The febrile parturient: choice of anesthesia

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INTRODUCTION

Fever is a common clinical problem in labor and delivery suites - worldwide. The febrile parturient presents a unique diagnostic dilemma and therapeutic challenge to both an obstetrician and an anesthesiologist involved in her care. Fever can result from a variety of infectious microorganisms, tissue trauma, malignancy, drug administration, endocrine and immunological disorders. However, infection is by far the most common cause of fever in the parturient. [1, 2] The infectious etiology of fever in a parturient may be pregnancy specific, such as chorioamnionitis, or not specific to pregnancy, such as urinary tract infection.

The risk to the mother and the fetus is significantly increased in pregnancy complicated by infection and fever. The diverse clinical manifestations of various infectious disorders combined with the unique anesthetic implications of pregnancy may result in life-threatening complications and significantly impact upon the practice of obstetric anesthesia.

The diagnosis of infection in pregnancy often raises questions about the safety of neuraxial anesthesia in febrile patients. Despite this concern, and lack of universal guidelines, it has now been well established that the presence of infection and fever in labor does not always contraindicate the administration of regional anesthesia. [2] The decision whether to administer regional anesthesia or not in a febrile parturient should be based on an individual risk-to-benefit ratio.

FEVER: DEFINITION AND PATHOPHYSIOLOGY

In humans normal body function depends on a relatively constant body temperature, which is regulated by hypothalamus. The balance between heat production and heat loss to the environment determines human body temperature. [3] The core temperature is usually 0.5 ºC higher than the oral temperature. There is a circadian fluctuation in temperature with the nadir at 6 a.m. and the peak at 8 p.m. In females there is a monthly cycle, in which the temperature increases at the time of ovulation and falls back to baseline at the onset of menstruation. The normal core body temperature in adults ranges from 36 to 38 ºC. [3] The human body has a set point temperature and temperature control mechanisms that constantly adjust body temperature, to maintain this level.

Fever is defined as an increase in core body temperature above 38 ºC, which is secondary to an increase in the hypothalamic set point. [1, 3] The human body temperature rarely exceeds 41ºC. Normal circadian fluctuation in body temperature with increase in the evening and decrease in the morning continues even in febrile patients. [4] Under normal circumstances, core body temperature is tightly regulated, with a variation of approximately 0.5ºC. While it is uncertain as to the benefits of fever, there are suggestions that the increased body temperature aids in the activation of the host immune response with augmentation of bactericidal, phagocytic and chemotactic properties of polymorphonuclear leukocytes. The negative aspects of fever include increased basal metabolic rate and increased cardiac demand.

FEVER: INTERACTION WITH PREGNANCY

Physiologic changes of pregnancy include an increase in the maternal basal metabolic rate.[5] Maternal body temperature in labor is also significantly affected by the degree of physical activity and intensity of uterine contractions. Pain associ-

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ated with uterine contractions causes the parturient to hyperventilate, which along with accompanying perspiration, leads to compensatory heat dissipation. Higher temperatures have been reported in laboring parturients who remained calm and inactive.[6] The maternal-fetal temperature gradient closely correlates with utero-placental blood flow and fetal oxygen delivery. Hyperthermia (defined as an increase in core body temperature above 38ºC) in a laboring patient results in higher maternal oxygen consumption and decrease in fetal oxygen delivery. [5, 6] Fetal temperature is about 0.5 ºC higher than maternal temperature.

Perinatal morbidity is significantly increased in pregnancies complicated by the presence of peripartum maternal infection and fever. [7] The anatomic changes associated with pregnancy may predispose women to certain infections. Urinary tract dilation is one of the most significant alterations induced by pregnancy. These changes are mediated by hormonal (progesterone) and mechanical factors, resulting in urinary stasis and predilection to urinary tract infections. It has been estimated that the incidence of pyelonephritis in pregnancy is approximately 1%.[7]

Maternal immune function is usually decreased even in normal pregnancy. [2, 7] Therefore, some febrile diseases may take a more severe course in pregnancy leading to transplacental transmission of infectious agent and fetal jeopardy. The source of fever should be identified and possible fetal implications considered. Upper respiratory or urinary tract infections, for example are less likely to pose a significant danger to the fetus as compared to HIV infection or chorioamnionitis. The possibility of peripartum transmission of infectious microorganisms will affect the obstetric and subsequent anesthetic management of these patients.

