counts remain above 30,000 per mcL, treatment is not required until 36-weeks gestation or 10 days prior to the anticipated delivery date (Rajasekhar, Gernsheimer, Stasi, & James, 2013). However, oral corticosteroid therapy is recommended if delivery is imminent, platelet counts are below 30,000 per mcL, or manifestations of bleeding are present (Rajasekhar et al., 2013). Oral corticosteroids are considered a first-line treatment and help to increase platelet counts by suppressing the immune response (Hindley, 2016; Rajasekhar et al., 2013). The corticosteroids of choice are prednisone or prednisolone (10-20 mg/day) because they do not readily cross the placenta (Rajasekhar et al., 2013). Unfortunately, there are risks associated with the use of corticosteroids

during pregnancy including weight gain, gestational diabetes, and maternal hypertension (Gernsheimer & McCrae, 2007; Hindley, 2016). Therefore, corticosteroids should be avoided in women who have hypertensive or diabetic conditions (Gernsheimer & McCrae, 2007; Hindley, 2016). An appropriate alternative therapy is intravenous immunoglobulin (IVIg) (1g/kg), which may be administered if significant side effects occur, corticosteroid therapy is ineffective, or a more rapid increase in platelets is required (Hindley, 2016; Provan et al., 2010; Rajasekhar et al., 2013). Side effects associated with IVIg include vomiting, headache, and hypotension, which can be attenuated by decreasing the rate of infusion (Hindley, 2016).

Generally speaking, platelet transfusion alone is not an effective treatment for ITP due to the rapid destruction of platelets associated with this syndrome (Provan et al., 2010). However, if a rapid increase in platelets is required for life-threatening bleeding or emergent delivery, platelet transfusion in conjunction with IVIg infusion is recommended (Provan et al., 2010; Rajasekhar et al., 2013; Stavroe & McCrae, 2009). A retrospective review of 40 patients with ITP who received concurrent platelet transfusion and IVIg for severe thrombocytopenia, active bleeding, and/or impending surgery concluded that the treatment was associated with minimal side effects, resolution of bleeding, and rapid restoration of platelet counts (Spahr & Rodgers, 2008). In fact, platelet transfusion not only reduces bleeding but will increase the post-transfusion platelet count by more than 20,000 per mcL in bleeding ITP patients (Provan et al., 2010). Unfortunately, there is limited evidence available regarding the optimal dose and timing for administration of IVIg and platelet therapy.

Mode of Delivery

American Society of Hematology (ASH) guidelines on the intrapartum management of ITP recommend that maternal condition and obstetrical indicators dictate the mode of delivery

(Rajasekhar et al., 2013). Previous evidence indicated that elective cesarean section reduced the risk of fetal intracranial hemorrhage. However, this evidence has been dispelled by numerous studies over the last two decades (Stavroe & McCrae, 2009). Gasim (2011) conducted a retrospective study of 38 pregnancies with known ITP in which 14 parturients delivered by cesarean section and 24 underwent vaginal delivery. The study reported a low incidence of poor neonatal outcomes that were unrelated to the mode of delivery and concluded that routine use of cesarean section should be avoided (Gasim, 2011). Similarly, a retrospective study spanning from 1988 to 2007 reviewed 104 pregnancies complicated by ITP and noted no association between intracranial hemorrhage and mode of delivery (Belkin, Levy, & Sheiner 2009).

Even if a trial of labor is deemed appropriate, the risk of cesarean section is present with every labor (Stavroe & McCrae, 2009). Therefore, the primary concern during parturition is maintaining a platelet count that will minimize the risk of maternal hemorrhage during both vaginal and cesarean delivery (Stavroe & McCrae, 2009). The ASH guidelines recommend a platelet count of 50,000 per mcL to minimize the risk of maternal hemorrhage during both vaginal and cesarean delivery because the incidence of hemorrhage is rare with platelet counts above this value (Myers, 2012; Stavroe & McCrae, 2009; Rajasekhar et al., 2013). If emergency delivery is required with a platelet count under 50,000 per mcL, platelet transfusion in conjunction with IVIg is recommended (Provan et al., 2010; Rajasekhar et al., 2013; Stavroe & McCrae, 2009).

