

Anesthesiology
66:551-553, 1987

Anesthetic Management of the Parturient Receiving Amiodarone

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General anesthesia for patients receiving the antiarrhythmic drug amiodarone has been associated with significant morbidity and mortality, including sinus arrest, heart block, atropine-resistant bradycardia, myocardial depression, and peripheral vasodilation associated with intractable hypotension.¹⁻⁴ Management of such patients with epidural or spinal anesthesia has not been described. We report here the use of an epidural anesthetic to manage a parturient with congenital pulmonic valvular stenosis who, prior to her pregnancy, had symptomatic episodes of ventricular tachycardia that required amiodarone for adequate control.

REPORT OF A CASE

A 33-yr-old, 70 kg, G1P0 patient had a heart murmur since birth. At the age of 20 yr, she began to notice dyspnea on exertion, and she exhibited episodes of atrial flutter. Her dyspnea slowly increased until, when she was 23 yr old, cardiac catheterization revealed pulmonic stenosis with a right ventricular pressure of 180/10 and pulmonary artery pressure of 20/0, and she underwent a pulmonic valvulotomy. Following the valvulotomy, the patient had recurrent episodes of atrial flutter and ventricular tachycardia associated with dizziness and syncope. These arrhythmias were poorly controlled with various combinations of digoxin, quinidine, and disopyramide. Cardiac catheterization at age 32 yr, 14 months prior to admission, revealed a right atrial pressure of 4 mmHg, mean right ventricular pressure of 30 mmHg, mean pulmonary artery pressure of 26 mmHg, pulmonary capillary wedge pressure of 6 mmHg, cardiac output of 3.1 l/min, mild residual pulmonic stenosis and insufficiency, and mild tricuspid insufficiency. Nine months prior to admission, while undergoing an exercise tolerance test, she developed ventricular tachycardia and syncope after 5 min of exercise at a heart rate 25% above resting level. At this point, amio-

darone therapy was instituted, achieving reasonable control of her arrhythmias at doses of 200-600 mg *p.o.*, *q.d.* One month later, she became pregnant.

At the 28th week of pregnancy, the patient was admitted to the hospital for treatment of gastroenteritis and dehydration. Her lungs were clear to auscultation. Her heart rate was regular, and a grade II/VI systolic murmur was detected at the lower left sternal border and over the pulmonic area. Electrocardiogram showed a normal sinus rhythm with first degree atrioventricular block, right axis deviation, and evidence of right ventricular hypertrophy. An echocardiogram was consistent with marked right ventricular dilation, hypertrophy, and a markedly dilated right atrium with tricuspid insufficiency, all of which may have been exacerbated by the hemodynamic effects of her pregnancy. Left heart structures exhibited normal size and function. Pulmonary function tests were normal. Hemoglobin was 13 gm/dl and hematocrit was 45%. Thyroid function tests were normal. Liver function tests revealed an elevated alkaline phosphatase of 216 μ /l.

After intravenous hydration and resolution of her gastroenteritis, the patient was discharged to her home. She returned to the hospital during her 35th week of gestation for observation and fetal surveillance, and remained for the duration of her pregnancy. During this time, an attempt was made to gradually decrease her dose of amiodarone, but she developed a symptomatic episode of ventricular tachycardia during the 40th week of her pregnancy while taking 200 mg *q.d.* The dose of amiodarone was increased to 600 mg *q.d.*, and a 24-h Holter monitor revealed approximately one premature ventricular contraction every 2 min and couplets, but no evidence of ventricular tachycardia.

At the 41st week of gestation, the patient was transferred to the intensive care unit (ICU) to begin induction of labor with oxytocin. Antibiotic prophylaxis was provided with gentamicin, 80 mg, and penicillin, 2 million units, intravenously. Prior to induction of labor, an epidural catheter was inserted at the L4-L5 interspace, a radial arterial catheter was inserted, and an 8.5 French catheter was inserted into the right internal jugular vein. Because the patient had a history of intractable arrhythmias when any catheter contacted her endocardium, extreme care was taken not to insert the guide wire into the right ventricle. No attempt was made to pass a pulmonary artery catheter for the same reason. A temporary pacing catheter and pulse generator were available in the patient's room, along with angiotensin II (Hypertensin CIBA), supplied by the manufacturer for possible treatment of refractory hypotension in this particular patient.