Presence of bacteria in blood samples alone (unassociated with fever/infection), obtained from parturients, seems quite common. It has been determined that even routine procedures in labor, such as insertion of a urinary catheter, may result in transient bacteremia. However, the clinical significance of these findings and anesthetic implications remain unclear. The overall incidence of maternal infection in labor has been estimated as 3.1%. [8] Animal studies have found evidence to suggest that bacteremia may increase the risk of meningitis after subarachnoid block. [9] The extrapolation of these data to humans is questionable and the importance to clinical practice uncertain.

FEVER: VIRAL ETIOLOGY IN PREGNANCY

Virus-associated symptoms in pregnancy are usually mild. The presumptive diagnosis can be made on the basis of epidemiological findings or social contacts. Viruses most commonly encountered in parturients include influenza virus, herpes simplex virus, hepatitis viruses, cytomegalovirus, papillomavirus and human immunodeficiency virus. Additionally, febrile diseases caused by measles, rubella and chickenpox viruses may appear during pregnancy.

Herpes Simplex Virus

Herpes simplex virus is a double-stranded DNA virus. It belongs to a large group of double stranded DNA viruses, which also encompasses varicella-zoster virus, cytomegalovirus and Epstein-Barr virus. Two types of herpes simplex virus have been identified. Herpes simplex virus (HSV) type 1 is generally associated with oral lesions (cold sores) and transmission occurs through oral secretions. Herpes Simplex Virus type 2 is associated with painful vesicular or papular lesions on mucous membranes or skin of the genital tract. Sexual contact remains the predominant mode of HSV type 2 transmission. Both types of HSV share the property of asymptomatic periods of latency interrupted by episodes of reactivation. During periods of latency the virus resides in the sensory neural ganglia. [10] Two cases of postpartum HSV endometritis have been reported in the literature. Both infants died from disseminated HSV infection. [11]

Anesthetic implications

The administration of regional anesthesia often raises concerns about neuraxial spread of the virus and possibility of a disseminated disease. The risk may be higher in primary infections with transient presence of the virus in the systemic circulation. [12] Differentiation between the primary (initial) and secondary (recurring) infection is of critical importance before the administration of anesthesia. Unfortunately, such a distinction often proves very difficult in clinical settings. [12] The transient viremia of primary infection is followed by permanent antibody production 4 to 6 weeks later. The coexistence of typical genital lesions with systemic symptoms (fever, myalgia and headache) usually suggests a primary infection, however, approximately 30% of these patients remain asymptomatic. The lack of symptoms may additionally cloud the differential diagnosis. [13] When primary infection is acquired in the peripartum period the risk of vertical transmission to the neonate is very high because of the presence of viremia. [14] The safety of regional anesthesia in primary infection with HSV has not been established. In contrast, viremia is rarely present in patients with secondary, recurrent HSV type 2 infection and several investigators have documented safety of regional anesthesia in these patients. [15-17] However, the presence of an active lesion at the site of needle insertion would obviously preclude regional anesthesia in both groups of patients.

Administration of labor epidural utilizing opioids (particularly morphine), has been suspected of reactivation of HSV-1 lesions in the thoracic and perioral locations. [18, 19] Similar findings have been reported with subarachnoid opioids. [20] The pathophysiology of this reactivation remains obscure, although pruritus, scratching, and activation of the nucleus of the fifth cranial nerve by opiate binding, have been postulated. [21, 22] This association, however, has not been confirmed by others and remains controversial. [23] It is noteworthy that no such association has been reported between neuraxial opioids and recurrence of HSV type-2 infections.