Neuraxial Anesthesia in the parturient with ITP

Management of ITP in pregnancy requires collaboration among the obstetrician, hematologist, anesthetist, and neonatologist (Hindley, 2016; Myers, 2012; Provan et al., 2010). Anesthesia should be consulted early in the pregnancy to make decisions regarding the analgesic

and anesthetic plan for delivery (Myers, 2012). Early pregnancy anesthetic counseling for women with ITP should include an explanation that neuraxial anesthesia may not be possible due to the platelet count at the time of delivery (Myers, 2012). In addition, education should be provided regarding the benefits, risks, and alternatives to neuraxial anesthesia (Myers, 2012). When a parturient with ITP is admitted, anesthesia should be notified, and the most recent platelet count should be made available (Hindley, 2016).

Currently, neuraxial anesthesia is considered the favorable method of obstetric analgesia and anesthesia (Nagelhout & Plaus, 2014). It has significant advantages over general anesthesia as a primary anesthetic for cesarean section including decreased risk of maternal mortality, pain relief, blood pressure stability, and more favorable neonatal outcomes (Provan et al., 2010; Nagelhout & Plaus, 2014). Unfortunately, coagulopathy is considered a contraindication to neuraxial anesthesia administration because it places the parturient at increased risk of spinal-epidural hematoma (Bernstein et al., 2016; Nagelhout & Plaus, 2014). Controversy exists regarding the lowest safe platelet count required for administration of neuraxial anesthesia in the parturient with thrombocytopenia. The ASH Clinical Practice Guide on Thrombocytopenia in Pregnancy does not recommend a definitive minimum platelet count for placement of neuraxial anesthesia in parturients with ITP (Rajasekhar et al., 2013). Instead, the guide suggests that a minimum platelet count of 80,000 per mcL may be appropriate but ultimately recommends that local practices and clinician discretion should guide administration of neuraxial anesthesia (Rajasekhar et al., 2013). Similarly, the International Consensus Report on the Investigation and Management of ITP also does not recommend a minimum platelet count for neuraxial anesthesia (Provan et al., 2010). However, studies included within the report indicate that a lower threshold

of 75,000 per mcL may be appropriate (Provan et al., 2010). Additionally, Huang, McKenna, and Babins (2014) report that:

> No recommendations exist from the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anesthesia, The American Society of Anesthesiologists, or the American College of Obstetrics and Gynecology addressing when it is safe to administer neuraxial techniques in the parturient with ITP or other coagulopathies (p. 128).

Due to inadequate evidence and conflicting reports, a minimum required platelet count cannot be supported. Until a consensus can be reached, it is suggested that the provision of neuraxial anesthesia be considered on an individual basis with the risks of the procedure carefully balanced against the benefits (Myers, 2012; Provan et al., 2010).

Several studies have proposed utilizing thromboelastography (TEG) and rotational thromboelastometry (ROTEM) to help guide safe anesthetic practices in the parturient with thrombocytopenia (Huang et al., 2014; Mauritz, Strouch, & Olufolabi, 2016; Provan et al., 2010). ROTEM and TEG are point-of-care tests that are used to assess coagulation and provide information regarding clot formation, stabilization, and dissolution (Mauritz et al., 2016). According to Provan et al. (2010), “using this technique, thrombocytopenia can be evaluated against the prothrombotic state of pregnancy, rather than monitoring platelet function alone” (p. 178). A prospective cohort study performed by Huang et al. (2014), utilized TEG in conjunction with platelet counts to assess the incidence of neurologic complications related to regional anesthesia in parturients with thrombocytopenia. The results from the three-year study suggest that neuraxial anesthesia can be safely performed in parturients with platelet counts greater than 56,000 per mcL and a normal TEG result (Huang et al., 2014). Similarly, a case study performed

by Mauritz et al. (2016) reported utilizing ROTEM to evaluate platelet function and guide the anesthetic management of a high-risk parturient with thrombocytopenia. With the use of ROTEM, a cesarean section was performed under spinal anesthesia without complication (Mauritz et al., 2016). There is potential in utilizing TEG and ROTEM to assess the risk of administering neuraxial anesthesia in the parturient with ITP. However, a recommendation for its use cannot be made at this time.

