Case Reports/Case Series

Case report: Pregnancy in hemodialysis-dependent end-stage renal disease: anesthetic considerations

[Présentation de cas : Grossesse et insuffisance rénale terminale sous hémodialyse : considérations anesthésiques]

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Purpose: To describe the obstetrical and anesthetic management of a parturient with end-stage renal disease.

Clinical features: A 38-yr-old woman had severe renal impairment due to Wegener's granulomatosis. She was on hemodialysis for 12 years following two failed kidney transplants. She had two unsuccessful pregnancies, two and 12 years previously. The antenatal care of the present pregnancy incorporated a multidisciplinary approach involving obstetrics, nephrology and anesthesiology. Labour was induced at 36 weeks gestation. Bupivacaine 0.0625% with fentanyl $2 \mu\text{g}\cdot\text{mL}^{-1}$ was injected through an epidural catheter inserted for labour analgesia. Lidocaine 2% with epinephrine $2.5 \mu\text{g}\cdot\text{mL}^{-1}$ was given later for Cesarean delivery. There was no associated maternal or neonatal morbidity. The management focused on minimizing hemodynamic disturbances while providing maximum pain relief.

Conclusions: For a successful outcome in the parturient with end-stage renal disease, a multidisciplinary approach is essential.

logie. Le travail obstétrical a été induit à 36 semaines de grossesse. De la bupivacaine 0,0625 % et du fentanyl $2 \mu\text{g}\cdot\text{mL}^{-1}$ ont été injectés via un cathéter péridural inséré pour l'analgésie du travail obstétrical. De la lidocaïne 2 % et de l'épinéphrine $2,5 \mu\text{g}\cdot\text{mL}^{-1}$ ont été administrés plus tard lors de l'accouchement par césarienne. Il n'y a pas eu de morbidité maternelle ou néonatale associée. La prise en charge a eu comme objectifs de minimiser l'instabilité hémodynamique tout en fournissant un soulagement maximal de la douleur.

Conclusion : Une approche pluridisciplinaire est essentielle dans la prise en charge d'une parturiente souffrant d'insuffisance rénale terminale.

PATIENTS with dialysis-dependent end stage renal disease (ESRD) are usually amenorrheic and infertile¹ and pregnancy is rare. Without careful multidisciplinary management, most pregnancies end in spontaneous or surgical abortions. In these pregnancies, the main fetal problems consist of polyhydramnios, intra-uterine growth retardation preterm delivery, low birth weight and stillbirth.^{1,2} Accurate maternal and fetal monitoring, including frequent examination of the fetomaternal circulation by Doppler sonography, is required to recognize the above-mentioned complications.³ Though there are no prospective randomized clinical trials examining the relationship between dialysis and fetal outcome, there is evidence that increasing solute clearance through more intensive dialysis is beneficial to the health of the fetus.²

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Objectif : Décrire la prise en charge obstétricale et anesthésique d'une parturiente souffrant d'insuffisance rénale terminale.

Éléments cliniques : Une femme de 38 ans souffrait d'une insuffisance rénale sévère secondaire à une granulomatose de Wegener. Elle avait été hémodyalysée pendant 12 ans, suite à l'échec de deux transplantations rénales, et avait eu deux grossesses infructueuses, deux et 12 ans auparavant. La prise en charge anténatale de la grossesse actuelle a donc nécessité une approche pluridisciplinaire, incluant les services d'obstétrique, de néphrologie et d'anesthésio-

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Prenatal care must include intensive surveillance for hypertension, pre-eclampsia, left ventricular failure due to volume overload, anemia, infection, intra-uterine growth retardation and preterm labour. There are no reports regarding management of analgesia for labour, although limited information is available regarding successful peripheral regional blocks in ESRD patients presenting for non-obstetric surgery.^{4,5} We describe the anesthetic management of a parturient with ESRD who was successfully managed by Cesarean delivery (CD) after a failed trial of labour. The subject gave written consent for the publication of this report.