Hepatitis

Hepatitis viruses type A, B, C, D and E have been identified. Viral hepatitis, which results from infection with these viruses vary in the mode of transmission and clinical expression. The onset of the disease may be gradual or fulminant. The incubation period and seroconversion may vary from 2 to 24 weeks. [24] The clinical symptomatology may include fever, anorexia, fatigue, nausea, vomiting and abdominal discomfort and jaundice. There is little surprise that some of these symptoms might draw insufficient attention since their occurrence in otherwise normal pregnancy is common. [25]

Anesthetic implications

Careful preanesthetic evaluation should determine the degree of hepatic impairment prior to administration of anesthesia of any kind. Although mild hepatitis does not significantly alter anesthetic management and pregnancy outcome, severe infection may have detrimental effect on the mother and her fetus. Laboratory evaluation should include serum electrolytes, creatinine, blood urea nitrogen, bilirubin, transaminases, and alkaline phosphatase, albumin and prothrombin time. Whenever possible maternal serum should be checked for the presence of Hepatitis B surface antigen (HbsAg). If a pregnant patient with acute viral hepatitis must undergo an emergency delivery, prompt correction of electrolyte abnormalities and dehydration is recommended. [2, 25]

When general anesthesia is selected for these parturients, anesthetic agents with known extrahepatic metabolism are recommended. Standard doses of intravenous induction agents are generally used since their action is terminated by redistribution rather than metabolism or excretion. Isoflurane remains the potent inhaled volatile anesthetic agent of choice because it has the least effect on hepatic blood flow. Factors such as hypotension, excessive sympathetic stimulation and high airway pressure should be avoided since they are causes of reduced hepatic blood flow.

Neuraxial blocks may be safely employed in febrile parturients with viral hepatitis provided thrombocytopenia is absent, coagulation studies remain normal and hypotension is avoided. [26] The risk of vertical transmission of hepatitis C to the fetus is significantly increased peripartum. [27] Universal safety precautions are recommended when handling blood and body fluids from these patients.

Human Immunodeficiency Virus

Human acquired immune deficiency syndrome (AIDS) has grown from negligible numbers in 1981 to a cumulative total of nearly 9 million cases reported by the World Health Organization as of 1997. [28] In the year of 2002, it is estimated that over 34 million individuals worldwide are infected with HIV – the vast majority of whom live in the developing world. [28-30] In the United States women have been identified as the fastest growing group of new AIDS patients. [29] Consequently it is not uncommon to find pregnant women who are HIV positive. [28-31] Early identification of HIV infection in pregnancy is of the utmost importance.

The diagnosis of HIV infection in pregnancy often raises questions about the safety of regional analgesia in these patients. [32] This controversy first began when it was suggested that the introduction of a spinal needle in the HIV patient would spread the disease into the central nervous system and therefore increase the patient's risk for development of the neurological sequelae of this disease. [33] It is now well established that HIV infection does not contraindicate the administration of regional anesthesia. [32, 34] HIV is a neurotropic virus and central nervous system infection takes place early in the course of the disease process. [32, 34, 35] Neurotropic predisposition of an HIV virus is responsible for symptoms of neurological dysfunction manifested clinically at the time of initial AIDS diagnosis in up to 40% of infected patients. [35]

The HIV positive patient, irrespective of her clinical condition, meets criteria for AIDS, by definition, when CD4+ T cell count falls below 200 cells/microliter. [36] High maternal viral load increases the likelihood of perinatal transmission of HIV. [37, 38] Clinical evidence suggests that most perinatal HIV transmissions occur during labor and delivery. [39, 40] Kind et al. [41] studied the effect of elective Cesarean section and zidovudine prophylaxis on vertical HIV transmission and concluded that elective Cesarean section and zidovudine prophylaxis appear to have an additive effect in the prevention of vertical HIV transmission. Because of the recent findings, many HIV-positive women are being advised to undergo elective cesarean section. [41]

Anesthetic implications

Anesthetic management of these patients must be tailored to the individual obstetric indications, urgency and route of delivery and presence of coexisting disease. HIV seropositivity alone, should not determine the preferred method of anesthesia. Careful physical examination and documentation of neurological deficits should be undertaken prior to induction of anesthesia. The coexistence of other sexually transmitted diseases such as hepatitis B and syphilis may be encountered. [34]

