● Evidence-Based Case Report

Anesthetic and Analgesic Management of Mitral Stenosis During Pregnancy

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Rheumatic mitral stenosis (MS) is the most common clinically significant valvular disease in pregnant women. Although its prevalence is less than 1% during pregnancy, its presence increases the risk of adverse maternal, fetal, and neonatal outcomes.[1-3] The ideal labor analgesia and cesarean anesthetic for this population, based on patient expectation, severity of disease, safety, and morbidity outcomes remain controversial. In this evidence-based case report, the anesthetic treatment of 2 patients with different severity of MS is presented. After the case presentations, the evidence or lack of evidence, the reasoning supporting various strategies of management, and a review of available guidelines and clinical recommendations are discussed.

Evidence-Based Medicine Search Procedures

The goal of evidence-based medicine is to define a clinical question and the information required to resolve the problem, conduct an efficient search of the literature, select the best relevant studies, apply rules of evidence to determine their relative validity, extract the clinical message, and apply that message to the clinical problem, with incorporation of the patient's values and expectations.[4-6] Ideal best evidence is in the form of prospective, randomized clinical trials. However, when such trials are unavailable, observational studies, followed by systematic clinical observations, clinical reports, and pathophysiologic reasoning should be used. Our clinical question in this evidence-based medicine review is, "What is the ideal cesarean anesthetic, labor analgesic, and perioperative management for parturients with mitral stenosis?" The literature search for our case presentation was conducted on the medical database MEDLINE. Individual key words that were searched include "mitral stenosis," "valvular heart disease," "pregnancy," "neuraxial anesthesia," "neuraxial analgesia," "labor analgesia," "cesarean delivery," "anesthetic technique," "epidural anesthesia," "spinal anesthesia," "epidural analgesia," "combined spinal-epidural analgesia," "perioperative outcomes," "perioperative management," and their combinations. We limited our search to articles available in English. These articles were graded from level I (most evidence) to level V (least evidence) (Table 1).[4-8] The available data on ideal anesthesia and analgesia for parturients with MS are limited, and the specific search yielded only 7 relevant level IV or higher articles. The perioperative anesthetic management and predictors of complications in parturients with MS yielded 7 studies with level III or higher evidence. Additional search was also performed for guidelines and recommendation in atrial fibrillation and anticoagulation therapy during pregnancy.

Case 1

A 28-year-old nulliparous woman, with an intrauterine pregnancy of 35-weeks gestation and a history of rheumatic MS (mitral valve area, 2 cm^2; left ventricular ejection fraction [LVEF], 40%, and dyspnea on moderate activity), presented for a prelabor anesthetic consultation. The patient's concerns were labor pain, complications and safety of delivery, analgesia and anesthesia, and bonding with the baby at delivery. The following evening, she presented with labor onset without cardiopulmonary decompensation or dysrhythmia. The anesthetic plan was combined spinal epidural analgesia (CSEA) with bupivacaine 1.25 mg, fentanyl 15 μg, and preservative-free morphine 0.1 mg intrathecally, and epidural patient-controlled analgesia with bupivacaine 0.125% and fentanyl 2 μg/mL. A

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Table 1. Grading of Level of Evidence

Level	Evidence
I	Evidence obtained from a systematic review or meta-analysis of all relevant randomized controlled trials.
II	Evidence obtained from a large randomized controlled trial.
III	Evidence obtained from a small randomized controlled trial or from cohort studies.
IV	Evidence obtained from nonrandomized controlled trial, case reports, descriptive studies, and observational studies.
V	Evidence obtained from expert opinions without explicit critical appraisal or are based on physiological reasoning.

NOTE. Adapted from references 4-8.

low-forceps, assisted vaginal delivery was planned, with a supplement pudendal block if needed, in an attempt to limit maternal expulsive efforts and stress during second-stage delivery. Despite adequate analgesia, the forceps delivery was unsuccessful, which led to an surgical delivery (cesarean delivery). Two-percent lidocaine 20 mL plus fentanyl 100 μg was incrementally administered epidurally to produce a surgical bilateral block of T4 level. A healthy neonate was delivered uneventfully. The patient had 3 episodes of mild to moderate hypotension: shortly after administration of the CSEA, during administration of epidural lidocaine for the surgical delivery, and shortly after delivery. Phenylephrine was used in 20 to 50 μg increments, along with lactated Ringer's solution, by titrating to effect against patient's hemodynamics and clinical signs and symptoms. The patient was observed overnight in the telemetry unit and discharged home on the third postpartum day without complications.