As discussed earlier, the major risk associated with administering neuraxial anesthesia to thrombocytopenic patients is the development of a spinal-epidural hematoma (Bernstein et al., 2016). A spinal-epidural hematoma is a collection of blood within the spinal neuraxis that can compress the spinal cord and nerve roots leading to irreversible neurologic dysfunction (Horlocker et al., 2010; Nagelhout & Plaus, 2014). The actual risk of developing neurological dysfunction following administration of neuraxial anesthesia is unknown (Horlocker et al., 2010). The estimated incidence in the obstetric population is 1 in 168,000 after epidural administration and unknown after spinal administration (Bernstein et al., 2016). Lee et al. (2017) conducted a retrospective cohort study and systematic review that included a total of 1,524 thrombocytopenic parturients. The study found that the risk of epidural hematoma was 11% for a platelet count less than 50,000 per mcL, 3% for 50,000 to 69,000 per mcL, and 0.2% for 70,000 to 100,000 per mcL (Lee et al., 2017). Similarly, a study containing 499 parturients with platelet counts less than 100,000 per mcL reported the risk of spinal-epidural hematoma to be 0 to 0.6% (Goodier, Lu, Hebbar, Segal, & Goetzl, 2015). Factors associated with the development of a symptomatic hematoma include spinal cord abnormalities, difficult needle placement, coagulopathy, increased needle size, and catheter placement (Horlocker et al., 2010; Provan et al., 2010). Due to these risk factors, Provan et al. (2010) suggest that spinal anesthesia delivered

by an experienced clinician may be a safer neuraxial anesthetic option for thrombocytopenic patients. However, there is limited evidence regarding appropriate anesthetic techniques that minimize the risk of hematoma formation. Again, a thorough risk-benefit analysis should be performed prior to administering neuraxial anesthesia to a parturient with ITP (Myers, 2012; Provan et al., 2010).

Anticipation and Management of Maternal Hemorrhage

The major complication associated with ITP in the parturient, although low, is excessive or spontaneous hemorrhage during the intrapartum and postpartum periods (Berkley & Kilpatrick, 2009; Hindley, 2016). An integral component of obstetric anesthesia is developing a plan for the management of maternal hemorrhage (Nagelhout & Plaus, 2014). Due to the potential for maternal hemorrhage, a CBC should be drawn, and a large bore IV cannula should be inserted as a precautionary measure (Hindley, 2016). Typically, it is not routine to order a blood type and screen for healthy low-risk parturients (Apfelbaum et al., 2016). The decision to order a blood type and screen are based on the history, anticipated hemorrhagic complications, institutional policy, and provider assessment (Apfelbaum et al., 2016). If type specific blood is not available in the event of an emergency, type O-negative blood is an acceptable alternative (Apfelbaum et al., 2016). Additionally, resources for hemorrhagic emergencies should be readily available as they are associated with reduced maternal complications (Apfelbaum et al., 2016). The ASA Practice Guidelines for Obstetric Anesthesia recommend the following resources for obstetric hemorrhagic emergencies: large bore IV catheters, fluid warmers, blood bank resources, massive transfusion protocol, rapid transfusion devices, and cell salvage equipment (Apfelbaum et al., 2016).

Maternal hemorrhage should be considered when blood loss is greater than or equal to one liter or clinical manifestations of hypovolemia develop within 24 hours of parturition (Shields, Goffman, & Caughey, 2017). When maternal hemorrhage develops, anesthetic focus shifts from the delivery of analgesia and anesthesia to the maintenance of vital organ perfusion and oxygenation (Nagelhout & Plaus, 2014). If severe hemorrhage develops with regional anesthesia in place, it is recommended to consider rapid sequence induction of general anesthesia (Nagelhout & Plaus, 2014). General anesthesia utilizing anesthetic agents that result in minimal hemodynamic depression may be the most appropriate anesthetic technique in the event of severe hemorrhage (Apfelbaum et al., 2016). Furthermore, it allows the clinician to manage volume resuscitation, focus on hemodynamic support, and ensure patient comfort (Nagelhout & Plaus, 2014).

