

ANESTHESIA FOR PARTURIENT WITH RENAL TRANSPLANTATION

Parikh BK, Shah VR, Bhosale GP, Praveen CS

ABBREVIATIONS

CBC : Complete blood counts

ECG : Electrocardiogram

GA : General anaesthesia

IV : Intravenous

NSAID : Non- Steroidal anti inflammatory drugs

CRF : Chronic renal failure

ETCO₂ : End-Tidal carbon dioxide

GFR : Glomerular filtration rate

NIBP : Non- Invasive blood pressure

USG : Ultrasonography

KEY WORDS

anaesthesia, pregnancy, renal transplantation

ABSTRACT

Pregnancy in renal transplant recipients is now becoming common and overall maternal and fetal outcome is good in patients with well functioning grafts in spite of several potential problems. Vaginal delivery is recommended but caesarian section is required in at least 25% patients. We report 2 cases of pregnant women who underwent caesarian section for the obstetric reasons. The potential maternal and fetal risks and details of anesthetic management of pregnant transplant recipients are reviewed here.

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^(1,2). However after renal transplantation, endocrine function improves rapidly and correlates closely with that of normal women of childbearing age, reaching the rate of 12 %¹.

The first case of successful pregnancy was reported in a woman who had received renal transplantation in 1958 from her identical twin sister. She did not receive any immunosuppressive medication³. Since then pregnancy in a renal transplant patient has become a reality and there have been hundreds of successful pregnancies reported in literature, however anaesthetic management of these patients is still rarely reported. These patients present a unique challenge to the obstetrician, the nephrologist and

Department of Anaesthesiology and Critical Care

ADDRESS FOR CORRESPONDENCE

Beena K. Parikh, MD. Asst. Prof., Department of Anaesthesiology and Critical Care.

Institute of Kidney Diseases & Research Centre and Institute of Transplantation Sciences

Civil Hospital Campus, Asarwa, Ahmedabad 380016, Gujarat, India

TEL: 0091 79 2268 5600/01/04/05 FAX: 0091 79 22685454 E mail: ikdrcad1@sancharnet.in

anaesthesiologist due to their desire to have normal child in the phase of altered physiology and presence of immunosuppressants.

Here, we report the anaesthetic management of two cases of parturients with renal transplantation who underwent delivery by caesarean section with good maternal and neonatal outcome.

CASE 1

A 33 year old female patient having CRF due to postpartum cortical necrosis underwent renal transplantation in June 1998 at our institute. After transplantation, she had stable graft function with maintenance doses of cyclosporine, azathioprine and prednisolone and was on regular follow up at our outpatient department. Two years after transplantation, she came to us with two months of amenorrhea and morning sickness. Ultrasonography (USG) showed gestational sac of 8 weeks with fetal cardiac pole. She was explained all the pros and cons of pregnancy and she decided to continue pregnancy.

Regular antenatal follow up was done. Serial assessment of renal function, complete blood counts (CBC), platelet counts and USG evaluation of the transplanted kidney and fetus was carried out. Hematinics and low dose aspirin were started. Her immunosuppressants were continued with dose adjusted to keep the trough plasma cyclosporine level within therapeutic range. At 22 weeks, she was diagnosed to have mild pregnancy induced hypertension and was put on Tab. Methyldopa, 250 mg three times a day. Routine CBC at 36 weeks revealed leucopenia. 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 caesarean section for cephalopelvic disproportion after confirming fetal maturity.

Preoperative workup 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 previous night of surgery, she was given Tab. Ranitidine, 150 mg and in the morning her routine immunosuppressants and anti-hypertensives were continued. After securing intravenous (IV) line, Inj. Ranitidine, 50 mg and Inj. Ondansetron, 8 mg were given 90 minutes before surgery to

prevent nausea, vomiting and aspiration associated with pregnancy and immunosuppressants. Antibiotic prophylaxis was given along with that. Till the delivery of baby, a 15° left lateral tilt was maintained. Adequate hemodynamic monitoring was provided in the form of non-invasive blood pressure (NIBP) monitoring, ECG, S_pO_2 and urine output. Preloading was done with 500 ml of normal saline. Lumbar puncture was done with strict aseptic precautions and 0.5 % Bupivacaine, 12.5 mg with Morphine, 0.2 mg was given in the subarachnoid space. A healthy child with normal APGAR score was delivered. Totally 1500 ml of crystalloids and 10 U of Oxytocin were given. Postpartum course was smooth. Inj. Hydrocortisone, 100 mg was given before surgery and six hourly post partum for 1st 24 hours.

