Alfentanil for urgent Caesarean section in a patient with severe mitral stenosis and pulmonary hypertension

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We present the case of a parturient with severe mitral stenosis and pulmonary hypertension who received general anaesthesia using alfentanil for urgent Caesarean section. Alfentanil promoted haemodynamic stability and allowed immediate postoperative extubation. Epidural morphine provided postoperative analgesia. This combination permitted early ambulation and prevention of thromboembolism. A disadvantage of this technique, neontal respiratory depression, was promptly reversed with a single dose of naloxone. The anaesthetic management of mitral stenosis in pregnancy is discussed and the neonatal pharmacokinetics of maternally administered alfentanil are presented.

On présente le cas d'une parturiente atteinte d'une sténose mitrale sévère et hypertension pulmonaire avant subi l'anesthésie générale avec de l'alfentanil pour une césarienne d'urgence. L'alfentanil a favorisé la stabilité hémodynamique et a permis une extubation rapide. La morphine en administration épidurale a fourni l'analgésie postopératoire. Cette combinaison a permis une mobilisation précoce et la prévention de l'embolie. Le désavantage de cette technique, la dépression respiratoire néonatale, a été rapidement antagonisé par une dose unique de naloxone. La conduite anesthésique de la grossesse chez les femmes atteintes d'une sténose mitrale est discutée et la pharmacocinétique néonatale et maternelle de l'alfentanil est présentée.

Key words
ANAESTHESIA: obstetrical, Caesarean section;
ANAESTHETICS: intravenous, alfentanil;
HEART: mitral stenosis.

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Mitral stenosis is the most common of the lethal cardiac lesions occurring in pregnancy, and is present in 0.3–1.2 per cent of parturients.[1,2] The maternal mortality is 5–17 per cent with severe disease,[1,2] and ranges from 30–50 per cent when accompanied by pulmonary hypertension.[3] Although carefully titrated lumbar epidural anaesthesia is often recommended for patients with uncomplicated mitral stenosis,[3] there is no consensus on the best anaesthetic technique for patients with severe disease. We present a patient with severe mitral stenosis and secondary pulmonary hypertension who required urgent Caesarean section for fetal distress.

Case report

A 28-yr-old, 165 cm, 77 kg, gravida 3, para 2 woman was admitted at 39 wk gestation for amniocentesis to assess fetal lung maturity before elective Caesarean section. Her medical history was significant for gestational diabetes and mitral stenosis. Her surgical history included an uncomplicated mitral commissurotomy 16 mo before this admission, and Caesarean section (for transverse lie) six years earlier under spinal anaesthesia. The postoperative recovery from the Caesarean section was complicated by multiple pulmonary emboli and heart failure.

Maternal echocardiography at the 24th wk of the present gestation revealed marked biatrial enlargement, right ventricular dilation, and an estimated pulmonary arterial systolic pressure of 51 mmHg. Trace mitral and tricuspid regurgitation, and mild aortic insufficiency were present. The mitral valve area was 1.1–1.5 cm^2. The left ventricular ejection fraction was estimated to be 60 per cent. The patient had no symptoms of heart failure, dysrhythmias, or decreased exercise tolerance during this pregnancy. Her only medication was heparin 5000 u subcutaneously every 12 hr, which was discontinued prior to amniocentesis.

Physical examination on admission revealed clear lung fields bilaterally, a nonradiating systolic murmur at the left lower sternal border and apex, and trace pedal oedema without jugular venous distension or hepatomegaly. The

TABLE Maternal haemodynamic measurements

Interval	*HR* *bpm*	*BP* *(mmHg)*	*CVP* *(mmHg)*	*PAP* *(mmHg)*	*PCWP* *(mmHg)*	*CO* $L \cdot min^{-1}$	*SVR* $dyne \cdot sec \cdot cm^{-5}$	*PVR* $dyne \cdot sec \cdot cm^{-5}$	*SVR* *PVR*
Pre-op baseline	74	120/74	8	75/35	15	5.4	1203	493	2.4
Pre-induction	94	175/95	8	120/55	20	5.4	1682	838	2.0
Post-induction	74	106/64	8	70/30	NA	3.5	1598	NA	NA
Post-delivery	75	120/65	13	80/35	30	7.5	749	213	3.5
Post-op ICU (T_0)	87	180/90	10	120/55	34	6.0	1465	568	2.6
1 hr Post-op ICU	72	130/70	7	80/40	19	6.1	1087	450	2.4
24 hr Post-op ICU	71	125/69	8	81/32	19	5.4	1179	434	2.7

ECG revealed sinus rhythm, left atrial enlargement, and an RSR′ pattern in V_1 consistent with right ventricular hypertrophy. Chest *x*-ray showed cardiomegaly, left atrial enlargement and engorged pulmonary vasculature with cephalization. Haemoglobin, haematocrit, coagulation variables, and serum electrolytes were all within normal limits. Peripheral oxygen saturation was 98–99 per cent while breathing room air.