Maternal hemorrhage requiring blood transfusion is the leading cause of maternal morbidity in the United States (Shields et al., 2017). Unfortunately, replacing intravascular volume at the rate it is being lost in severe hemorrhage may require the use of blood bank resources and massive transfusion protocols (Apfelbaum et al., 2016; Nagelhout & Plaus, 2014). Intraoperative cell salvage should be considered, especially in situations involving limited banked blood availability or patient refusal of banked blood administration (Apfelbaum et al., 2016). Furthermore, a rapid increase in platelets may be required for thrombocytopenic parturients with life-threatening bleeding (Provan et al., 2010). As discussed earlier, platelet transfusion in conjunction with IVIg infusion may reduce bleeding by rapidly restoring platelet counts (Provan et al., 2010; Rajasekhar et al., 2013; Stavroe & McCrae, 2009). Ultimately, the utilization of a massive transfusion protocol and clear communication amongst the multidisciplinary care team will promote improved patient outcomes by initiating laboratory

studies, restoring fluid volume, correcting coagulopathies, and rectifying the primary cause of bleeding (Apfelbaum, 2016; Nagelhout & Plaus, 2014; Shields et al., 2017).

Discussion

The patient in this case review was undergoing elective, repeat cesarean section at 36-weeks gestation with a history of chronic ITP. Antepartum management of the patient's ITP was limited due to the fact that she did not present for prenatal care until late in the third trimester. Therefore, serial platelet counts were not drawn throughout the pregnancy, and the ITP was not medically managed with oral corticosteroids or IVIg therapy.

Elective cesarean section was the patient's only option for delivery due to her history of three previous cesarean sections and incomplete uterine rupture. This coincides with the evidence, which recommends that the maternal condition and obstetrical indicators should guide the mode of delivery. As previously discussed, a platelet count of 50,000 per mcL is recommended to minimize the risk of maternal hemorrhage during both vaginal and cesarean delivery. Although the platelet count was considered stable at 87,000 per mcL and no bleeding manifestations were noted, the major maternal complications associated with ITP in the parturient is hemorrhage. Therefore, precautionary measures were taken prior to the start of the case, which included maintaining communication with blood bank, having two units of typed and screened blood available in the operating room, obtaining two large bore IV catheters with blood tubing attached, and confirming that rapid transfusion devices were readily available. Likewise, this corresponds with the evidence presented within the review.

The decision to perform spinal anesthesia as the primary anesthetic was based on the patient's stable platelet count and absence of bleeding manifestations. This intervention may be considered controversial. Until a consensus is reached, the evidence suggests that a thorough

risk-benefit analysis is appropriate. Additionally, TEG and/or ROTEM were not utilized to further assess coagulation, though, there is limited evidence to support this intervention. The spinal anesthetic was placed in one attempt by an experienced anesthetist utilizing a 25-gauge pencil point spinal needle. It is feasible that these interventions may have minimized the patient's risk of hematoma formation, however, the evidence is inconclusive.

Conclusion

ITP is an autoimmune disorder that accelerates the rate of platelet destruction and leads to persistent thrombocytopenia. Most pregnancies complicated by ITP are uneventful and result in good outcomes. However, frequent monitoring of maternal and fetal wellbeing as well as collaboration among the multidisciplinary care team members is required to mitigate complications. Management of ITP ultimately depends on the patient's clinical manifestations and platelet counts. These factors not only dictate prenatal medical management and mode of delivery, but also the anesthetic plan throughout parturition.

Although it is well documented that the risk of spinal-epidural hematoma increases as the platelet count decreases, a decisively safe platelet count for the administration of neuraxial anesthesia in thrombocytopenic patients has yet to be identified. A consensus among national medical specialty societies needs to be achieved regarding this value. Additionally, emerging research on the utilization of TEG and ROTEM to help guide safe anesthetic practices in the parturient with thrombocytopenia is promising. However, further research is needed before definitive recommendations can be made.

Undoubtedly, a parturient with ITP presents a unique challenge to the anesthesia care team that requires thorough anesthetic planning and vigilant monitoring. With the development of consistent guidelines among national medical specialty societies and further research

regarding the management of the condition, anesthetic management of this population can be improved.