Respiratory system involvement with oropharyngeal and esophageal pathology may make HIV infected patients more prone to regurgitation, difficult intubation and aspiration. Opportunistic pulmonary infections may necessitate prolonged mechanical ventilation in the postoperative period. Careful examinations of the cardiovascular (subclinical cardiomyopathy), renal (nephropathy) and hematologic (neutropenia, thrombocytopenia) systems, are indicated in preanesthetic assessment of these patients. Patients with AIDS may exhibit electrolyte disturbances, such as hyponatremia, which may be due to adrenal infection by cytomegalovirus or mycobacteria. These, if severe, should be corrected before induction of anesthesia. Although thrombocytopenia may occur in the HIV-positive patient, it is rare for the platelet count to be low enough as to impact on the choice of anesthetic. If, however, the platelet count falls below 50,000/mm the risks of bleeding and epidural hematoma may increase. [41] Treatment of complications of neuraxial anesthesia including management of post dural puncture headache should not differ from the standards of care for healthy patients. Specifically, should post-dural puncture headache occur, an epidural blood patch with autologous blood is safe and effective in the HIV infected patient. [43]

When general anesthesia is selected, dose adjustments for history of drug abuse (acute versus chronic), compromised hepatic and renal function, or generalized muscle wasting are necessary. The HIV related pulmonary pathology may require a higher fraction of inspired oxygen concentration. [2, 32] Increased sensitivity to opioids and benzodiazepines has been reported in HIV infected pregnant patients. Concern, has been raised by some, that potent volatile agents may additionally depress the already compromised immune system in HIV infected patients. [43]

The risk of occupational exposure to infected blood and body fluids should never be underestimated when caring for HIV-infected patients. Necessary safety measures (universal/standard precautions) must be employed when handling blood and blood products of all patients, not just the ones who are known to be HIV positive. [44, 45] There is a "window" period between the primary HIV infection and seroconversion, during which the diagnosis can be delayed, yet viral transmis-

sion can occur. The use of gloves prevents 98% of an anesthesiologist's contact with patient's blood and body fluids. [44, 45] The risk of HIV transmission from a needle stick injury with HIV infected blood is approximately 0.32%. [46]

FEVER: BACTERIAL ETIOLOGY IN PREGNANCY

Bacterial infections of the skin, respiratory system and genitourinary tract in pregnancy can evolve into a systemic illness with bacteraemia, leading to maternal and fetal complications. The most common bacterial infections in pregnancy include urinary tract infections, chorioamnionitis, respiratory tract infections and postpartum endometritis. Systemic bacterial illness irrespective of its origin may lead to serious maternal and fetal consequences, if left untreated. The incidence of maternal infection in labor is estimated at 3.1%. [47] Septicemia has been reported in 0.07% of pregnant patients. The most common etiology is gram-negative organisms (95%), with the remaining being caused by gram positive and other bacteria. [48]

Urinary tract infections

Urinary tract infections are the most common bacterial infections encountered during pregnancy. Urinary tract infections include a spectrum of disorders ranging from asymptomatic bacteriuria to pyelonephritis. Asymptomatic bacteriuria is diagnosed in approximately 10% of pregnant women. [2, 49, 50] The incidence of pyelonephritis in pregnancy, which requires prompt treatment, has been estimated at 1-2%. [50]

Anesthetic implications

Most parturients with pyelonephritis are dehydrated secondary to fever, vomiting and anorexia. [49, 50] These changes may lead to electrolyte imbalances, which should be corrected prior to administration of anesthesia. Hemodynamic alterations may be present in a parturient with pyelonephritis even in the absence of overt sepsis. Antibiotic therapy is indicated before induction of regional anesthesia. There is no evidence that regional anesthesia is detrimental in febrile patients with urinary tract infection.[2]

Chorioamnionitis

Acute intra-amniotic infection, or chorioamnionitis, historically has been associated with maternal morbidity and mortality. [51, 52] The incidence of intra-amniotic infection in term pregnancy at delivery varies from 0.5-10.5%. [51] The hallmark of the diagnosis is an increased maternal temperature of 37.8 C or higher associated with uterine tenderness, foul-smelling amniotic fluid and generalized symptoms of infection. [53, 54] Chorioamnionitis accounts for 20-40% cases of neonatal sepsis and neonatal respiratory tract infections. [55] With prolonged chorioamnonitis, neonatal morbidity is substantially increased. [56] Grether et al. found that intrauterine exposure to maternal infection markedly increased the risk of cerebral palsy in term infants. [57] Prompt efforts to initiate treatment and induce delivery are indicated.

