Anaesthesia for Caesarean section in a parturient with quintuplet gestation, pulmonary oedema and thrombocytopaenia

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The case of a 32-year-old parturient with a quintuplet pregnancy is described. The pregnancy had been complicated by premature labour which was treated with ritodrine tocolysis. Betamethasone was administered to hasten fetal lung maturation. The ritodrine therapy was complicated with fluid overload and pulmonary oedema requiring intravenous diuretic treatment. The patient presented urgently for Caesarean section, with fluid overload and worsening thrombocytopaenia. Life-threatening pulmonary oedema was manifest in the immediate preinduction period, following insertion of a pulmonary artery catheter and surgery was delayed to improve the mother's condition with intravenous diuretic therapy. Induction was carried out with the patient in the sitting position, with cricoid pressure maintained to protect the airway as the patient was lowered to a wedged, supine position. Intravenous nitroglycerin was used to control blood pressure. Low pressure mask-bag ventilation was utilized to maintain oxygen saturation and the patient was intubated and ventilated with positive end-expiratory pressure. Positive pressure ventilation was continued for 24 hours postoperatively. The perioperative course is reviewed and followed by a discussion of the anaesthetic considerations for multiple gestation pregnancies.

Key words:

ANAESTHESIA: obstetric; COMPLICATIONS: preterm labour, multiple gestation, pulmonary oedema; SYMPATHETIC NERVOUS SYSTEM, SYMPATHOMIMETIC AGENTS: ritodrine, beta-mimetics.

Multiple gestation pregnancies are fraught with risk for both mother and fetuses. Maternal morbidity and mortality are increased compared with singleton pregnancies. The incidence of fetal and neonatal demise is increased as well, and premature labour and delivery appears to be the single most important factor responsible. Premature labour is a common complication of pregnancy in the parturient with a multiple gestation. Therapy for preterm labour includes both agents to inhibit uterine contractions as well as agents to increase fetal lung surfactant production, facilitating fetal lung maturation. These agents are not without side-effects and life-threatening complications have been reported. We present the case of a parturient with a quintuplet gestation complicated by preterm labour. Tocolysis, although successful in prolonging labour by 14 days was complicated by maternal fluid overload and pulmonary oedema.

Case report

The patient, a 32 year-old female, Gravida 2, with a quintuplet pregnancy at 27 weeks gestational age, was admitted to hospital because of an effacing cervix. She went into premature labor on the day of admission and tocolysis was initiated with intravenous ritodrine, while betamethasone was administered to hasten fetal lung maturation. For the next 14 days, up to and including the day of delivery, tocolysis was maintained with ritodrine, administered either intravenously or orally. Early in the course of therapy the patient complained of dyspnoea and was noted to be gaining weight. Daily furosemide therapy was initiated to control fluid retention. Nine days before delivery, orthopnoea was evident and physical examination revealed pitting oedema to waist level. Four days prior to delivery there was clinical evidence of pulmonary oedema and the furosemide dose was increased. The patient was now assuming a sitting posture around the clock, because any degree of recumbency caused dyspnoea. Despite worsening symptoms of pulmonary oedema, the

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patient resisted intervention in the form of operative delivery, hoping to increase gestational age for fetal optimization.

Six days prior to delivery thrombocytopenia of $109 \times 10^9 \cdot L^{-1}$ was noted on haematologic examination. When the platelet count dropped from $95 \times 10^9 \cdot L^{-1}$ to $72 \times 10^9 \cdot L^{-1}$ within a 24 hr period, the decision to proceed to Caesarean delivery was made.

A planning committee had been formed in anticipation of the quintuplet delivery. Representatives from the Departments of Obstetrics, Pediatrics, Neonatology, Anaesthesia, Nursing Services and Respiratory Technology had met to ensure availability of both manpower and equipment for the birth. The existing twin-isolette neonatal resuscitation room was augmented by equipping an adjacent delivery room to receive three of the five quintuplets. Teams of neonatologists, neonatal intensive care nurses and respiratory technologists were available to care for the newborns.

The patient was brought into the delivery/operating room. Electrocardiographic leads and a blood pressure cuff as well as a pulse oximeter were placed. Initial blood pressure and heart rate were 160/110 mmHg and 120 beats $\cdot min^{-1}$ respectively. A large bore intravenous line and a left radial artery line were established with local anaesthesia. The mother was positioned in 30° reverse Trendelenburg position, with a wedge under her right hip, and the right internal jugular vein was cannulated and a pulmonary artery catheter inserted. During insertion of the central line, despite continuous administration of oxygen by mask, the patient complained of increasing dyspnoea. Following insertion of the pulmonary artery catheter, the patient was returned to the sitting position. She was noted to be clinically cyanosed with a pulse oximeter saturation reading of 82 per cent (SpO_2). She was both hypertensive and tachycardiac at 160/100 mmHg and 130 beats per minute, respectively. Crackles were auscultated to both shoulders, over anterior and posterior lung fields and she was coughing frothy, pinkish sputum.