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Anesthetic Considerations for the Parturient with Immune Thrombocytopenic Purpura

Leah A. Davis, SRNA

UND Nurse Anesthesia
University of North Dakota

Introduction

- Immune thrombocytopenic purpura (ITP) is an autoimmune disorder that accelerates the rate of platelet destruction and leads to persistent thrombocytopenia.
- ITP accounts for 5% of pregnancy-associated thrombocytopenia.
- The condition in the parturient is associated with complications that include:
  - Maternal hemorrhage
  - Fetal intracranial hemorrhage
  - Spinal-epidural hematoma with neuraxial anesthesia

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Case Information

- Planned repeat cesarean section for pregnancy at 36-weeks gestation
- 23-year old female
- 155 cm
- 90 kg
- No known drug allergies
- ASA physical status level 2

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Pre-operative Evaluation

- Past Medical History:
  - Chronic ITP
  - Iron deficiency anemia
- Surgical History:
  - 3 previous cesarean sections
  - Laparoscopic cholecystectomy
- Obstetric History:
  - G4P3
  - Late prenatal care in 3rd trimester
  - No medical management of ITP during pregnancy
- Anesthetic History:
  - Uncomplicated

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Pre-operative Evaluation Continued

- Pre-operative vital signs:
  - Heart rate: 72/min
  - Blood pressure: 122/70 mmHg
  - Respirations: 12/min
  - Room air oxygen saturations (SpO2): 99%
  - Temperature: 36.1° Celsius
- Mallampati score: 2
- Pertinent labs:
  - HGB: 12.4 g/dL
  - HCT: 37.2%
  - PLT: 87,000/mcL (stable)
  - Type and screened for 2 units PRBCs (available in OR)

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Anesthetic Course

- Pre-op:
  - 1L bolus LR via 20-gauge IV catheter
- Intrathecal administration:
  - Sitting position, one attempt at L3-4 space
  - 20-gauge introducer needle and 25-gauge, 3.5 inch pencil point spinal needle
  - Injection of 1.6 mL 0.75% bupivacaine, 20 mcg fentanyl, and 0.2 mg morphine
  - Level of blockade: T6 distribution
- Spontaneously breathing with nasal cannula at 3 L/min
- Additional 18-gauge IV catheter placed with NS and blood tubing attached
- Other medications administered:
  - 100 mcg phenylephrine IV, 2 g cefazolin IV, 4 mg ondansetron IV, 1L bag LR with 20 units oxytocin.

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Intraoperative Issues

- Hypotension:
  - Treated with 100 mcg phenylephrine IV
- Nausea:
  - Treated with 4 mg ondansetron IV

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Post-operative Course

- Total procedure time: 1 hour and 25 minutes
- Neonate transferred to NICU and parturient transferred to PACU
- Complaint of itching in PACU
  - Treated with 25 mg diphenhydramine IV
- Intake/Output:
  - Volume replacement:
    - Normal saline: 1000 mL
    - Lactated ringers: 1400 mL
    - Lactate ringers with 20 units oxytocin: 500 mL
  - Estimated blood loss: 500 mL
  - Urine Output: 400 mL
- Patient and neonate discharged home on post-operative day 4

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Pathophysiology

- ITP is an autoimmune disorder that involves the formation of IgG antiplatelet antibodies that recognize specific antigens on platelet membranes.
- The binding of the IgG antibodies to the platelet membrane marks the platelet for destruction by the reticuloendothelial system in the spleen.
- This accelerates the rate of platelet destruction and leads to persistent thrombocytopenia.
- Most commonly presents as an asymptomatic disorder that is detected with routine lab testing.
- Some may present with a history of gingival bleeding, epistaxis, easy bruising, and/or petechiae.

(Berkley & Kilpatrick, 2009; Stavroe & McCrae, 2009; Wyszynyski et al., 2016)

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Complications

- Current literature indicates that women with ITP have a low risk of complications and can safely tolerate pregnancy.
- Major complication for the parturient is hemorrhage.
- Major complication in the fetus is the development of fetal thrombocytopenia and subsequent fetal intracranial hemorrhage.
  - Maternal IgG antibodies are actively transported into fetal circulation thru the placenta.
  - Highest risk of hemorrhage occurs in neonates with platelet counts less than 50,000/mcL.
  - Intracranial hemorrhage can occur during delivery, but may not appear until 2-5 days postpartum.