Anesthetic implications

There is no evidence that neuraxial blocks are contraindicated in a febrile parturient with intra-amniotic infection. [2] Since most obstetricians administer parenteral antibiotics once the diagnosis of chorioamnionitis has been established, it is justified to delay administration of labor analgesia until after the parturient has received antibiotics.[58] However, administration of regional anesthesia prior to antibiotic therapy in parturients with intra-amniotic infection and proven bacteremia has not proven deleterious. [59, 60]

Pneumonia

Because of efficient host defense mechanisms bacterial pneumonia is rather uncommon in healthy parturients. In contrast, alcoholism or drug abuse in pregnancy may impair consciousness and predispose to inhalation of bacteria-containing secretions leading to pneumonia. Bacterial pneumonia is characterized by development of transient chills, followed by a rapid increase in body core temperature. Approximately 66% of cases of pneumonia in pregnancy are bacterial in origin. [61] The etiology of pneumonia in pregnancy is no different than in the non-pregnant state. [2, 61] Streptococcus pneumoniae is the most commonly isolated pathogen.

Anesthetic implications

Pregnancy-specific physiologic changes in the respiratory system such as decreased functional residual capacity, increased oxygen consumption, capillary engorgement, hypersecretion of respiratory tract mucosa and decreased cellular immunity, may predispose to the development of pneumonia. A chest radiograph should confirm the diagnosis. The parturient with pneumonia is susceptible to the development of pulmonary edema. [61] Supplemental oxygen administration should maintain SpO_2 above 95% and PaO_2 above 70-80 mmHg.

Continuous labor analgesia may attenuate the increased oxygen consumption in patients with pneumonia. [62] Ideally intravenous antibiotics should be administered as soon as possible before induction of regional anesthesia. When general anesthesia is selected, rapid desaturation should be anticipated resulting from increased oxygen consumption characteristic of both pregnancy and infection.

FEVER: SEPTIC SHOCK

Septic shock may potentially complicate most infectious disorders of pregnancy. Fortunately this complication is infrequent and usually occurs during the postpartum period. Once septic shock has developed, mortality is very high (33-66%). [63, 64] The most common etiologies include chorioamnionitis, pyelonephritis, endometritis and toxic shock syndrome. [64] Septic shock can be subdivided into early (hyperdynamic) and late (hypovolemic) phases.

The early phase of septic shock (up to 24 hours) is characterized by hypotension, hypoperfusion, low systemic vascular resistance and increased cardiac output. Progression to the late phase is associated with significant fluid losses and decreased cardiac output. Peripheral vascular resistance is increased and manifested clinically by cold and cyanotic extremities. Oliguria and myocardial depression are characteristically present. Increased concentrations of fibrin degradation products mirror the presence of disseminated intravascular coagulation (DIC). An adult respiratory distress syndrome (ARDS) may also develop. The diagnosis of septic shock is usually established by development of pronounced hypotension in the presence of peripheral vasodilation. Rapid and aggressive treatment with intravenous fluids, vasopressors and antibiotics is required.

Anesthetic implications

The appropriate therapy for septic shock usually includes intravenous administration of broad-spectrum antibiotics and intensive fluid resuscitation, guided by cardiovascular monitoring. If abdominal delivery is indicated the need for emergent delivery must be often weighed against the need for insertion of invasive monitors and resuscitative efforts aimed at restoring optimal maternal condition for delivery. The late phase of septic shock is associated with low cardiac output, intravascular fluid deficits, hypotension and coagulopathy, a combination that usually precludes the administration of regional anesthesia.

Hemodynamic stability of maternal circulation and maintenance of uterine perfusion should determine the choice of anesthetic agents for induction and maintenance of general anesthesia. Prolonged induction of anesthesia should be avoided to prevent neonatal depression at delivery. The selection of induction agents should be based on their predicted cardiovascular response, and agents that support the cardiovascular system, such as etomidate or ketamine, should be selected.