A diagnosis of pulmonary oedema was made, the mask was exchanged for a non-rebreathing mask, furosemide 80 mg was given intravenously and arterial blood gases were drawn. The pH was 7.39, $PaCO_2$ 33 mmHg and PaO_2 52 mmHg. A brisk diuresis began almost immediately following the administration of furosemide and a second dose of furosemide, 40 mg intravenously, was given 30 minutes after the first to sustain the diuresis. With diuresis of 1100 ml there was improvement, both symptomatically and in the SpO_2 , which returned to 92 per cent. It was decided then to proceed with the induction.

The surgical team was asked to scrub and gown and the

patient's abdomen was prepped while she remained sitting. Blood pressure prior to induction was 180/110 mmHg and this was reduced to 140/90 mmHg with 125 μg of intravenous nitroglycerin in three divided doses. The patient was anaesthetized in the sitting position, with cricoid pressure applied. Anaesthesia was induced with lidocaine 100 mg, thiopentone 300 mg and succinylcholine 120 mg IV. The patient lowered to the supine position and low-pressure, mask-bag ventilation was carried out while cricoid pressure was maintained. SpO_2 increased from 92 to 98 per cent and then intubation was carried out as the patient was being draped. Ventilation was controlled and 100 per cent oxygen was administered with positive end-expiratory pressure (PEEP) maintained. Isoflurane was administered at 0.4 per cent end-tidal concentration, monitored by mass spectrometer. A lower segment Caesarean section was carried out and the five fetuses were delivered without incident and in good condition. Approximately one litre of ascitic fluid was expelled from the peritoneal cavity upon opening of the peritoneum and blood loss was estimated at 1500 ml. Pulmonary artery wedge pressure measured after delivery of the infants was 24 mmHg.

Following delivery, the anaesthetic was converted to a balanced technique with fentanyl, vecuronium, nitrous oxide and oxygen. Haemodynamics were notably stable after induction and throughout the operative period. Repeat arterial blood gases intraoperatively, on controlled ventilation with PEEP, showed a pH of 7.34, $PaCO_2$ of 42 mmHg and PaO_2 of 316 mmHg.

The patient was taken to the Recovery Room intubated and ventilated and, after it was ascertained that her condition was stable, she was transferred to the Intensive Care Unit. She was extubated on the second postoperative day, made an uncomplicated recovery and was discharged home on the ninth postoperative day.

Discussion

The perioperative course of our patient provides an excellent case study of the problems of the parturient with a multiple gestation pregnancy. Featured were: premature labour; beta-mimetic tocolysis complicated by fluid overload and pulmonary oedema; and pre-eclampsia. We shall discuss these features, as they apply to our patient and to the parturient with a multiple gestation pregnancy, in general.

The physiologic changes of pregnancy are well described.^{1,2} Increases in blood volume, red cell mass and cardiac output have been studied in singleton, twin and triplet pregnancies (Table I).^{3,4} For multiple gestations of higher order, little information is available, and extrapolation of existing twin-triplet data represents the best estimate for changes in cardiovascular parameters. With

TABLE 1 Increases in cardiovascular parameters with pregnancy (per cent)

	<i>Singleton</i>	<i>Twin</i>	<i>Triplets</i>
Blood volume	49	67	97
Red cell mass	31	40	50
Cardiac output	44	48	48

regard to the respiratory system, it would be expected that the cephalad displacement of the diaphragm seen in the singleton pregnancy would be exaggerated in the multiple pregnancy resulting in further decreases in functional residual capacity and inspiratory capacity. Incompetence of the lower oesophageal sphincter would be expected to occur earlier in the gestation in the multiple pregnancy than in a singleton cohort, with obvious implications for anaesthesia practice.

Anaemia, toxemia and haemorrhage, both antepartum and postpartum, are more common in parturients with a multiple gestation pregnancy. In a review of a series of triplet pregnancies, antepartum haemorrhage was seen in five per cent of pregnancies, pre-eclampsia in 19 per cent, anaemia in 14 per cent and pre-term labour in 78 per cent.⁵ The maternal mortality rate is increased two to three times compared with singleton pregnancies.⁶

Fetal loss in the multiple gestation pregnancy is very common. The combined stillbirth and neonatal mortality rate in a series of triplet pregnancies was reported as 232/1000. Preterm labour and birth order were the two most important factors, relating to neonatal mortality, that were isolated.⁵ In a series of 1655 sets of twins mortality was somewhat higher compared to singletons. Placentae from the twin pregnancies were noted to be smaller than the singleton placentae from 21 to 22 weeks to term and there was some suggestion that the placenta was a factor limiting growth and gestational age in twin pregnancies.⁷