Case 2

A 32-year-old, term nulliparous woman was admitted for progressively increasing shortness of breath, tachycardia, bibasilar rales, room-air oxygen saturation of 93%, and a history of severe MS (mitral valve area, 1.2 cm^2; pulmonary artery [PA] systolic pressure, 60 mm Hg; and LVEF, 25%) associated with pulmonary hypertension and dyspnea at rest. A PA catheter and a radial artery line were placed. Initial measurements indicated a PA pressure of 58/28 mm Hg, a pulmonary capillary wedge pressure (PCWP) of 25 mm Hg, and a cardiac index of 3.0 L/min/m_2. The patient's symptoms improved after the administration of a diuretic and a beta-blocker. The hemodynamics improved: PA pressure, 48/21 mm Hg; PCWP, 20 mm Hg; cardiac index, 3.4 L/min/m_2; and oxygen saturation, 97%, with oxygen by nasal cannula. The patient was anxious, and her main concerns were maternal and fetal safety and complications from delivery, analgesia, and the anesthetic. With earlier presence of late fetal heart-rate decelerations, an epidural catheter was inserted without complication in anticipation of a potential operative delivery. Before administration of an epidural test dose, the fetus experienced fetal bradycardia not resolved with the usual resuscitation, which led to an emergency surgical delivery. Because the epidural catheter was untested, a general anesthetic was planned. After administration of aspiration prophylaxis, preoxygenation, and surgical skin preparation, a modified rapid-sequence induction was used with intravenous etomidate and succinylcholine. Esmolol and sufentanil were titrated in divided doses, along with an infusion of intravenous nitroglycerin, during the induction phase to minimize increases in PA pressure and pulmonary vascular resistance (PVR). Anesthesia was maintained with 100% oxygen, isoflurane, and titrated doses of midazolam, sufentanil, and muscle relaxant. A healthy neonate, with 1-minute and 5-minute APGAR scores of 3 and 8, respectively, was delivered and did not require resuscitation. Shortly after delivery of the placenta, the patient expereinced new and acute-onset atrial fibrillation (AF) with ventricular rate, 150 bpm; blood pressure, 80/45 mm Hg; and PCWP, 37 mm Hg. While preparing for electrical cardioversion, intravenous esmolol, 0.5 mg/kg, and phenylephrine, 100 μg, were administered immediately and repeated once shortly afterward. In addition, intravenous digoxin in divided doses and furosamide were administered. Before electrical cardioversion could be attempted, the patient converted to a sinus rhythm rate of 90/min, and the blood pressure rose to 102/60 mm Hg and the PCWP fell to 28 mm Hg. The patient remained stable, was extubated uneventfully, received postoperative fentanyl epidural patient-controlled analgesia, and was monitored overnight in the intensive care unit. The patient was discharged on postpartum day 3 on digoxin, a beta-blocker, and a diuretic; subsequent postpartum evaluations revealed gradual cardiac improvement.

Discussion

Preoperative Management

MS can prevent normal emptying of the left atrium and filling of the left ventricle, which results in a reduced stroke volume, a fixed cardiac output, elevated left atrium and PA pressures, and eventually pulmonary edema. In severe cases, the right ventricle can develop compensatory hypertrophy

that leads to an increased PVR, pulmonary hypertension, and right heart failure. The specific cardiovascular alterations that occur during labor that can worsen symptoms in patients with MS include an increase in heart rate, an increase in blood volume, acute changes in CO, and venous return that can lead to an increase in left atrial irritability. All of these can lead to an elevated transmitral gradient and left atrium pressure and result in acute pulmonary edema. The time of maximum risk for these patients is during late pregnancy, labor, and immediately postpartum. Recent studies have identified several independent predictors (mitral valve area $<$ 1.5 cm^2, New York Heart Association functional class $>$ class II, LVEF $<$ 40%, and prior cardiac events) of adverse maternal cardiac complications in parturients with cardiac diseases.[1-3] The overall mortality is reported to be less than 1% in patients with mild disease and 5% to 15% in patients with severe disease or with atrial fibrillation.[9,10] The risk of a primary adverse cardiac event (pulmonary edema or symptomatic arrhythmia, stroke, arrest, or death) in pregnancies with 0, 1, or more than 1 predictors is 5%, 27%, and 75%, respectively.[1] Kasab et al.[11] have shown that pregnant patients with symptomatic mitral stenosis can be treated safely with beta blockade, which significantly reduces the incidence of pulmonary edema. Patients with severe symptoms who undergo valvuloplasty or valve surgery before pregnancy appear to have fewer complications during pregnancy than do those treated medically.[12] Therefore, preconception or early counseling regarding management and risk of adverse cardiac outcomes is important, especially in patients with severe mitral stenosis.