(Berkley & Kilpatrick, 2009; Hindley, 2016; Provan et al., 2010; Stavroe & McCrae, 2009)

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Prenatal Medical Management

- CBC should be drawn:
  - Monthly in the 1st and 2nd trimester, bimonthly in the 3rd trimester, and weekly as the anticipated delivery date approaches.
  - More frequent monitoring may be required depending on the severity of the thrombocytopenia.
- Treatment is not required until 36-weeks gestation or 10 days prior to the anticipated delivery date if there is no evidence of bleeding and platelet counts remain above 30,000/mcL.
- Treatment is recommended if delivery is imminent, platelet counts are below 30,000/mcL, or bleeding is present.
  - First line therapy = oral corticosteroids (prednisone or prednisolone)
  - Alternative therapy = intravenous immunoglobulin (IVIg)

(Hindley, 2016; Gernsheimer & McCrae, 2007; Provan et al., 2010; Rajasekhar, Gernsheimer, Stasi, & James , 2013)

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Prenatal Medical Management Continued

- Platelet transfusion in conjunction with IVIg infusion is recommended if a rapid increase in platelets is required for life-threatening bleeding or emergent delivery.
  - Platelet transfusion alone is not an effective treatment for ITP due to the syndrome's rapid destruction of platelets.
  - A retrospective review by Spahr & Rodgers (2008) concluded that concurrent platelet transfusion and IVIg treatment was associated with minimal side effects, resolution of bleeding, and rapid increase in platelet counts.
  - Provan et al. (2010) found that platelet transfusion in conjunction with IVIg will increase the post-transfusion platelet count by more than 20,000/mcL in bleeding ITP patients.

(Provan et al., 2010; Rajasekhar et al., 2013; Spahr & Rodgers, 2008; Stavroe & McCrae, 2009)

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Mode of Delivery

- Maternal condition and obstetrical indicators dictate the mode of delivery.
- Previous evidence indicated that elective cesarean section reduced the risk of fetal intracranial hemorrhage. However:
  - Belkin, Levy, & Sheiner (2009) conducted a retrospective study that found no association between intracranial hemorrhage and mode of delivery and concluded that routine use of cesarean section should be avoided.
  - Similarly, a retrospective study by Gasim (2011) reported a low incidence of poor neonatal outcomes that were unrelated to the mode of delivery.
- The primary concern during parturition is maintaining a platelet count greater than 50,000/mcL to minimize the risk of hemorrhage during both vaginal and cesarean delivery.

(Belkin et al., 2009; Gasim, 2011; Provan et al., 2010; Rajasekhar et al., 2013; Stavrae & McCrae, 2009).

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Neuraxial Anesthesia

- ITP increases the risk of spinal-epidural hematoma formation.
- No definitive recommendation exists regarding the minimally safe platelet count required for administration of neuraxial anesthesia in the parturient with thrombocytopenia.
  - The ASH Clinical Practice Guide on Thrombocytopenia in Pregnancy suggests that a minimum platelet count of 80,000/mcL may be appropriate.
  - Studies included within the International Consensus Report on the Investigation and Management of ITP indicate that a lower threshold of 75,000/mcL may be appropriate.
  - No recommendations exist from the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anesthesia, The American Society of Anesthesiologists, or the American College of Obstetrics and Gynecology.

(Bernstein et al., 2016; Huang, McKenna, & Babins, 2014; Myers, 2012; Nagelhout & Plaus, 2014; Provan et al., 2010; Rajasekhar et al., 2013)

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Neuraxial Anesthesia Continued

- Several studies have proposed utilizing thromboelastography (TEG) and rotational thromboelastometry (ROTEM) to guide safe anesthetic practices in the parturient with thrombocytopenia.
  - The use of TEG and ROTEM allows thrombocytopenia to be evaluated against the prothrombotic state of pregnancy, rather than monitoring platelet function alone.
  - The results from a prospective cohort study by Huang et al. (2014) suggest that neuraxial anesthesia can be safely performed in parturients with platelet counts greater than 56,000/mcL and a normal TEG result.
  - Similarly, a case study performed by Mauritz, Strouch, and Olufolabi (2016) reported utilizing ROTEM to safely perform a cesarean section under spinal anesthesia in a high-risk parturient with thrombocytopenia.