Incremental doses of phenylephrine were injected to test the maternal and the fetal response to alpha-agonist therapy. These injections were made following insertion of the arterial and central venous catheters, prior to any epidural analgesic administration and with constant fetal heart rate monitoring. The patient exhibited no change in blood pressure with intravenous doses of 5, 10, 15, 20, 30, or 50 μ g of phenylephrine separated by periods of approximately 2 min. A response was obtained to 70 μ g of phenylephrine; before injection, blood pressure was 157/82 mmHg, heart rate 78 beats/min, and central venous pressure (CVP) 3 mmHg, compared to values of 169/93 mmHg, 68 beats/min, and 7 mmHg, 90 s following injection. After injection of 100 μ g of phenylephrine, arterial pressure reached a maximal value of 188/103 mmHg, heart rate of 65 beats/min, and CVP of 7 mmHg, re-

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Received from the Departments of Anesthesia and Medicine, The Pennsylvania State University College of Medicine, Milton S. Hershey Medical Center, Hershey, Pennsylvania 17033. Accepted for publication October 31, 1986.

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Key words: Anesthesia; obstetric. Heart, arrhythmia: amiodarone; treatment. Sympathetic nervous system: amiodarone; sympatholytic agents.

TABLE 1. Hemodynamic Response to Labor, Epidural Anesthesia, and Operative Delivery

	Baseline*	Epidural Fentanyl†	Epidural Chloroprocaine‡	2 H Postop	1 Day Postop
Systolic blood pressure (mmHg)	145	147	120	140	126
Diastolic blood pressure (mmHg)	84	85	70	75	59
Mean blood pressure (mmHg)	109	105	87	95	78
Heart rate (beats/min)	70	85	75	75	53
Cardiac output (l/min ⁻¹)	3.7	5.7	3.5	3.0	3.2
Cardiac index (l · min ⁻¹ · m ⁻²)	2.0	3.2	1.9	1.7	1.7
Systemic vascular resistance (dyn-sec-cm ⁻⁵)	2200	1400	1600	2600	1800
Central venous pressure (mmHg)	5	7	2	0	6
Fetal heart rate (beats/min)	135	149	125		

* Before onset of labor.

† ½ h after epidural fentanyl administration during first stage of labor.

‡ Following epidural chloroprocaine administration for cesarean section but before delivery (sensory anesthetic level T4).

spectively. Fetal heart rate remained between 120 and 130 beats/min while doses of phenylephrine were administered, with good beat-to-beat variability. A cardiac output of 3.7 l/min was measured with the use of indocyanine green dye 1 h after the test doses of phenylephrine were injected; at this time, blood pressure was 145/84 mmHg, heart rate 70 beats/min, CVP 5 mmHg, and the calculated systemic vascular resistance (SVR) was 2240 dyn-sec-cm⁻⁵.

Following the above measurements, an oxytocin infusion was started for induction of labor. When contractions became uncomfortable, fentanyl, 100 µg, was injected into the epidural catheter with good relief of the labor pains. One-half hour after epidural fentanyl administration, an indocyanine green dye cardiac output of 5.7 l/min was measured between contractions, with a blood pressure of 147/85 mmHg, and calculated SVR of 1400 dyn-sec-cm⁻⁵ (table 1). Twenty-four hours after an intermittent oxytocin infusion was started, and 1.5 h after the injection of fentanyl into the epidural catheter, fetal monitoring revealed the sudden onset of recurrent variable decelerations. Cesarean section was planned. In anticipation of urgent cesarean section, 18 cc of 2% chloroprocaine was slowly administered via the epidural catheter over 30 min, resulting in a T10 sensory level, a blood pressure of 150/90 mmHg, and a fetal heart rate of 135 beats/min. In the operating room, oxygen was administered via a 100% non-rebreathing mask and a slow epidural injection of 35 cc of 3% chloroprocaine was performed, resulting in a T4 sensory level. With the sensory epidural level of T4, blood pressure ranged from 100–130/45–70 mmHg, heart rate from 65–70 beats/min, and CVP from 1–2 mmHg. Cardiac output was 3.5 l/min with a calculated SVR of 1600 dyn-sec-cm⁻⁵. The patient remained comfortable during the cesarean section, and a 2850 gm baby girl was delivered with Apgar scores of 8 at 1 min and 9 at 5 min. Following delivery, phenylephrine infusion at a rate of 40 µg/min was used for 45 min to maintain a systolic blood pressure of 110 mmHg, and an additional 10 cc of 3% chloroprocaine was administered through the epidural catheter to maintain a T6 sensory level. During the operative procedure, 1850 ml of lactated Ringers solution were administered.

Postoperative pain was relieved by continuous epidural administration of fentanyl. Two hours postoperatively, after the recovery of sensation in her legs, the patient's blood pressure was 140/75 mmHg, heart rate was 75 beats/min, CVP was 0 mmHg, cardiac output was 3.0 l/min, and systemic vascular resistance 2600 dyn-sec-cm⁻⁵. The morning of the first postoperative day, receiving an epidural fentanyl infusion of 60 µg/hr, the patient's blood pressure was 126/59, heart rate was 53, CVP was 6, cardiac output was 3.2 l/min, and SVR was 1800 dyn-sec-cm⁻⁵. Amiodarone at a dose of 200 mg daily was continued postoperatively. The patient was transferred from the ICU 3 days after delivery, and went home with her daughter 5 days later.