Amniocentesis resulted in blood tinged amniotic fluid. The L/S ratio was 1.8, and the PG level was 0.0, indicative of fetal lung immaturity. Shortly thereafter, persistent abdominal pain and uterine contractions developed, and $MgSO_4$ therapy was begun for tocolysis. Over the next six hours the contractions continued, fetal heart rate beat-to-beat variability decreased, and late decelerations developed. An urgent Caesarean section was scheduled, and the patient was given gentamycin 80 mg IV, ampicillin 1000 mg IV, ranitidine 50 mg IV, metoclopramide 10 mg IV, and sodium citrate 30 cc PO prophylactically. Urinary, arterial, and pulmonary arterial catheters were inserted and the patient was taken to surgery.

After preoxygenation and surgical skin preparation, cricoid pressure was applied and a rapid sequence induction performed using intravenous lidocaine 100 mg (1.3 $mg \cdot kg^{-1}$) alfentanil 10 mg (125 $\mu g \cdot kg^{-1}$), thiopentone 250 mg (3.25 $mg \cdot kg^{-1}$) and succinylcholine 100 mg (1.3 $mg \cdot kg^{-1}$). The trachea was intubated within 90 sec. Anaesthesia was maintained throughout the 105 min using 100 per cent oxygen, enflurane 0–0.5 per cent, incremental doses of alfentanil (total 16.5 mg) and an intravenous infusion of succinylcholine for muscle relaxation.

A 3940 g male was delivered two minutes after induction of anaesthesia. Apgar scores were one at one minute, three at five minutes, and six at ten minutes. Umbilical cord blood obtained at delivery for blood gas analysis revealed venous pH 7.16, PCO_2 65mmHg, PO_2 10 mmHg; and arterial pH 7.11, PCO_2 63 mmHg, and PO_2 8 mmHg. The trachea was intubated and the lungs were ventilated with 100 per cent O_2, and he was given naloxone 0.04 mg IM immediately after delivery. Fifteen minutes later the trachea was extubated and he was discharged from the Neonatal ICU after 12 hr of uneventful observation.

Prior to emergence from anaesthesia, the patient was placed in the right lateral decubitus position and epidural morphine, 5 mg in 10 ml, was administered at the L_{3-4} interspace. She was then allowed to awaken, was responsive and comfortable, and the trachea was extubated in the OR. On arrival in the ICU, arterial blood gas analysis showed pH 7.40, PCO_2 32 mmHg, PO_2 247 mmHg, and SaO_2 99 per cent (FiO_2 0.4). Eight hours later, arterial blood gas analysis revealed pH 7.40, PCO_2 40 mmHg, PO_2 87 mmHg, and SaO_2 97 per cent (FiO_2 0.21). A second dose of epidural morphine, 5 mg in 10 ml, was given 12 hr later, before the onset of pain or the administration of other analgesics. The patient reported no pruritus or nausea, and her respiratory rate never decreased below 10 $\cdot min^{-1}$. The maternal haemodynamic measurements before, during, and up to 24 hr following Caesarean section are shown in the Table.

Subcutaneous heparin, 5000 u every 12 hr, was begun 18 hr postoperatively. The patient required no parenteral pain medications for 30 hr, and was out of bed within 18 hr. She was discharged from the hospital with her infant on the fourth postoperative day without further problems.

Discussion

Patients with mitral stenosis often tolerate the haemodynamic changes of pregnancy poorly. Because of the increases in blood volume and cardiac output associated with pregnancy, symptoms from even mild or moderate mitral stenosis may become severe as the pregnancy progresses. These haemodynamic changes account for a 25 per cent incidence of pulmonary congestion,[1] and a 5–17 per cent mortality rate in the puerperium.[1–3] The primary anaesthetic considerations in uncomplicated mitral stenosis include prevention of rapid ventricular rates, maintenance of sinus rhythm, avoidance of large, rapid decreases in SVR, and prevention of increases in central blood volume with concomitant increases in PAP.[1] To this end, patients usually receive a carefully

titrated segmental epidural block for labour and vaginal delivery.[1-3] For Caesarean section, either epidural or general anaesthesia may be used as long as these haemodynamic limitations are considered.[1,2]

In patients with pulmonary hypertension, whether primary or secondary to mitral disease, the peripartum mortality rate is 30–50 per cent.[4,5] When patients develop pulmonary hypertension, they also develop right heart strain and become exquisitely sensitive to reductions in preload and to increases in pulmonary vascular resistance. For patients with pulmonary hypertension requiring Caesarean section under general anaesthesia, slow induction of deep anaesthesia using high-dose narcotics or halothane and controlled ventilation seems to be the preferred technique,[1,3] despite the risk of maternal aspiration.

As this patient had both severe mitral stenosis and pulmonary hypertension, our goal was to provide a stress-free induction of and emergence from anaesthesia, avoiding the increases in heart rate, SVR, and PVR, commonly associated with tracheal intubation and extubation. The need for early ambulation to prevent thromboembolic complications made a technique avoiding postoperative mechanical ventilation while providing profound analgesia of paramount importance. An additional consideration was the need to minimize drug-induced neonatal depression.

