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Original Research Article

Anesthesia management of renal transplantation: A retrospective analysis

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ABSTRACT

Background: Transplantation provides a near normal life and excellent rehabilitation compared to dialysis and is preferred method of treatment for end stage renal disease patients.
Materials and Methods: After ethics committee approval, a retrospective analysis of recipients of renal transplantation was done at our hospital from January 2010 to December 2014. Preoperative patient status, fluid management, hemodynamic parameters, anesthesia management, and perioperative complications were recorded and analyzed.
Results: Total 100 patients were recorded, 92% living and 8% were cadaveric related transplant. 92% were done electively. Most common co-morbidity recorded was hypertension in 49% patients. Predominant cause of end stage renal disease was chronic glomerulonephritis (41%). General anesthesia was technique of choice in all patients, 27 also received epidural. Invasive blood pressure monitoring was done in 3 patients with cardiac co-morbidities. 15% patients required blood transfusion. CVP maintained > 12 mmHg and maximum at de-clamping. Mean arterial pressure maintained above 95 mmHg. Ionotropic support required in 2 patients. 76% patients were transfused with only crystalloid (NS and/or RL) while 24 patients received a combination of both crystalloid and colloid. 97% patients were extubated postoperatively while 3% required ventilator support. Recovery time with desflurane was significantly less as compared to other inhalational agents. One patient died postoperatively.
Conclusion: Recent advances in surgical techniques, anesthesia management and immunosuppressive drugs have made renal transplantation safe and predictable. Preoperative patient optimization, intraoperative physiological stability and postoperative care of renal transplant patients have contributed to the success of renal transplant program in our hospital.

1. Introduction

Transplantation provides a near normal life and better rehabilitation as compared to dialysis. It is the treatment of choice for patients with end-stage renal disease,[1] and is much more cost effective than maintenance dialysis.[2] Understanding the minute alterations in Physiology, is important in providing successful and safe perioperative management.[3] Co-morbid diseases in chronic renal failure patients are common and frequently severe. Cardio-vascular complications have been described in 10% of renal transplant recipients. Associated co-morbid diseases increase the complexity of anesthesia management.[4] Vigilant intraoperative monitoring, optimization of intravascular fluid volume status to maintain maximum kidney perfusion, to avoid fluid overload, and early correction of electrolyte abnormalities (especially Potassium) are the crux of short and long term success of renal transplants.[5]

With the expanding criteria for taking patients for kidney transplantation, anesthesiologists are likely to be encountered with more problems of the interaction of other co-morbid diseases and multiple drug therapies in the near future.[4] Anesthesia management has changed along with

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the advances and developments in medical and surgical field. This study is to analyze preoperative assessment and patient optimization, intraoperative hemodynamic monitoring, postoperative management and complications in renal transplant recipient.

2. Materials and Methods

At first, approvals from ethics committee (project no. EC/73/2015) and concerned departments (nephrology and urology) were taken. As this is a retrospective study, waiver of consent was obtained from ethics committee. After that, records of living and cadaveric kidney transplants conducted from January 2010 to December 2014 were reviewed at our hospital. As per the hospital policy, all events that occurred were noted manually and a copy of perioperative anesthesia notes written by the concerned anesthesiologist was preserved. We noted age, sex, type of transplant, cause of chronic kidney disease, preoperative details, dialysis history, preoperative optimization and investigations, anesthesia management, monitoring details and the outcome were also recorded.

In the given duration 100 record sheets were available with good data. Live related donors (92 patients) belonged to ASA 1 and 2 grades. All living donor nephrectomies, including some laproscopic nephrectomies were performed under general anesthesia. However, our study focused on anesthesia management of the recipients of kidney transplant.

2.1. Statistical analysis

Data was statistically described in terms of mean (±SD), frequencies (number of cases) and percentages where appropriate. Comparison of quantitative variables between the study groups was done by Student's t-test for two independent samples. A probability value (p value) of <0.05 was considered statistically significant. All statistical calculation was done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 21.