CASE 2

A 28 year old female with CRF due to chronic glomerulonephritis underwent renal transplantation in May 1998 at our institute. After transplantation the graft function was good on maintenance dose of Prednisone, 10 mg/kg BW/ day, Azathioprine, 75 mg /day and cyclosporine, 2 mg/kg BW/ day. She was receiving Tab. Nifedipine, 20 mg twice a day for her hypertension. One year after transplantation she conceived and was explained about her high risk pregnancy. Regular follow up was done and besides controlled hypertension, whole course of her pregnancy was uneventful. At 34 weeks of gestation, she developed premature rupture of membranes with no progress of labour. So an emergency caesarean section was planned.

Anaesthetic options (general vs. regional) with risks and benefits of both were explained and she opted for general anesthesia (GA). She underwent emergency caesarian section in the evening. She had taken her routine doses of anti-hypertensives and immunosuppressive drugs before caesarian section. Inj Hydrocortisone, 100 mg, Inj Ranitidine, 50 mg and Inj. Metoclopramide, 10 mg were given IV as soon as decision for surgical delivery was taken. Preparation for unexpected difficult intubation was done. On the operation table she was given 15° left lateral tilt. She was monitored with ECG, S_pO_2 , end tidal TCO_2 , urine output and peripheral nerve stimulator. Disposable anaesthetic circuit was used. Preoxygenation was done for 3 minutes. Crash induction was done with Inj. Thiopentone sodium, 5 mg.kg⁻¹ and Inj. Succinylcholine, 2 mg.kg⁻¹ with Sellick's maneuver. To attenuate the pressor response to laryngoscopy and



ARTICLES

intubation, Inj. Lignocaine (2 %) 1.5 mg.kg⁻¹ was given. She was intubated with portex 7 mm disposable cuffed tube. She was maintained with O₂ + N₂O + Atracurium+ Isoflurane (0.6-1 %). She delivered a normal healthy child with APGAR score of 6 and 9 at 1 and 5 minutes respectively. Intraoperatively, patient received 1200 ml of fluids and 10 units of Oxytocin. Inj. Fentanyl, 2µg.kg⁻¹ was given after the birth of the baby. Postoperative residual muscle paralysis was reversed and patient was extubated when awake. Postoperative course was uneventful. Postoperative pain relief was provided with Inj. Tramadol, 2 mg.kg⁻¹ 8 hourly.

DISCUSSION

The ideal time for conception after renal transplantation is between second and fifth year of transplantation if the patient has stable graft function (S.creatinine <2 mg/dl) on maintenance dose of immunosuppression with no evidence of recent episodes of acute rejection, hypertension controlled on minimal medication, proteinuria < 500 mg/ 24 hours and a normal graft USG^{3,4}. In the first year after transplantation, cytomegalovirus remains the most frequent cause of fetal complications such as prematurity and low birth weight, whereas after five years, graft dysfunction may start secondary to chronic rejection^{1,3}.

All post-transplant pregnancies should be considered as high risk and close monitoring by obstetrician and transplant physician is mandatory. Antenatal assessment includes serial measurement of renal functions and hematological parameters, control of blood pressure, aggressive treatment of any infection and meticulous fetal surveillance⁵. Immunosuppressive therapy is usually maintained at pre-pregnancy levels with frequent monitoring of blood levels, adjusting dosage according to pharmacokinetic changes during pregnancy². Incidence of acute rejection is low (between 3-9 %) due to the privileged immunological state of pregnancy^(3,5)

Ideally vaginal delivery is recommended as there is no risk of mechanical injury to the transplanted kidney or obstruction to the birth canal¹. Caesarean sections are purely necessary for the obstetric indications as in the above two cases. There is incidence of 25 % caesarean section rate which is much higher than expected, presumably reflecting fear that vaginal delivery would be hazardous for mother and/or child. When caesarean section is necessary, lower segment approach is usually feasible, but previous urological surgery may make

this difficult⁶. Care must be taken not to damage ureter or compromise graft blood supply.