A carefully titrated epidural anaesthetic would have met these goals. However, the deteriorating fetal condition and subsequent urgency of the Caesarean section precluded this possibility. A variety of techniques including nitroglycerine, nitroprusside, trimethaphan, and beta-adrenergic blockade has been proposed to blunt the haemodynamic responses to intubation.[7-10] Lidocaine, 1.5 $mg \cdot kg^{-1}$, given as a bolus prior to induction and intubation has also been advocated,[12] but its efficacy in this situation is unpredictable.[13] The vasoactive drugs mentioned above may also be useful, but do not provide analgesia, and all have considerable drawbacks such as reflex tachycardia, fetal cyanide toxicity or ileus, tachyphylaxis, or myocardial depression. High-dose fentanyl or sufentanil techniques may provide more haemodynamic stability, but generally require postoperative mechanical ventilation and have prolonged and unpredictable half-lives in newborns which may result in prolonged neonatal depression.[4,15] Alfentanil offers the haemodynamic advantages of other narcotics, but its short half-life minimizes the need for postoperative ventilatory support and would theoretically avoid prolonged neonatal depression. However, even in high doses, narcotics may be incomplete as the sole induction agent in young, unpremedicated adults.[16] Therefore, we chose the combination of alfentanil, lidocaine, and a reduced dose of thiopentone to produce a stress-free induction of anaesthesia in this very anxious patient, while avoiding postoperative narcosis and mechanical ventilation.

As shown in the Table, on arrival in the OR the patient's systemic and pulmonary arterial pressures, SVR, PVR, and heart rate were markedly elevated, reflecting her anxiety and pain. Following induction of anaesthesia, these values decreased slightly below baseline, and were accompanied by a modest reduction in cardiac output. Following delivery, PA pressures, CVP, and CO increased without associated increases in heart rate, SVR, or PVR. Therefore, we believed these changes indicated an appropriate response to postdelivery autotransfusion and did not reflect significant ventricular failure. By the end of surgery both SVR and PVR had returned to their baseline values, with little change in the SVR:PVR ratio.

During surgery a low concentration of enflurane was administered to decrease the possibility of maternal awareness, and the cardiovascular effects of such a small amount (0.3 MAC) were negligible. Small, intermittent boluses of alfentanil were administered to provide a stable intraoperative course. The short duration of action of alfentanil allowed awake extubation at the end of the procedure, and may have accounted for the easily reversed neonatal depression.

In addition to the usual risks of postoperative atelectasis and pneumonia, this patient was at extremely high risk for postoperative pulmonary embolism. Therefore, epidural morphine was used to provide prolonged analgesia and allow early ambulation and pulmonary toilet without adverse cardiovascular effects.[17,18] The gradual but marked decrease in PA pressures over the first postoperative hour may be attributed to the onset of analgesia from the first dose of epidural morphine, and the patient remained pain-free and was out of bed within 18 hr postoperatively.

The biggest disadvantage of this technique was neonatal narcosis. When delivered, the infant was severely depressed and the umbilical cord blood gas analysis revealed evidence of uteroplacental insufficiency. In this case, the degree of depression due to alfentanil is unclear, but it has been shown that while newborns are not adversely affected by low (10 $\mu g \cdot kg^{-1}$) maternal doses of alfentanil,[19] at higher doses (35–100 $\mu g \cdot kg^{-1}$), there can be marked neonatal depression.[20-22] Despite a low fetal/maternal ratio of 0.29 for total alfentanil,[23] there is much less protein binding in the neonate 71–73 per cent) than in the mother (85–88 per cent), and the concentration of free drug is the same in both maternal and neonatal plasma.[20,23] Equilibrium between maternal and fetal blood is reached in less than ten minutes,[23] and therefore it appears that placental transfer of alfentanil is both rapid

and extensive. The elimination of alfentantl in the newborn seems to be slower than in adults,[20,23] and in one animal model, neonatal plasma levels of alfentanil were actually higher two hours after delivery than they were at birth.[23] All these factors, and the fact that the infant in our case responded rapidly to naloxone, suggest that alfentanil contributed to the neonate's depression at birth.

The use of alfentanil in general anaesthesia for urgent Caesarean section in a patient with severe mitral stenosis and pulmonary hypertension is presented. This is the first reported case of the use of alfentanil in this situation. It provided cardiovascular stability so that no vasoactive medications were needed. Alfentanil allowed immediate postoperative tracheal extubation, epidural morphine provided excellent postoperative analgesia, and the combination permitted early ambulation and prevention of thromboembolism. A disadvantage of this technique, neonatal respiratory depression, was easily reversed with a single dose of naloxone. Thus, an integrated anaesthetic plan using a short-acting systemic narcotic (alfentanil) intraoperatively, and a long-acting spinal narcotic (epidural morphine) postoperatively facilitated an excellent outcome and early discharge for this severely ill patient and her neonate in a potentially life-threatening situation.

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