Ideal Anesthetic and Analgesic Management

In case 1, the patient was hemodynamically stable and clinically asymptomatic, which placed her at low risk of an adverse cardiac event. Therefore, invasive monitoring was not used for this patient.[1,9,13,14] The goal of our anesthetic management was to provide adequate maternal analgesia, minimize maternal endogenous catecholamine release, prevent tachycardia, and maintain optimal preload and normal sinus rhythm while avoiding a rapid decrease in afterload or acute increase in preload.[13-15] An assisted forceps delivery was planned in an attempt to limit the maternal Valsalva maneuvers and stress associated with expulsive efforts. Because patients with MS may have a limited ability to increase CO, prevention of aortocaval compression or rapid decreases in SVR maintains venous return, PCWP, and left ventricular end-diastolic volume at near baseline levels, which, in turn, limit the need for compensatory increases in cardiac output.[16,17] Labor epidural analgesia and CSEA have been administered successfully in carefully monitored parturients with MS when epidural local anesthetic is titrated incrementally and when combined with intrathecal or epidural opioids.[13-15,17-21] Kee et al.[19] reported, in 3 parturients with moderately severe MS, the use of intrathecal fentanyl (25 μg) followed by diluted epidural bupivacaine and fentanyl infusion, without significant hemodynamic changes or requirement of local anesthetic boluses.[19] We chose a CSEA[19] in an attempt to minimize initial sympathetic block and hypotension during the first stage of labor. Morphine was included in an attempt to prolong the duration of the intrathecal analgesia and minimize the subsequent amount of epidural local anesthetic required.[20] Morphine can be excluded because of its potential side effects.

The intravenous preload was restricted to 250 mL because excessive hydration can lead to pulmonary edema in patients with MS. Hypotension was treated quickly and aggressively with titrated phenylephrine and crystalloid. Epinephrine was avoided in all epidural solutions to reduce the risk of tachycardia and potentially acute peripheral vasoconstriction. During the second stage of labor or an operative delivery, epidural anesthesia and analgesia can facilitate the gradual increase of venous capacitance to accommodate the acute increases in venous return and CO that occur in the immediate postpartum period and lead to pulmonary edema. Ziskind et al.[17] showed that parturients with severe MS benefited from epidural anesthesia with appropriate degrees of Trendelenburg position to obtain optimal PCWP pressure and cardiac indexes and reduce maternal heart rate during operative delivery. Clark reported PCWP increases of 10 to 18 mm Hg in the immediate postpartum period after vaginal delivery in parturients with severe MS.[14] In addition, he suggested that intravenous albumin may increase plasma colloid oncotic pressure and limit the development of pulmonary edema.[14] However, the use of colloid versus crystalloid remains controversial.

In case 2, the clinical presentation placed the patient at significant risk of adverse cardiac events, such as pulmonary edema, symptomatic arrhythmia requiring treatment, stroke, or cardiac arrest/death[2] during labor and, especially, immediately postpartum. In additional to the usual management of patients with MS as described in case 1, invasive monitoring (PA catheter and arterial line) was used in this patient to closely monitor and optimize hemodynamic variables.[14] Epidural anesthesia was planned for the surgical delivery in an attempt to

reduce the impact of an acute increase in preload typically observed after delivery. The sustained fetal bradycardia precluded the use of the epidural catheter. Time was insufficient to gradually and incrementally establish surgical anesthesia. A relatively rapid administration of epidural local anesthetic could have resulted in sympathectomy and hypotension and led to a poorly tolerated reflex tachycardia and a worsening of the patient's pulmonary hypertension and edema. The potential hazards of general anesthesia include acute increases in PVR and heart rate during laryngoscopy and intubation, decreased venous return during positive pressure ventilation, and negative inotropic effects of certain inhalation anesthetic agents. Our primary goal was to minimize sympathetic stimulation and tachycardia. Because of the severity of our patient's MS, we chose a balanced anesthetic that included a relatively high dose of narcotic for cesarean delivery and a beta-blocker.[9,13,22,23] We attempted to minimize hemodynamic changes and sympathetic stimulation during induction with esmolol. Although maternally administered esmolol has been associated with fetal bradycardia and hypoxemia,[24,25] the benefits of reducing the sympathetic responses and controlling heart rate during laryngoscopy and intubation outweighed the fetal risk. Nevertheless, the neonatology team was notified and was present at delivery and was prepared to treat possible neonatal side effects.