FEVER: THE SAFETY OF REGIONAL ANESTHESIA

It is a common concern among anesthesiologists that administration of regional anesthesia to a febrile parturient may spread the infectious agent to the central nervous system and lead to neurological sequelae. However, to date no epidemiologic study has documented a causal relationship between dural puncture in the presence of bacteremia and the subsequent development of complications such as meningitis and epidural abscess. [65]

Hlavin et al. [66] reported a 0.2-1.2 per 10,000 incidence of spontaneous epidural abscess in the general hospital population of patients. Kindler et al. [67] reported 2 cases of epidural abscess in a series of 4162 pregnant patients who received labor epidural analgesia. Another case of an epidural abscess was described in a patient who received epidural anesthesia for cesarean section. [68] The development of Streptococcus-induced bacteremia and meningitis after spinal anesthesia was reported by Ngan Kee. [69] Mamourian et al. [70] reported three MRI confirmed cases of spinal-epidural abscess following combined spinal-epidural injections. Recently, three more cases of meningitis following increasingly popular combined spinal-epidural anesthesia (CSEA) have been described. [71, 72] Review of the older literature also documents association of spinal-epidural abscess and regional anesthesia. [73] Interestingly, the majority of spinal-epidural infections appear to be related to the surgical procedure or hematogenous spread of infectious agent rather than to regional anesthetic technique. [73]

To date there are no well-established guidelines for the anesthesiologist in the choice of anesthesia for the febrile parturients. Anesthetic management of a febrile patient should be based on an individual risk-to-benefit ratio, obstetrical indications, urgency and route of delivery. If general anesthesia is selected for the febrile pregnant patient, associated risk factors such as aspiration of gastric contents, neonatal depression and the potential for a difficult airway should be anticipated. [74] The history and physical examination, aided by the laboratory investigations, will usually identify the etiology of fever. Spinal, epidural or CSEA may be safely administered in the presence of maternal infection and fever. Administration of empiric antibiotic therapy is recommended by most authorities and should be initiated as soon as possible, prior to induction of anesthesia. [75] Because oxygen consumption is increased in febrile patients supplemental oxygen should be administered with regional anesthesia to these parturients.

The induction of CSEA has been associated with more rapid cervical dilatation when compared to conventional labor epidural analgesia. [76] Because prolonged labor is a significant risk factor for maternal fever, CSEA may be associated with a lower incidence of fever compared to conventional epidural analgesia and may therefore become the recommended technique for these patients.

FEVER: GENERAL ANESTHESIA FOR THE FEBRILE PARTURIENT

General anesthesia still remains a viable option for selected patients with infection and fever. It offers rapid onset of induction, reliability and predictability necessary in emergency situations. However, despite technical advances in airway management, the consequences of failed intubation and/or aspiration of gastric contents may be catastrophic. Maternal mortality rate is 16 times higher in pregnant patients who undergo abdominal delivery under general anesthesia as compared to those who receive regional anesthesia. [74] Laboring patients with infection and fever seem more likely than non-febrile parturients to receive general anesthesia. Uncertainty of fetal tolerance of labor in the presence of infection, possible legal implications of delayed delivery and concerns of appropriate labor analgesia may create some urgency and lead to abdominal delivery.

Preanesthetic evaluation of the infected parturient should include the cause and duration of fever. Upper respiratory tract infections in febrile parturients may increase oropharyngeal and bronchial secretions and lead to increased airway irritability. Fever increases maternal oxygen consumption and may compromise transplacental oxygen delivery to the fetus. Preoxygenation with 100% O_2 prior to induction of general anesthesia is important in optimizing maternal and fetal hemoglobin oxygen saturation. [77] Aspiration prophylaxis, volume expansion and correction of electrolyte abnormalities are necessary. In critically ill patients the need to proceed with emergency delivery should be weighed against the need for insertion of invasive monitoring devices such as central line or Swan-Ganz catheter and resuscitation efforts aimed at restoring optimal maternal condition for delivery.