3. Results

100 patients who underwent renal transplantation from Jan 2010 to Dec 2014 were in the age limit of 10 to 50yrs, with median age being 30 to 40yrs. Of the total patients, 8 underwent cadaveric renal transplant while 92 underwent living related transplant. (Figure 1) There was predominance of male patients with 81 males and 19 females. 6 patients were pediatric.

The causes of end stage renal disease (ESRD) were chronic glomerulonephritis (CGN)-41%, chronic interstitial nephritis (CIN) 19%, polycystic kidney disease (PCKD)-5%, obstructive nephropathy (Ob.N)-5%, diabetic

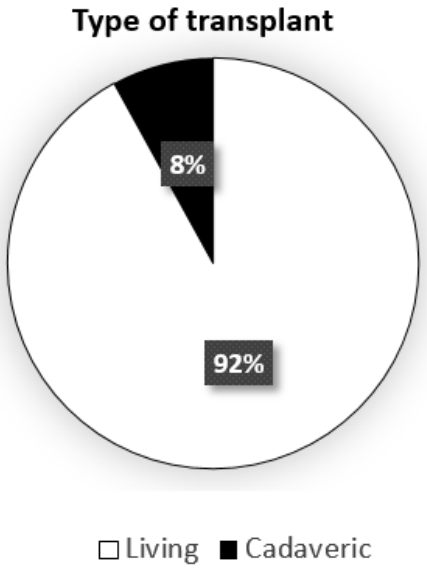

Fig. 1:

nephropathy (DN)-4%, Hereditary nephropathy -3%, Reflux nephropathy -3%, focal segmental glomerulosclerosis (FSGS)- 2%, membranoproliferative glomerulonephritis (MPGN) -1% and in 17% patients other causes were noted. (Figure 2)

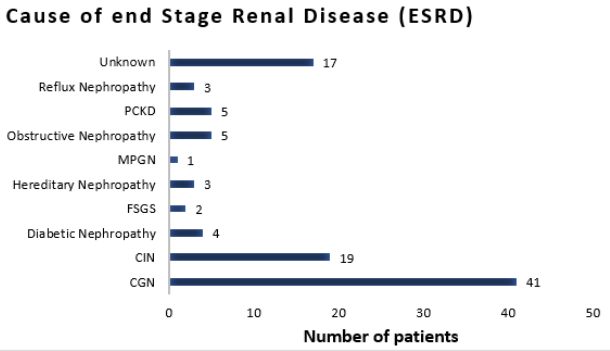

Fig. 2:

3.1. Preoperative status

All 100 patients in our study underwent hemodialysis within 24 hours before the procedure. Anemia was a common finding in most of the patients. Average hemoglobin was 8.2 g%, Hb was less than 8.2 g% in 9% of the patients and Iron supplement was given in all. Out of total, 29 also received erythropoietin and 14 received preoperative blood transfusion. Serum potassium levels were in the range of 2.8 to 6 meq/l with an average of 4.03 meq/l (±0.66SD). Serum creatinine levels ranges from 1.3 to 10.9mg/dl with

an average of 5.7mg/dl (±4.86SD).

Chest X-ray showed 8 patients had bilateral pleural effusion. Preoperative Electrocardiogram of 22 patients showed left ventricular hypertrophy, ST-T abnormalities (8), tall T wave (6), left atrial enlargement (9) and right bundle branch block (2). Ejection fraction was <30% in 1 patient, <40% in 2, between 40-50% in 30. Preoperative echo showed 2 patients with pericardial effusion and 1 had left ventricular thrombus. Human leukocyte antigen (HLA) matching was done in all.

Three-drug regimen of immunosuppressants including methylprednisolone, which was divided in three phases, was used to decrease graft rejection. Various drugs used for immunosuppression were Steroids, Cyclosporin, Tacrolimus, Sirolimus, Basiliximab, OKT 3, Azathioprine and Antilymphocyte globulin.

3.2. Anesthesia management

General anesthesia was the technique of choice in all 100 cases. Epidural was put in 27 cases along with general anesthesia. Living related renal transplants were performed electively while cadaveric done in emergency or semi-electively. Ranitidine hydrochloride 150mg was given orally one hour before surgery as pre-medication, in addition to the patients' regular medications.