Premature labour is more common than term labour in multiple gestation pregnancies. Up to 60 per cent of twins and 80 per cent of triplets are premature. Because prematurity is the most important risk factor leading to stillbirth and neonatal mortality, there is great effort directed towards treating preterm labour and prolonging gestation. The incidence of both respiratory distress syndrome and neonatal mortality are reduced when premature labour is treated at less than 33 weeks gestation.⁹ Beta-mimetic agents for labour tocolysis, combined with corticosteroids to hasten fetal lung maturation, represent the most utilized mode of treatment for preterm labour.

Ritodrine, a beta-adrenergic agonist, with predominant beta₂ specificity, has been demonstrated, in multiple studies, to be more effective than placebo in the treatment of preterm labour.⁸ Ritodrine acts by increasing intracellular concentrations of cAMP, via activation of adeny-

cyclase. The increased levels of cAMP inhibit myosin light chain kinase, interfere with actin-myosin coupling and result in uterine relaxation. Ritodrine tocolysis is not without side-effects. Hyperglycaemia, hypokalaemia, fluid overload with dilutional anaemia and pulmonary oedema, hypotension, cardiac arrhythmias and myocardial ischaemia have all been reported in patients treated with ritodrine.⁹

Ritodrine leads to sodium and water retention, expanding extracellular space and, in some patients, results in pulmonary oedema. Patients treated with ritodrine demonstrate positive fluid balance when compared to controls.¹⁰ When ritodrine is delivered in a saline vehicle, this positive fluid balance is augmented. In a study comparing saline and glucose solutions for ritodrine administration, there was a significantly increased incidence of maternal pulmonary oedema in the group receiving saline.¹¹ There have been case reports as well as a retrospective study suggesting that the combination of corticosteroids and beta-mimetic agents increases the risk of maternal pulmonary oedema.^{12,13} However, there does not appear to be enhanced fluid retention caused by combination therapy compared to ritodrine treatment alone, when studied prospectively.¹¹ Twin gestation appears to predispose the mother to the development of pulmonary oedema while being treated with the beta-mimetic agent, terbutaline.¹³ Finally, there have been case reports of maternal pulmonary oedema, during ritodrine therapy for preterm labour, in patients in whom there was no evidence of fluid overload. This suggests the potential for either non-cardiogenic pulmonary oedema with capillary leak or alternatively, myocardial failure.^{14,15} Strict intake and output measurements, daily weights and frequent examination for evidence of fluid overload or pulmonary oedema should be routine care for all patients on ritodrine therapy.

Ritodrine inhibits hypoxic pulmonary vasoconstriction and loss of this physiologic compensation in a parturient with pulmonary oedema may lead to increased ventilation-perfusion inequalities, with hypoxaemia out of proportion to the existing pulmonary oedema.¹⁶ Close monitoring of arterial oxygen content is mandatory in patients undergoing ritodrine tocolysis, especially if it is complicated by maternal pulmonary oedema.

Arrhythmias, with and without evidence of myocardial ischaemia, have been reported in patients on ritodrine.⁹ Included have been premature ventricular contraction, premature nodal contraction and atrial fibrillation. These arrhythmias have responded to withdrawal of the drug and oxygen therapy. Previously undiagnosed cardiac lesions have been unmasked by beta-mimetic therapy, including atrial septal defects and idiopathic hypertrophic subaortic stenosis.¹⁷ Myocardial ischaemia, infarction and mater-

TABLE II Anaesthetic considerations in multiple pregnancy

Maternal

Physiologic changes of pregnancy augmented
 Increased incidence of toxemia
 Increased anaemia
 Increased incidence premature labour
 Prolonged labours
 More frequent ante/postpartum haemorrhage
 Maternal mortality higher
 Retained placentae more common

Fetal

Prematurity 6–10 times more common
 Abnormal presentation more frequent
 Perinatal mortality rate increased
 Asphyxia more common
 Small for gestational age

nal death have occurred during beta-mimetic therapy.¹⁸ Continuation of therapy in the setting of serious cardiac complications is contraindicated.

The hyperglycaemia associated with ritodrine therapy results from activation of hepatic phosphorylase and mobilization of hepatic glycogen. Ketoacidosis and subsequent fetal death have been reported during tocolytic therapy in an insulin-dependent diabetic parturient.^{19,20} Serum insulin levels are increased via beta-mimetic stimulation of the pancreatic islet cells and hypokalaemia may result from the insulin-mediated movement of potassium and glucose from the extracellular to the intracellular space. Glucose administration should be appropriately restricted in non-diabetic patients and insulin-dependent diabetics must be managed very cautiously. Evidence of ketoacidosis or maternal hyperglycaemia should prompt rapid intervention and correction.