Anaesthesiologist would be involved in the care of these patients for either labour analgesia or for operative procedure. Anaesthetic considerations include:

- Effect of pregnancy on renal allograft
- Side effects of immunosuppressive drugs in mother and fetus, relevant to anaesthesiologist
- Interaction of immunosuppressants with anaesthetic drugs and techniques

In normal pregnancy glomerular filtration rate increases by about 30-50 % during first and second trimester, and decreases during the third trimester. This hyperfiltration of pregnancy is related to increased plasma flow; with concomitant increase in intraglomerular pressure^(7,1). Similar changes are seen in transplanted kidney, which theoretically predisposes the patient to loss of renal function. However in majority of the patients studied, pregnancy does not appear to cause excessive or irreversible problems with graft dysfunction if the function of the transplanted organ is stable prior to pregnancy.

The immunosuppressive drugs commonly used in renal transplantation are cyclosporine, azathioprine or mycophenolate mofetil and steroids. The side effects of cyclosporine important from anaesthetic point of view are hypertension, hyperlipidemia, nephrotoxicity, neurotoxicity and hepatotoxicity^{3,7}. Hypertension is due to increase in systemic vascular resistance and calcium channel blockers are preferred drugs for its treatment. Nephrotoxicity is the major complication of cyclosporine due to renal arteriolar vasoconstriction leading to reduction of glomerular filtration rate and creatinine clearance⁸. The drugs dependant on kidneys for elimination should be used with caution and nephrotoxins should be avoided in perioperative period. Thorough neurological examination is also important in patients on cyclosporine as it contributes to tremors, seizures and paraesthesia. Documentation of paraesthesia is important if regional anaesthesia is planned.

The major complication of azathioprine and mycophenolate mofetil is bone marrow suppression especially leucopenia^{3,8}. So, complete blood examination is necessary before surgery. In our case 1, leucopenia was found which was corrected preoperatively. 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^{7,8}.

Considering the long term side effects of immunosuppressive drugs, preoperative assessment include a battery of laboratory investigations like CBC, renal function tests, S. electrolytes, blood glucose, liver function tests, viral serology and coagulation profile².

Transplant patients may have pelvic osteodystrophy related to previous renal failure and dialysis or steroid therapy⁹. The incidence of avascular necrosis of femoral head is about 20% in transplanted patients. Some of the patients may have diabetes mellitus. In such cases, strict diabetic management profile is needed, because of increased complication rate by two fold compared to other pregnant renal allograft recipients⁶. Preeclampsia may be over diagnosed in these patients due to proteinuria and hypertension induced by cyclosporine^{3,6}.

Apart from side effects of immunosuppressants, exposure to anaesthesia and surgery alters many facets of immunocompetence. Exposure to anaesthesia and surgery depresses both T cell and B cell responsiveness as well as phagocytosis. Though local and inhaled anaesthetics (nitrous oxide) produce dose dependant inhibition of mobilization and migration of polymorphonuclear leucocytes necessary for phagocytosis, these effects are probably insignificant clinically, considering the usual duration of anaesthesia and doses of drugs administered². Immunocompetence during surgery can be affected by direct and hormonal effect of anaesthetic drugs, immunological consequences of other drugs used, type of surgery and coincident infection. The incidence of post operative 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 anaesthesia or by deepening the plane of anaesthesia and by inhibiting the stress response with the help of drugs in G.A².

The choice of anaesthetic technique depends on functional status of transplanted kidney, the cardiovascular status, hematological status and indication of cesarean section. In absence of renal dysfunction, anaesthetic management is similar to that of a normal parturient, except for prophylactic antibiotic and stress dose of steroids in all patients with transplanted kidney^{6,8}. Strict aseptic precautions should be maintained during intravascular access, intubation or while performing regional techniques and the use of disposable anaesthesia accessories are required².

