

Anesthesia for parturient with renal transplantation

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Abstract

Management of successful pregnancy after renal transplantation is a unique challenge to nephrologist, obstetrician, and anesthesiologist, as these patients have altered physiology and are immune-compromised. We present the anesthetic management of three postrenal transplant patients scheduled for cesarean section. While conducting such cases, cardiovascular status, hematological status, and function of transplanted kidney should be assessed thoroughly. Side effects of immunosuppressant drugs and their interaction with anesthetic agents should be taken into consideration. Main goal of anesthetic management is to maintain optimum perfusion pressure of renal allograft to preserve its function.

Key words: Anesthesia, pregnancy, renal transplantation

Introduction

Successful renal transplantation in women of child-bearing age is increasing in recent years. Women with chronic renal failure (CRF) suffer from altered reproductive and sexual functions; hence, conception is rare for women on dialysis, the incidence being one in every 200 patients.^[1] However, after successful renal transplantation, endocrine function improves rapidly and correlates closely with that of normal women of childbearing age.^[1] These patients present a unique challenge to the obstetrician, nephrologist, and anesthesiologist due to the presence of altered physiology and immune-suppressants.

We report the anesthetic management of three cases of parturients with renal transplantation who underwent delivery by cesarean section with good maternal and neonatal outcome.

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Case Reports

Case 1

A 33-year-old woman having CRF due to postpartum cortical necrosis underwent renal transplantation. After transplantation, she had stable graft function with maintenance doses of cyclosporine, azathioprine, and prednisolone and was on regular follow-up at outpatient department. Two years after transplantation she conceived.

Regular antenatal follow-up was done. Serial assessment of renal function, complete blood counts (CBC), platelet counts, and ultrasonographic evaluation of the transplanted kidney and fetus were carried out. Hematinics and low-dose aspirin were started. Her immunosuppressants were continued with dose adjusted to maintain plasma cyclosporine level within therapeutic range (Co - 150–200 ng/ml). At 22 weeks gestation, she was diagnosed to have mild pregnancy induced hypertension and was put on oral methyldopa, 250 mg three times a day. Routine CBC at 36 weeks revealed leucopenia (TLC = 1500/mm³). Azathioprine was suspected to be responsible for the same and was discontinued. Both oral and parenteral folic acid supplements were given to treat leucopenia. After correction of leucopenia within a week, patient was referred for elective cesarean section for cephalopelvic disproportion after confirming fetal maturity.

Preoperative work up included thorough systemic examination and review of graft function, hematology, and electrocardiogram (ECG). She was explained about spinal anesthesia and her informed consent was obtained. On

the night before surgery, she was given ranitidine 150 mg orally and in the morning her routine immune-suppressants and antihypertensives were continued. Ranitidine 50 mg, ondansetron 8 mg, and hydrocortisone 100 mg were given intravenously (IV) 90 min before surgery to prevent nausea, vomiting, and aspiration associated with pregnancy and immunosuppressants. Antibiotic prophylaxis was given along with that. Adequate hemodynamic monitoring was provided in the form of noninvasive blood pressure (NIBP) monitoring, ECG, peripheral oxygen saturation (S_pO_2), and urine output. After preloading with 500 ml of normal saline, 0.5% bupivacaine 12.5 mg with morphine 0.2 mg was given in the subarachnoid space. A total of 1500 ml of crystalloids was administered. 20 U of oxytocin were given IV after childbirth and carboprost 250 μ g was given intramuscularly (IM) after removal of placenta. 15° left lateral tilt was maintained till the delivery of the baby. A 2.2-kg healthy child with normal APGAR score was delivered. Postpartum course was smooth. Hydrocortisone, 100 mg, was continued and was given 6 hourly for 24 h postoperatively to provide a cover for the surgical stress.

Case 2

A 28-year-old woman with CRF due to chronic glomerulonephritis underwent renal transplantation at our institute. After transplantation the graft function was well maintained on prednisone 10 mg/kg/day, azathioprine 75 mg/day, and cyclosporine 2 mg/kg/day. She was receiving nifedipine 20 mg twice a day for hypertension. One year after transplantation she conceived. Regular follow-up was done and her pregnancy was uneventful with controlled hypertension. At 34 weeks of gestation, fetal distress developed and an emergency cesarean section was scheduled under general anesthesia (GA).