Case report

A 38-yr-old gravida 3 para 0 woman was referred at 30 weeks gestation. Her past medical history included chronic renal failure (CRF) secondary to Wegener's granulomatosis at age 15. She had two unsuccessful renal transplants and was now maintained on home hemodialysis (HD), 14 hr per week (two hours per day). She had conceived twice in the past but both pregnancies ended in spontaneous abortions, two and 12 years prior to the present pregnancy. She also had experienced a past episode of prolonged apnea following succinylcholine for a routine anesthetic.

There was intensive interdisciplinary cooperation amongst nephrologists, obstetricians and anesthesiologists during her pregnancy, labour and delivery. The total weekly dialysis period was increased from 14 to 21 hr per week (three hours per day) with close attention to electrolyte and acid-base management. The serum bicarbonate was maintained between 18–20 mEq·L⁻¹ by using low bicarbonate dialysate, and electrolyte imbalance was avoided.

The patient's weight gain was monitored by a nutritionist and she was allowed unlimited protein intake. Erythropoietin (EPO), intravenous iron, calcium carbonate, folic acid and multivitamins were administered. At 32 weeks of gestation, maternal steroids were prescribed to maximize fetal lung maturity. The patient's blood pressure was monitored three times daily, pre-dialysis, post-dialysis and once during the latter part of the day. At 34 weeks gestation, mild hypertension (140–150/90–93 mmHg) was observed, but no antihypertensive medications were prescribed.

She remained on close obstetric monitoring throughout. Daily non-stress tests were done to assess fetal growth. At 33–34 weeks gestation, the resistive index of the umbilical artery indicated early placental insufficiency, and induction of labour was planned at 36 weeks. Labour analgesia had been discussed with

TABLE Laboratory parameters four hours after dialysis on the day of induction

Laboratory tests	4 hr post dialysis
Hemoglobin (g·L ⁻¹)	123
Platelet count (× 10 ⁹ ·L ⁻¹)	271
International normalized ratio	0.9
Prothrombin time (sec)	29
Fibrinogen (g·L ⁻¹)	6.73
Urea (mmol·L ⁻¹)	11.6
Creatinine (μmol·L ⁻¹)	254.6

her, and she requested epidural analgesia for pain relief.

On the day of induction, she underwent a three-hour dialysis in the morning using the left arm arterio-venous fistula. A bolus of 1500 U heparin was given intravenously, followed by an infusion of 800 U·hr⁻¹. Her laboratory parameters prior to epidural insertion are presented in the Table.

The epidural was inserted approximately six hours after dialysis, with the patient in the sitting position. Routine monitors were applied and a 19G epidural catheter (Flexitip plus®, Arrow International, Reading, PA, USA) was inserted via a 17G Tuohy needle at the L3–4 inter-space, without difficulty or complication. An initial dose of 0.0625 % bupivacaine 5 + 5 mL was given. Analgesia was maintained with patient-controlled epidural analgesia consisting of bupivacaine 0.0625% + fentanyl 2 μg·mL⁻¹ at a basal rate of 5 mL·hr⁻¹, and patient-controlled boluses of 5 mL every 15 min with a maximum of 25 mL·hr⁻¹. Good analgesic effect was achieved.

Labour was augmented with oxytocin after the membranes were ruptured. Maternal position was optimized using left uterine displacement whenever feasible. After five hours in labour, full cervical dilation was achieved and mento-anterior face/brow presentation was discovered. With each contraction the patient developed variable fetal decelerations. Some vaginal bleeding ensued, although the patient remained hemodynamically stable. Placental abruption was suspected, and urgent CD became mandatory.

The epidural was topped up with 2% lidocaine containing 2.5 μg·mL⁻¹ epinephrine and fentanyl to a total of 300 mg lidocaine and 60 μg fentanyl. Effective anesthesia was readily achieved, without maternal hemodynamic instability. Vasopressors were used electively to maintain blood pressure within 15% of baseline values (mean blood pressure 116/69 ± 18.6/16.8 mmHg). A total of 100 μg phenylephrine

and 15 mg ephedrine *iv* was administered to prevent, rather than treat hypotension. The estimated blood loss was 700 mL (including 200 mL of clot found on opening the lower uterine segment). Intravenous fluid was limited to 400 mL Ringer's lactate and 800 mL normal saline.