Atrial Fibrillation in MS Parturients

Siu et al.[2] reported a 75% risk of primary cardiac complications in patients with 2 or more risk factors, as was the case in our case 2 patient. Szekely and Saith[10] found that parturients with moderate MS have an increased incidence of atrial fibrillation (AF) associated with significantly increased maternal mortality. Therefore, new onset AF must be treated aggressively in parturients with MS. Despite the limited fluid administration, the use of nitroglycerin and a beta-blocker to minimize increased PVR, our case 2 patient developed AF shortly after delivery. She responded pharmacologically while being prepared for electrical cardioversion. Direct current cardioversion should be considered and can be performed safely during pregnancy,[26] especially in hemodynamically compromised patients. Although the American Heart Association/American College of Cardiology/European Society of Cardiology guidelines and most experts suggest electrical cardioversion for patients in this situation, evidence indicates that pharmacologic agents can control the ventricular rate and achieve chemical cardioversion.[27,28] Beta-blockers, calcium channel blockers, and digoxin can be used to control heart rate, whereas procainamide and quinidine are recommended if suppressive antiarrhythmic therapy is required during pregnancy because they have the longest history of safety in parturients.[29-31] Newer agents such as amiodarone, sotalol, propafenone, and flecainide have been advocated for nonpregnant patients; however, the efficacy and safety of their general use as first-line pharmacologic therapy for acute-onset AF in parturients are not well established.[30,31] Furthermore, amiodarone is an Food and Drug Administration category D drug that has been associated with neonatal hypothyroidism, congenital anomaly, and teratogenicity.[30,31] Theoretically, metoclopramide should be avoided because it has been associated with tachyarrhythmias.[32]

Anticoagulation Therapy in Parturients With MS

In the Framingham Heart Study, patients with rheumatic heart disease and AF had a 17-fold risk of stroke compared with age-matched control subjects, and the risk was 5 times greater than in those with nonrheumatic AF.[33,34] No controlled studies are available to guide anticoagulation therapy in hemodynamically compromised patients receiving electrical cardioversion for acute onset AF. In a nonrandomized trial of 437 patients with acute onset of AF receiving cardioversion, the incidence of emboli was 0.8% in those with anticoagulation therapy, compared with 5.3% in those without anticoagulation therapy.[35] Furthermore, atrial thrombus was found in 15% to 29% of nonanticoagulated patients with AF of duration longer than 48 hours to 72 hours, respectively.[36,37] Whether pregnancy increases the risk of thromboembolism in patients with AF is not clear. The significant risk of systemic embolism in patients with MS and persistent AF warrants the use of anticoagulation therapy, but no definitive results of clinical trials are available to guide anticoagulant therapy during pregnancy. Warfarin seems to provide greatest maternal protection during pregnancy but has been associated with a 2-fold fetal loss rate when compared with unfractionated heparin. Based on limited available data, several authors recommend the use of warfarin to achieve a target international normalized ratio of 2.0 to 3.0 throughout pregnancy except during the periods between 6 and 12 weeks and after 36 weeks, during which closely monitored use of unfractionated heparin is suggested.[16,38-40] Low-molecular-weight heparin has been used in parturients and is probably safe, but data are insufficient to support the efficacy and safety for use throughout pregnancy.[16,38-40]

Summary

The anesthetic management for labor and delivery for 2 parturients with different severities of MS and under different but commonly occurring obstetric situations was presented. A carefully and gradually titrated lumbar epidural analgesia or CSEA, with consideration to optimize preload, afterload, heart rate, and rhythm, can be used for analgesia and anesthesia in nearly all patients with MS. However, when contraindications to regional anesthesia are present, general anesthetic can be safely administered for cesarean delivery, but care should be used to avoid the significant increases in heart rate, SVR, and PVR commonly associated with induction and emergence. With either regional or general anesthesia techniques, invasive monitoring should be reserved for patients with severe disease.

Women with MS should be evaluated by a cardiologist before becoming pregnant whenever possible. In parturients who develop severe symptoms during pregnancy, mitral valvuloplasty under radiography or tranesophageal echocardiography during the second trimester improves delivery and fetal outcomes.[12,41] Parturients with MS should be evaluated by a cardiologist once every trimester and more often if complications ensue, although serial echocardiography during pregnancy generally is not warranted.[16] For optimal maternal and fetal outcomes, these patients must be managed through multidisciplinary evaluation, including early consultation by an anesthesiologist so that an anesthetic plan can be discussed and formulated well in advance. This evidence-based case report reveals the lack of strong evidence available in the literature for ideal analgesic or anesthetic management of these parturients, but it also shows how clinically individualized and personalized care can achieve optimal individual outcomes. As Brown[42] stated, "the important part of patient care is caring for the patient." Further studies are urgently needed in the areas of efficacy and safety in anticoagulant and antiarrhythmic therapy during pregnancy.

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