DISCUSSION

The patient's history of amiodarone therapy represented a primary anesthetic concern in the management of this case. Amiodarone is a class III antiarrhythmic agent which increases the duration of the action potential and has been shown to be effective for a variety of ventricular and supraventricular tachyarrhythmias.⁵ Its primary use is to control ventricular tachycardia and ventricular fibrillation that is resistant to treatment with other commonly used antiarrhythmic agents. Amiodarone may produce a number of side effects, including bradycardia, thyroid function abnormalities, pulmonary infiltrates, and corneal microdeposits. It has an extremely long half-life for elimination (>30 days).⁶ Therefore, discontinuation of amiodarone in the preoperative period would be impractical. Most of the reported interactions between amiodarone and anesthetics have been observed during anesthesia for cardiac surgical procedures. In patients receiving amiodarone and undergoing general anesthesia for non-cardiac surgery, Liberman and Teasdale noted nodal rhythm, bradycardia, and/or hypotension persisting as long as 48 h postoperatively.³ Navalgund *et al.* reported sinus arrest in one additional non-cardiac surgical patient.⁴ In part because of these reports, we chose epidural narcotics to provide pain control during labor and epidural local anesthetics to provide surgical anesthesia.

Administration of amiodarone has been shown in humans to cause both coronary artery and peripheral vasodilation.⁷ The mechanism of the drug's action on the peripheral vasculature involves, in part, inhibition of α -adrenergic-mediated vasoconstriction, probably by interfering with vascular smooth muscle excitation-contraction coupling.⁸ *In vitro*⁸ and in anesthetized dogs,^{9,10} amiodarone has produced a partial, non-competitive inhibition of the vascular response to the alpha and beta agonists isoproterenol, epinephrine, and norepinephrine. Thus, we tested the response of our patient to small doses of

phenylephrine prior to the use of epidural anesthesia. Our patient did, in fact, show a somewhat blunted response to phenylephrine, requiring a dose of 1 $\mu\text{g}/\text{kg}$ to produce any change in arterial pressure, despite the relatively low dose of amiodarone she was receiving. For this reason, angiotensin II (Hypertensin CIBA), which increases vascular tone by a non-adrenergic mechanism, was available for intravenous infusion in our patient.¹¹

During cesarean section, a total dose of 45 cc (1350 mg) of chloroprocaine, injected over 1 h, was required to achieve and maintain a T4 to T6 sensory level. This unusually large chloroprocaine dose was needed, in part, because several small doses, rather than one larger dose, of epidural anesthetic were used initially to minimize any precipitous change in the patient's hemodynamic status. The large total dose of chloroprocaine could increase the likelihood of an amiodarone-local anesthetic interaction. In most circumstances, both fetal and maternal blood levels of chloroprocaine are low after epidural administration, because of rapid chloroprocaine metabolism by maternal plasma cholinesterase.¹² Were significant plasma levels of chloroprocaine to develop, however, the cardiovascular effects of the local anesthetic and amiodarone could be expected to be additive or even synergistic. Both drugs decrease myocardial contractility, increase the effective refractory period of the ventricular muscle, slow impulse conduction through the heart, and decrease peripheral arteriolar tone leading, in the extreme case, to cardiovascular collapse.^{13,14} Administration of epidural chloroprocaine in our patient resulted in no signs of local anesthetic central nervous system toxicity. Further, although our patient's cardiac index did decrease to 1.9 $\text{l} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ after chloroprocaine administration, blood pressure, central venous pressure, and systemic vascular resistance remained within normal levels.

With the use of epidural anesthesia, extreme caution was taken to maintain the patient's intravascular blood volume. CVP was monitored continuously. Blood pressure and CVP remained stable until delivery of the infant. Following delivery, blood pressure was maintained with a phenylephrine infusion, rather than large volumes of intravenous fluid, which may have precipitated right heart failure in this patient. If hypotension had occurred before delivery, phenylephrine would probably have been employed as well, in spite of its potential to constrict the uterine artery, since ephedrine might have precipitated arrhythmias in this patient.

In summary, we have described for the first time the use of epidural anesthesia to manage a parturient who had undergone pulmonic valvulotomy for congenital pulmonic stenosis and required amiodarone for the control of severe arrhythmias. Whether regional or general anesthesia is employed, however, invasive hemodynamic monitoring with the capability to institute temporary ventricular pacing in the event of bradycardia or complete heart block may help to increase the safety of anesthesia in this group of patients.

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