Central neuraxial blocks are not contraindicated in renal allograft recipients if coagulation status is normal. It reduces chances of pulmonary aspiration, avoids complications related to airway management, and provides superior postoperative pain relief with less foetal depression². Spinal anaesthesia can be used if cardiovascular status is healthy because of its faster onset of action and less dose requirement than epidural anaesthesia. Spinal anaesthesia with a narrow gauge needle can also be given in patients with marginal coagulation profile. If patient has significant cardiovascular disease or severe preeclampsia, epidural anaesthesia is preferred as desired level of block can be achieved by small incremental doses with gradual fall of BP.

G.A. is used in cases where regional anaesthesia is contraindicated due to patient's refusal, altered coagulation profile, obstetric reason or compromised cardiac function. Crash induction should be done despite the surgery being a planned one to prevent aspiration². Suxamethonium can be used for intubation if serum potassium is less than 5.5 meq/liter. Intraoperative management includes careful attention to serum sodium and magnesium levels and avoidance of hyperventilation which can be done by maintaining the ETCO₂ with in normal range. Choice of non-depolarizing 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 agents⁸. Neuromuscular function should be monitored with peripheral nerve stimulator in these patients particularly if they are receiving magnesium. At the end, patient should be extubated after complete reversal of neuromuscular block and when fully awake with protective reflexes intact.



ARTICLES

Meticulous perioperative fluid and electrolyte management is essential as transplanted kidney is denervated and hypotension may make kidney susceptible to acute tubular necrosis due to nephrotoxicity of cyclosporine. Special care must be taken to keep patient well hydrated and maintain urine output more than 1ml/ kg BW/ hr. Benefit of invasive monitoring to guide fluid therapy should be weighed against risk of infection.

Postoperative pain relief is provided with narcotics by epidural or spinal route if regional anaesthesia is used or by parenteral opioids if G.A. 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.

Despite transplacental exposure of immunosuppressive drugs to foetus, congenital anomalies and other adverse effects are infrequent⁵. Azathioprine may give rise to neonatal leucopenia and thrombocytopenia unless maternal leucocyte count is maintained at or above 10000 cells /mm^{3,2}. It has also been reported to cause low birth weight, chromosomal breaks, prematurity, jaundice and respiratory distress syndrome³. Fetal defects like adrenal insufficiency, cleft palate, hare lip, cardiac septal defects, neurological and behavioral disturbances are common in children born to mothers using steroids especially during second trimester^{1,7}. Active cytomegalo virus infection during pregnancy is associated with congenital anomalies and in neonate it may lead to death. Therefore, involvement of neonatologist since early pregnancy and during delivery is advisable.

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.

REFERENCES

1. Lessan-Pezeshki M., Pregnancy after renal transplantation: points to consider. *Nephrol Dial Transplant.* 2002;17(5): 703-7.
2. Athma Prasanna : Anaesthesia for parturient with renal transplant. *The Indian Anaesthetist's Forum –online journal* (www.theiaforum.org) October 2003(1).
3. Edgar IP, Makowski L, Harris P. Parenthood following renal transplantation. *Kidney Int* 1980; 18: 221-33.
4. Lindheimer MD, Katz AI., Pregnancy in renal transplant patient. *Am J Kidney Dis.* 1992; 15(2) 173-76.
5. Stratta P, Canavese C, Giacchino F, et al. Pregnancy in kidney transplantation: satisfactory outcomes and harsh realities. *Journal of Nephrology* 2003; 16:792-06.
6. Davison JM, Dialysis, Transplantation and pregnancy. *Am J Kidney Dis.* 1991;17(2): 127-32.
7. Tripathi KD, *Essentials of medical pharmacology* (5th edition) , Jaypee brothers Medical publications, New Delhi (264-265,785-789).
8. Shah VR: Immunosuppressants and anaesthetist. *Transplantation India* 2003; 2(1):7-12.
9. Davison JM, : Renal Transplantation and pregnancy. *Am J Kidney Dis.* 1987; 9(4): 374-80.

Education is Social process....

Education is growth....

Education is not preparation for

life; education is life itself.

- JOHN DEWEY