Patient received her routine doses of antihypertensives and immunosuppressive drugs. Hydrocortisone 100 mg, ranitidine 50 mg, and metoclopramide 10 mg were given IV. Preparation for unexpected difficult intubation was made. The operating table was given 15° left lateral tilt. ECG, S_pO_2 , end-tidal carbon-dioxide ($EtCO_2$), and urine output was monitored. Disposable breathing circuit was used. After preoxygenation for 3 min and crash induction of anesthesia was done with thiopentone sodium 5 mg/kg and succinylcholine, 2 mg/kg along with application of Sellick's maneuver. To attenuate the pressor response to laryngoscopy and intubation, lignocaine 1.5 mg/kg was given. Trachea was intubated with a 7-mm cuffed endotracheal tube. Anesthesia was maintained with nitrous oxide, oxygen, and isoflurane up to 1% and muscle relaxation was provided with atracurium, titrated with peripheral nerve stimulator. A 2.5-kg normal healthy child was delivered, with APGAR score of 6 and 9 at 1 and 5

min, respectively. Intraoperatively, patient received 1200 ml of fluids. 20 units of oxytocin in infusion and methyl ergometrine 0.2 mg IV were given to help contract the uterus. Fentanyl 2 mcg/kg was given for analgesia after childbirth. At the end of the surgery, postoperative residual muscle paralysis was reversed and trachea extubated. Postoperative pain relief was provided with tramadol, 2 mg/kg IV 8 hourly. Postoperatively, hydrocortisone 100 mg was given 6 hourly for 24 h. Postoperative course was uneventful.

Case 3

A 29-year-old woman underwent renal transplant as she had chronic glomerulonephritis. After transplantation, she had stable graft function with maintenance dose of prednisolone 10 mg and tacrolimus 2 mg. For control of hypertension she was on nifedipine 20 mg thrice daily. Two and half year after transplant she planned a pregnancy. The pregnancy course was uneventful but at gestational term, an emergency cesarean section was scheduled because of nonprogress of labor.

Pantoprazole 40 mg and ondansetron 4mg were given IV and IV fluid was started. 2.2 ml of 0.5% bupivacaine was given intrathecally using 27-G Quincke needle. Patient's blood pressure was 180/100 mmHg. Infusion of nitroglycerine (NTG) was started and its dose was titrated according to BP reading. NTG was continued throughout the surgery and up to 4 h postoperatively. A 2-kg healthy normal child was delivered. Intraoperatively 500 ml of normal saline and 1000 ml of Ringer's lactate were infused. 20 U of oxytocin was given IV as infusion and carboprost (250 mcg) IM were given after removal of placenta.

Discussion

All post-transplant pregnancies should be considered as high risk and close monitoring by obstetrician and transplant physician is mandatory. Anesthesiologists are involved in the care of these patients for both labor analgesia or for operative procedure. Anesthetic considerations include:

- Effect of pregnancy on renal allograft;
- Side effects of immunosuppressive drugs in mother and fetus, relevant to anesthesiologist;
- Interaction of immunosuppressants with anesthetic drugs and techniques.

Pregnancy does not appear to cause excessive or irreversible problems with graft dysfunction if the function of the transplanted organ was stable prior to pregnancy.^[2]

The immunosuppressive drugs commonly used in renal transplantation are cyclosporine, tacrolimus, azathioprine, or mycophenolate mofetil and steroids. The important side effects of

cyclosporine, generally seen with long-term use of these agents, are hypertension, hyperlipidemia, nephrotoxicity, neurotoxicity, and hepatotoxicity.^[3,4] Vast majority of the patients are already hypertensive before the renal transplant and on medication for control of blood pressure. Hypertension is due to increase in systemic vascular resistance and calcium channel blockers are preferred for its treatment. Two of the patients were receiving oral nifedipine for control of blood pressure. Nephrotoxicity is the major complication of cyclosporine due to renal arteriolar vasoconstriction leading to reduction of glomerular filtration rate and creatinine clearance.^[5] The drugs dependant on kidneys for elimination should be used with caution and nephrotoxins should be avoided in perioperative period. Thorough neurological examination is important in patients on cyclosporine as it contributes to tremors, seizures, and paresthesia. Documentation of paresthesia is important if regional anesthesia is planned. None of our patients had neurological symptoms because of the immunosuppressive medication.

Newer immunosuppressive regimens, including tacrolimus, compare favorably with older regimens in reducing hypertension and pre-eclampsia.