Maternal cardiovascular stability and maintenance of uteroplacental blood flow should determine the choice of anesthetic agents for induction and maintenance of general anesthesia in febrile parturients. Prolonged anesthetic induction should be avoided to prevent neonatal depression at delivery. [78] While rapid sequence induction with cricoid pressure and intravenous administration of sodium thiopental [79] or propofol and succinylcholine is the standard technique, induction agents that support the cardiovascular system such as etomidate or ketamine should be considered. Sodium pentothal may depress myocardial contractility in critically ill parturients, thus the use of etomidate is advocated by some in these patients. Use of ketamine has been recommended, although its hemodynamic effects may be unpredictable in critically ill patients (including parturients) with depleted cat-

echolamine stores. [80]

Succinylcholine-induced hyperkalemia may be a problem in febrile patients, especially with prolonged sepsis. [81] Therefore, it is important to correct fluid and electrolyte abnormalities before induction of anesthesia, and avoid succinylcholine in patients with hyperkalemia. Rocuronium is an alternative to succinylcholine when a nondepolarizing agent is preferred for rapid sequence induction of general anesthesia for cesarean section. [82] It offers fast onset and intermediate duration of action and may be used for neuromuscular block in parturients requiring general anaesthesia if succinylcholine is contraindicated, but is associated with greater interpatient dose-response variability than succinylcholine. Drug interactions such as between muscle relaxants and antibiotics should be anticipated and appropriate dose adjustment undertaken to prevent prolonged muscle paralysis.

FEVER: EPIDURAL ANALGESIA AND MATERNAL "FEVER"

Several authors have recently investigated the controversy as to whether there is causual relationship between epidural labor analgesia and maternal intrapartum "fever". [83-86] Although it is clear that maternal temperature increases in some women who receive labor epidural analgesia, the cause of the increase is controversial. [84] The mechanisms of the association between labor analgesia and maternal fever have not been fully elucidated. [83, 84, 86, 87]

It is known that induction of epidural anesthesia for surgical procedures (including, in pregnant patients) causes sympathectomy and vasodilation associated with increased heat loss and hypothermia. Hypothermia results from redistribution of body heat from the core to the periphery, where the heat is lost to the environment. [88] To the contrary, labor epidural analgesia has been reported to cause a gradual increase in maternal core body temperature and result in hyperthermia. [2, 83] The mechanism of maternal hyperthermia following induction of epidural analgesia remains unclear. Possible explanations include cessation of hyperventilation that follows pain relief, increased incidence of shivering and decreased sweating. [88, 89]

Camann et al. [90] studied maternal temperature changes in 53 laboring women who received either epidural analgesia or parenteral opioids for pain in labor. Tympanic and oral temperatures were monitored in each study group. Administration of epidural analgesia did not affect maternal temperature for the first four hours after the induction of analgesia. However, an increase in maternal temperature in the epidural group was noted, beginning approximately five hours after initiation of the block. No maternal temperature changes were reported in parturients receiving parenteral opioids for labor analgesia. There was no difference in temperature changes between patients receiving epidural infusions of local anesthetics alone versus epidural infusions of local anesthetics combined with opioids.

Fusi et al. [89] compared patients receiving epidural infusion of bupivacaine for labor analgesia with those receiving intravenous injections of meperidine. Maternal temperature increases averaging 0.14 ºC/h were reported after induction of epidural analgesia. No increase in maternal temperature was noted following intravenous meperidine. It is noteworthy that both investigators (Camann et al. and Fusi et al.) administered higher concentrations of bupivacaine than those currently employed in obstetric anesthesia practice. [89, 90] Interestingly, the temperature increases attributed to epidural analgesia in both studies were subclinical and never exceeded 38 ºC. Fusi et al. suggested that increase in maternal temperature resulted from thermoregulatory and vascular modifications caused by labor analgesia. [89]

Other authors have reported similar increases in maternal core temperature in association with induction of epidural analgesia. [91, 92] The observed temperature increase in laboring patients averaged 0.10 ºC per hour of epidural analgesia, usually following a lag of 4 to 5 hours. In contrast to subclinical maternal temperature elevation reported by Fusi et al. [89] and Camman et al. [90], Herbst et al. [93] analyzed overt maternal fever (38 ºC or greater) in 250 women who were matched to 250 other women without fever. More women in the fever group received epidural analgesia (83% versus 53% in the control group), circumstantially implicating epidural analgesia as a cause not only of subclinical temperature elevation but also overt, clinical fever. [93] The authors concluded that, despite other risk factors such as prolonged labor and preterm rupture of membranes, there was clearly an independent association between epidural analgesia and increase in maternal temperature. [93]