(Huang et al., 2014; Mauritz et al., 2016; Provan et al., 2010)

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Spinal-Epidural Hematoma

- A spinal-epidural hematoma is a collection of blood that can compress the spinal cord/nerve roots leading to irreversible neurologic dysfunction.
  - A retrospective cohort study by Lee et al. (2017) found that the risk of epidural hematoma was 11% for a platelet count less than 50,000/mcL, 3% for 50,000 to 69,000/mcL, and 0.2% for 70,000 to 100,000/mcL.
  - Similarly, a study by Goodier, Lu, Hebbar, Segal, & Goetzl (2015) containing parturients with platelet counts less than 100,000/mcL reported the risk of spinal-epidural hematoma to be 0 to 0.6%.
- Risk factors for the development of a symptomatic hematoma include spinal cord abnormalities, difficult needle placement, coagulopathy, increased needle size, and catheter placement.
  - Provan et al. (2010) suggests that spinal anesthesia delivered by an experienced clinician may be a safer neuraxial anesthetic option for thrombocytopenic patients.

(Bernstein et al., 2016; Goodier et al., 2015; Horlocker et al., 2010; Lee et al., 2017; Nagelhout & Plaus, 2014; Provan et al., 2010)

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Management of Maternal Hemorrhage

- Maternal hemorrhage requiring blood transfusion is the leading cause of maternal morbidity in the United States.
- If severe hemorrhage develops with regional anesthesia in place, it is recommended to consider rapid sequence induction of general anesthesia.
  - This allows the clinician to manage volume resuscitation, focus on hemodynamic support, and ensure patient comfort.
- Intraoperative cell salvage should be considered.
  - Especially important in situations involving limited banked blood availability or patient refusal of banked blood administration.
- A rapid increase in platelets may be required for thrombocytopenic parturients with life-threatening bleeding.
  - Platelet transfusion in conjunction with IVIg infusion may reduce bleeding by rapidly restoring platelet counts.

(Apfelbaum et al., 2016; Nagelhout & Plaus, 2014; Provan et al., 2010; Shields, Goffman, & Coughey, 2017)

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Recommendations

- Frequent monitoring of maternal and fetal wellbeing as well as collaboration among the multidisciplinary care team is required to mitigate complications.
- Prenatal management should include serial CBC monitoring and administration of oral corticosteroids or IVIg depending on clinical manifestations and maternal platelet counts.
- The routine use of cesarean section should be avoided. The mode of delivery is dependent on maternal condition and obstetrical indicators.
- The primary goal during delivery is to minimize the risk of maternal hemorrhage by maintaining a platelet count greater than 50,000/mcL during both vaginal and cesarean delivery.

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Recommendations Continued

- life-threatening bleeding or emergent delivery may necessitate platelet transfusion in conjunction with IVIg infusion.
  - Further research is needed regarding the optimal dose and timing for administration of IVIg and platelet therapy.
- Further research is needed regarding the minimally safe platelet count required for administration of neuraxial anesthesia.
- Further research is needed regarding the use of TEG/ROTEM to help guide safe neuraxial anesthetic practices.

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Conclusion

- The patient underwent repeat cesarean section at 36-weeks gestation with a history of chronic ITP.
  - Serial platelet counts were not drawn and the ITP was not medically managed.
- Cesarean section was the patient's only option for delivery due to her history of 3 previous cesarean sections and incomplete uterine rupture.
- The platelet count was stable at 87,000/mcL and no bleeding manifestations were noted.
  - Precautionary measures for hemorrhage were taken prior to the start of the case.
  - TEG and/or ROTEM were not utilized to further assess coagulation.
  - The spinal was placed in one attempt by an experienced anesthetist utilizing a 25-gauge pencil point spinal needle

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Conclusion Continued

- A parturient with ITP presents a challenge to the anesthesia care team that requires thorough anesthetic planning and vigilant monitoring.
- With the development of consistent guidelines and further research, anesthetic management of this population can be improved.

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Thank You
Are There Any Questions?

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University of North Dakota