The major complication of azathioprine and mycophenolate mofetil (MMF) is bone marrow suppression especially leucopenia;^[3,5] so complete blood examination is necessary before surgery. In case 1, leucopenia was found which was corrected preoperatively by parenteral and oral folic acid. Preoperative liver function tests should be done as these drugs may cause elevation of liver enzymes.

Side effects of glucocorticoids are well documented and include sodium retention, hypertension, diabetes, peptic ulcer disease, Cushingoid syndrome, poor skin integrity, osteoporosis, and delayed wound healing. Care of patients includes gentle handling to prevent skin damage and fractures, antacid prophylaxis, and thorough airway examination.^[6] Ranitidine prophylaxis was given to all the three cases. In case 2, where GA was given, difficult airway cart was kept ready anticipating difficult intubation, and disposable anesthesia circuit/tubes were used.

Considering the long-term side effects of immunosuppressive drugs, preoperative assessment should include laboratory investigations such as CBC, renal function tests, electrolytes, blood glucose, and liver function tests.

Apart from side effects of immunosuppressants, exposure to anesthesia and surgery alters many facets of immunocompetence. Exposure to anesthesia and surgery depresses both T cell and B cell responsiveness as well as phagocytosis. Immunocompetence

during surgery can be affected by direct and hormonal effect of anesthetic drugs, immunological consequences of other drugs used, type of surgery, and coincident infection. The incidence of postoperative infection is related to surgical trauma and to an associated release of cortisol and catecholamines that are known to inhibit phagocytosis. This hormonal response is mediated through the sympathetic nervous system. The attenuation of sympathetic nervous system stimulation is desirable during surgery. This can be done by giving regional anesthesia or by deepening the plane of GA and by inhibiting the stress response with the help of drugs.

The choice of anesthetic technique depends on functional status of transplanted kidney, the cardiovascular status, hematological status, and indication of cesarean section. In absence of renal dysfunction, anesthetic management is similar to that of a normal parturient, except for prophylactic antibiotic and stress dose of steroids in all patients with transplanted kidney.^[5,6] Renal transplant recipients with functioning kidney grafts may have normal creatinine levels. However, glomerular filtration rate and effective plasma flow are likely to be low, and drugs excreted via kidney may have prolonged action. Strict aseptic precautions should be maintained during intravascular access, intubation or while performing regional techniques and the use of disposable anesthesia accessories is recommended. Central neuraxial blocks are not contraindicated in renal allograft recipients if coagulation status is normal

Immunosuppressive drugs can affect the pharmacology of many anesthetic drugs. Amongst intravenous anesthetic agents, propofol does not alter cyclosporine concentration. Cyclosporine tends to enhance pentobarbital anesthesia and fentanyl analgesia in mice by an unknown mechanism. Intraoperative management includes careful attention to sodium and magnesium levels and avoidance of hyperventilation which can be done by maintaining the EtCO₂ within the normal range.

Amongst inhalational agents, enflurane should be avoided in patients with renal transplantation because of hepatotoxicity of fluoride metabolite. However, sevoflurane is thought to be safe. To maintain therapeutic levels, cyclosporine or tacrolimus should be given 4 h preoperatively because of reduced gastric emptying. Choice of nondepolarizing muscle relaxant depends on renal status of patient. However, the drug that relies least on renal elimination like atracurium is the optimal choice. The solubility agent of cyclosporine (cremaphor) has been shown to augment the action of neuromuscular blocking agents.^[5] Neuromuscular function should be monitored particularly if the patient is receiving magnesium. Clinically relevant dose of azathioprine do not antagonize neuromuscular blocking drugs in humans

Meticulous perioperative fluid and electrolyte management is essential as hypotension may make the transplanted kidney susceptible to acute tubular necrosis. Special care must be taken to keep patient well hydrated and maintain urine output more than 1 ml/kg/h.

Postoperative pain relief is provided with narcotics by epidural or spinal route if regional anesthesia is used or by parenteral opioids if GA is given. Non steroidal anti-inflammatory drugs should be avoided as they increase the risk of gastrointestinal bleeding, reduce renal blood flow through prostaglandin inhibition and exacerbate cyclosporine toxicity.

In conclusion, a clear understanding of physiological changes secondary to renal transplantation and changes brought about by pregnancy on renal allograft recipient would contribute for safe management of parturient.

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