Glosten et al. [94] evaluated the effect of epidural analgesia on sweating in non-pregnant volunteers. A higher core temperature was needed to induce sweating in patients who received epidural analgesia. Additionally, decreased sweating was reported below the level of sensory block, most likely resulting from the blockade of sympathetic nerve fibers. Panzer et al. [95] showed that many parturients do not perspire, even in the presence of fever. Shivering was frequently not related to hypothermia, and sweating was not triggered by hypothermia in the studied subjects. Simultaneous sweating and shivering were reported. Kim et al. [96] reported that shivering associated with epidural analgesia was primarily caused by normal, physiologic thermoregulatory mechanisms. In contrast, other investigators concluded that shivering was primarily caused by a nonthermogenic mechanism. [97, 98]

A possible detrimental effect of maternal fever on the fetus has been a subject of significant controversy. Macaulay et al. [99] monitored intrauterine and fetal scalp temperature in a group of 57 parturients. Increased intrauterine temperature was noted in patients who received labor epidural analgesia. Three of 57 fetuses had scalp temperature exceeding 39 ºC. [99] Camann et al. [90] concluded that epidural analgesia is unlikely to increase maternal temperature sufficiently to have an adverse effect on the fetus.

Lieberman et al. [91] reported an association between epidural analgesia, maternal fever and neonatal sepsis evaluation. The study, which originally intended to evaluate active management of labor, reported the incidence of fever ranging from 7% to 36% in parturients receiving epidural analgesia. Fever was reported in 7% of parturients receiving epidural analgesia with labor duration less than 6 hours, and increased to 36% of parturients who were in labor for more than 18 hours. The incidence of fever in laboring patients who did not receive epidural analgesia remained approximately 1%, regardless of the duration of labor.

Neonatal sepsis evaluation was performed in 34% of neonates born to febrile mothers in the epidural group, compared

with 9.8% in the non-epidural group. Interestingly, the incidence of confirmed neonatal sepsis was not different between the two study groups, and was reported in less than 1% of neonates. Unfortunately, the study was not randomized and the two groups of patients differed significantly. Additionally the specific criteria for neonatal sepsis evaluations were not precisely established, and over 63% of neonatal sepsis evaluations were performed for reasons other than maternal fever. Nevertheless, logistic regression analysis, confirms the association between epidural analgesia and fever even after consideration of other variables. [100]

Philip et al. [100] prospectively randomized 613 laboring women to either an epidural or intravenous meperidine analgesia study group. The epidural labor analgesia was independently associated with maternal temperature increase when compared with intravenous meperidine administration. The frequency of neonatal sepsis evaluations was strongly associated with the presence of maternal fever.

In summary, there seems to be enough evidence to support the association between epidural labor analgesia and maternal temperature elevation, especially after four or more hours since the induction of anesthesia. [89-91, 93, 99, 100] However, most of the studies have not been randomized, and therefore patient selection bias cannot be eliminated. In contrast, there is no evidence that frequency of confirmed neonatal sepsis is increased in neonates born to mothers who received epidural analgesia for labor. The association between labor epidural analgesia and neonatal sepsis evaluation (work-up) is less clear. Many factors other than maternal fever are involved in the decision-making process leading to initiation of a neonatal sepsis evaluation.

Finally, most randomized studies compared temperature changes in patients who received epidural analgesia with control groups who received parenteral meperidine. [100] Meperidine is known to selectively decrease the shivering threshold and is widely used as a treatment of postoperative shivering. Therefore, its selection as control group remains questionable and further investigations are needed.

CONCLUSION

The administration of epidural anesthesia in healthy parturients in labor has been associated with a modest increase in maternal core temperature. However, there is lack of evidence to suggest that this transient increase in maternal temperature adversely affects the fetus.

There are many anesthetic challenges in the management of the febrile parturient, both in elective manner and emergency situations. The anesthesiologist may safely administer regional anesthesia to the majority of patients with fever and established infection, provided that sepsis is not present in the area of injection. However, it seems prudent to determine the etiology of fever and infection and initiate appropriate therapy with antibiotics prior to induction of labor analgesia.[101]

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