A baby weighing 1729 g was delivered with APGAR scores of 6 and 8, at one and five minutes, respectively. Oxytocin and antibiotics were given. Epidural morphine 3 mg was given at the end of the procedure for postoperative analgesia. Oral acetaminophen was the only postoperative analgesic required. The postpartum course of the mother was uneventful. The baby was admitted to the neonatal intensive care for ten days due to prematurity and feeding problems. She was discharged home on the tenth day, doing well.

Discussion

Although patients on dialysis (hemo- or peritoneal) have reduced fertility, there are many reported successful pregnancies in these patients. Hemodialysis causes a shift of blood flow away from the feto-placental unit. Once viability has been reached, fetal surveillance during HD is of utmost importance, given the acute fluid shifts that can occur, and the resulting potential for acute hypotensive episodes. Changes in amniotic fluid volume, the pulsatile index of the umbilical artery, and fetal heart rate have been documented during HD, further emphasizing the need for close fetal surveillance.⁶ Cardiovascular instability and hypotension may compromise fetal wellbeing. Mother and fetus should therefore be monitored before, during and after HD. In addition, dialysis may cause polyhydramnios because of fluid shifts and decreased plasma oncotic pressure.

Dialysis regime

Increasing the dialysis dose is known to prolong gestation, resulting in higher birth weight infants with better chances of survival. Dialysis time of more than 20 hr per week is known to result in 75% infant survival, contrasting with 33.3% in women receiving 15–19 hr per week.⁷ More frequent rather than longer dialysis sessions appear to be the method of choice, as this regimen may reduce the dialysis-induced hypotensive episodes, with consistent reduction in preterm labour and fetal distress. Increased dialysis time provides a less uremic environment allowing better growth for the fetus.³ This also allows liberal maternal dietary and fluid intake to satisfy fetal demand. It may also improve blood pressure control and reduce the amplitude of volume shifts. No randomized prospective trials of pregnant women on dialysis exist, but retrospec-

tive data suggest that maintaining BUN values ≤ 50 mg·dL⁻¹ (17.85 mmol·L⁻¹) is an appropriate goal.⁸

Electrolyte abnormalities and alkalosis may be associated with an intensive dialysis regimen. Alkalosis may result from vomiting of pregnancy, generalized tendency of respiratory alkalosis during pregnancy with absence of adaptive mechanisms of the kidney, excessive consumption of bicarbonate salts and high carbonate dialysate.

Anticoagulation

Anticoagulation is commonly used during dialysis. The use of heparin throughout pregnancy is associated with several potential maternal problems, including hemorrhage, and heparin-induced thrombocytopenia and osteoporosis, which can be associated with an increased fracture risk.⁹ There are guidelines for the management of patients on unfractionated heparin.^{10,11} The assessment of platelet function is a safety measure¹² but was not available in our hospital. Hemodialysis without anticoagulant is an alternative to systemic anticoagulant therapy for mothers with an active bleeding episode, or for those who are at risk of hemorrhage during the pregnancy.¹³ This patient had no evidence of an active bleeding disorder. Neither unfractionated heparin nor low molecular weight heparin cross the placenta and these drugs are considered safe for the fetus.

Anemia

A drop in hematocrit is observed in pregnant patients with ESRD. These patients are dependent on exogenous EPO for red cell production. Doubling the dose of EPO should produce enough red blood cells to satisfy pregnancy requirements, reverse the drop in hematocrit, and achieve the target hematocrit of 30–35%.³ Intravenous iron in doses of 1 g above usual requirements should be considered in these patients as oral absorption is poor.

Other concerns

Tocolytic drugs are the cornerstone of pharmacologic management of preterm labour. The goal is to prolong pregnancy to term or long enough for adequate gestational age and lung development. However, the side effects of these drugs must be considered. Tocolysis was not done in this case as induction was planned at 34–36 weeks due to suspected placental insufficiency. These patients may also be susceptible to several types of infections, including viral hepatitis B and C and methicillin-resistant staphylococcal aureus.

Anesthetic considerations

There are multiple anesthetic considerations in the parturient with HD-dependent ESRD. These patients are usually hypertensive and may have pre-eclampsia. They may also present with left ventricular failure due to fluid overload and/or anemia. Dialysis and its associated requirement for heparin may lead to coagulation abnormalities, with an increased risk of complications of regional anesthesia.