When approaching a parturient such as described in our case presentation, consideration must be given to both mother and her tiny, dependent charges (Table II). Preoperative assessment must be thorough. *In situ* intravenous catheters should be sufficient to allow for rapid volume infusion, through fluid warmers, in anticipation of greater than usual blood loss. Fetal depression must be minimized by avoidance of long induction–delivery and uterine–incision–delivery times. Sufficient paediatric staff should be present to resuscitate the newborns, thus allowing the anaesthetist to pay undivided attention to the mother.

In addition to the routine electrocardiographic, temperature and stethoscope monitoring, an arterial line is highly desirable. Central pressure monitoring is near mandatory in such seriously ill patients. Central venous pressure may not be a true reflection of left-sided filling pressures in seriously ill parturients and for this reason, a pulmonary artery catheter may be the preferred central monitoring line.²¹

Air embolism has recently been demonstrated to be a common occurrence during Caesarean section.²² The potential for significant air embolism may be greater in the setting of the large multiply pregnant uterus and the generous hysterotomy used to facilitate extraction of the fetuses. The pulmonary artery catheter has proven to be a valuable tool in monitoring for occurrence of air embolism, enhancing the desirability of the pulmonary artery catheter as the central line for monitoring.²³

In patients recently treated with beta-mimetics for tocolysis, presenting for anaesthesia, consideration must be given to a heightened potential for arrhythmias as well as the abating vasodilatory effects of the beta-mimetic on the peripheral vasculature. Patients treated with beta-mimetics have an increased risk of arrhythmias at time of induction and anaesthetic agents with sympathomimetic effects should be avoided or used with great caution.⁸ As serum levels of the beta-mimetic decrease there is increased vascular tone, resulting in a fluid shift back to the central compartment, which when combined with recumbent positioning for surgery, may result in central compartment overload and pulmonary oedema at the time of induction or shortly thereafter. The ability to provide positive-pressure ventilation with positive-end-expiratory pressure should be present at time of induction.

A slow intravenous induction may be preferable to a rapid sequence induction in these patients. The airway should be protected with cricoid pressure and low-pressure mask-bag ventilation is preferred to apnoeic oxygenation in patients with borderline oxygen status. Positive-pressure, controlled ventilation with PEEP support, if necessary, is indicated. If pulmonary oedema presents preoperatively, a short delay and intravenous diuretic treatment may rapidly improve the mother's condition. A variable period of postoperative ventilation with PEEP support is warranted, as diuretic therapy progresses.

We have presented the case of a 32-year-old parturient with a quintuplet pregnancy. Premature labour and ritodrine therapy, complicated by significant volume overload and pulmonary oedema, as well as thrombocytopenia and pre-eclampsia combined to yield a seriously ill parturient presenting for urgent Caesarean section. The degree of fluid overload and pulmonary oedema was underestimated preoperatively because of the patient's assumption of the sitting position for several days preoperatively. Supine positioning, modified by 30° reverse Trendelenburg and left-lateral wedged positioning resulted in life-threatening pulmonary oedema. We have described our approach to this patient specifically and outlined some thoughts on perioperative management of these patients in general.

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Résumé

On présente le cas d'une femme de 32 ans enceinte de quintuplet. La grossesse fut compliquée par un travail prématuré qui fut traité par la ritodrine. La bétaméthasone fut administrée afin d'accélérer la maturation pulmonaire fœtale. Le traitement à la ritodrine fut compliqué par la surcharge volémique et un œdème pulmonaire requérant l'administration de diurétique par voie intraveineuse. La patiente s'est présentée à l'urgence pour une césarienne avec une surcharge volémique et aggravation de sa thrombocytopénie. Un œdème aigu pulmonaire était manifeste avant l'induction et suite à l'insertion d'un cathéter dans l'artère pulmonaire la chirurgie fut retardée afin d'améliorer la condition de la mère par des diurétiques intraveineux. L'induction fut faite en position assise avec une pression cricoïde maintenue afin de protéger les voies aériennes quand la patiente fut mise en position couchée. La nitroglycérine intraveineuse fut utilisée afin de contrôler la pression artérielle. La ventilation manuelle au masque à basse pression a été utilisée afin de maintenir une saturation d'oxygène et la patiente fut intubée et ventilée avec la pression positive en fin d'expiration. La ventilation avec une pression positive en fin d'expiration fut continuée pour 24 heures dans la période postopératoire. Une revue de la période périopératoire est faite et ceci est suivi par une discussion des considérations anesthésiques dans les cas de grossesse à gestation multiple.