The safety of neuraxial block in such patients is not documented or proven. There are many reports detailing the safe and successful use of peripheral regional blocks in dialysis-dependent patients if there is no platelet dysfunction or coagulation abnormality.¹⁴ Peripheral regional anesthesia techniques have been used in patients with ESRD for the creation of arteriovenous fistulae.⁵ Moderately high doses of ropivacaine (225 mg) and bupivacaine (150 mg) in these patients did not cause toxicity. Reduced duration of activity but higher plasma levels of local anesthetics in patients with CRF have been reported.¹⁵ Uremia-induced changes in acid-base status, hemodynamic parameters and protein binding (at α -1 glycoprotein) have been suggested. Even though the duration of action of local anesthetic agents appears to be reduced, elimination of these drugs can be delayed in uremic patients so that monitoring for toxicity is recommended. Gould *et al.*¹⁶ reported bradycardia and hypotension after an axillary block with 250 mg bupivacaine in a patient with CRF. Rice *et al.*¹⁷ have reported toxicity with 150 mg bupivacaine in a patient with renal failure. In the case reported here, cumulative doses of local anesthetics were bupivacaine 78 mg for five hours of labour, and lidocaine 300 mg for CD. No signs or symptoms of toxicity were observed. There are no previously reported cases which describe the safe use of regional analgesia for labour in a patient on long-term HD.

Cesarean delivery should be reserved for the usual obstetric indications, while being prompted most often by failure to progress after premature rupture of membranes. For urgent CD, selection of anesthetic technique can be challenging in a potentially volume contracted, hypertensive, immunosuppressed, possibly pseudo-cholinesterase deficient and recently anticoagulated patient. Invasive monitoring may be indicated if the patient is unstable, if volume status is uncertain, or if there is any cardiovascular compromise. Transthoracic echocardiography and transesophageal echocardiography for monitoring cardiac function may be worth considering in higher risk individuals, while recognizing that these monitors are relatively invasive and inconvenient during labour and operative delivery.

Fluid preloading is discouraged, as small increases in left ventricular volume may cause a pronounced

increase in end-diastolic pressure leading to pulmonary edema.¹⁸ The use of vasopressors to maintain hemodynamic stability and minimize volume overload is preferred. Several randomized clinical trials of preload *vs* no preload in women with normal renal function undergoing CD¹⁹ have found that preloading produces a marginal, if any, reduction in the incidence of hypotension. Whatever the type of infused solution, rapid administration may cause a significant increase in central venous pressure, pulmonary capillary wedge pressure and hemodilution, with possible detrimental consequences. Therefore, we chose to use vasopressors instead of a high volume preload during CD. We opted to use intermittent boluses instead of a continuous infusion of vasopressor to maintain blood pressure within 15% of the baseline values.

Pseudocholinesterase levels are reduced during pregnancy, though parturients do not develop prolonged respiratory impairment following administration of standard doses of succinylcholine. Pseudocholinesterase deficiency should also be considered in these patients due to immunosuppression. The patient described in this report had previously experienced a single episode of prolonged apnea following succinylcholine, despite subsequently testing negative for atypical pseudocholinesterase.

Though the ratios of morphine-3-glucuronide and morphine-6-glucuronide to morphine are higher in patients with renal impairment, epidural morphine administration is known to result in lower metabolite production in comparison to other routes of administration, as it avoids first pass metabolism.²⁰ Therefore, use of a small dose of morphine by the epidural route was considered safe in this instance.

Most babies born to dialysis patients require neonatal intensive care unit admission because of prematurity. Even those born close to term should be monitored closely, as they generally have solute diuresis and may become seriously volume contracted. Neonatal intensive care management is mandatory.

In conclusion, intensive vigilance and prudence is warranted in the management of ESRD parturients. A multidisciplinary team of renal, obstetric, neonatal and anesthesiology physicians, nurses and nutritionists is required to ensure safety of the mother and child. A stable patient on a tightly controlled HD regimen is the key to successful labour analgesia for delivery. Local anesthetics for labour and delivery are not contraindicated, but their altered metabolism provides the potential for increased variation in clinical response, warranting cautious administration and careful monitoring of clinical endpoints.

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