Peripheral intravenous access was secured in the hand opposite to that of fistula. For induction, Propofol (2mg/kg) in 83% and thiopentone (5mg/kg) in 17% cases, was used. Maintenance of neuromuscular blockade with atracurium [0.6mg/kg] in 96 patients, rocuronium (0.6mg/kg) in 3 and vecuronium (0.1 mg/kg) in 1 patient. All patients were intubated and ventilated. Anesthesia was maintained with N_2O in oxygen (40:60) supplemented with 1-2% isoflurane (46), 4-6% desflurane (34), 1-2% sevoflurane (20) with fresh gas flow of 2-3 l/min. Fentanyl 2-3mcg/kg (93) or pentazocine 0.5mg/kg (7) was given for analgesia.

Intraoperative monitoring included heart rate, oxygen saturation, non-invasive blood pressure, end tidal CO2 and electrocardiogram in all patients. (Figure 3)

Central venous line was placed in all patients for central venous pressure (CVP) monitoring and 3 patients required invasive blood pressure monitoring. Average duration of surgery was 3.96hrs (±0.86SD). 76 patients were transfused with only crystalloid (NS and/or RL) while 24 patients received a combination of both crystalloid and colloid. 15 patients required intraoperative blood transfusion. All patients received injection furosemide average 1 to 1.5 mg/kg at the time of de-clamping to promote diuresis. Total ischemia time noted was on an average 54.9 min (±12.36SD). For every one-minute of warm ischemia time ten minutes of cold ischemia time was permitted. Kidney was placed in ice slush with a continuous perfusion of cold saline. Hemodynamic parameters were recorded hourly as well as according to intraoperative events. Vasopressor infusion was used in 2 patients during surgery.

Neuromuscular blockade was reversed with neostigmine 0.05mg/kg, and glycopyrrolate 8mcg/kg. Postoperatively, most of the patients were extubated, however, postoperative ventilatory support was needed in 3 patients

3.3. Postoperative care

Patients were transferred to post kidney transplant care unit. Rescue analgesia was provided with intravenous (i.v.) tramadol (50-100mg) in 48 patients, both i.v. tramadol and i.v. pentazocine (25-30mg) in 25 patients, 23 patients received epidural top up of 0.125% bupivacaine 8 hourly, 4 patients were given epidural plus i.v. tramadol.

Acute tubular necrosis (ATN) developed in 11 patients, pulmonary edema in 6 and 5 had pneumonia. Acute graft rejection was seen in 10 patients, which responded to thymoglobulins and immunosuppressants. Re-exploration needed in 2 patients either for thrombus in vessels or hematoma in the allograft. Postoperative mortality (over 6 months postoperatively) of 1 patient was seen. (Table 1) The rest of the patients received life-long triple drug immunosuppression.

Table 1: Shows the percentages of postoperative complications encountered in recipients of renal transplant

Post-op Complications	Number of patients	%
None	66	66.0%
Acute graft Rejection	10	10.0%
ATN	11	11.0%
Pneumonia	5	5.0%
Pulmonary edema	6	6.0%
Re-exploration	2	2.0%
Total	100	100.0%

4. Discussion

The treatment of choice in patients with end stage renal disease is renal transplantation, in both adults and children.[1,3,5–7] Although, there has been tremendous advances in field of renal replacement therapies, dialysis and other replacement therapies place major restrictions on patients and their families.[7] Adult data clearly depicts kidney transplantation is more cost effective, decreases long term mortality and also provides better quality of life as compared to long term dialysis.[2,3,7,8] Moreover, in patients undergoing long term dialysis, risk of cardiovascular disease is 10 to 30 times higher, and more than 50% deaths result from cardiovascular disease in dialysis patients.

Current audit shows that renal transplantation at our hospital has been successful. Proper planning, good team efforts, communication between all members participating in a transplant team in conjunction with good preoperative preparation of patients, are the factors responsible for better

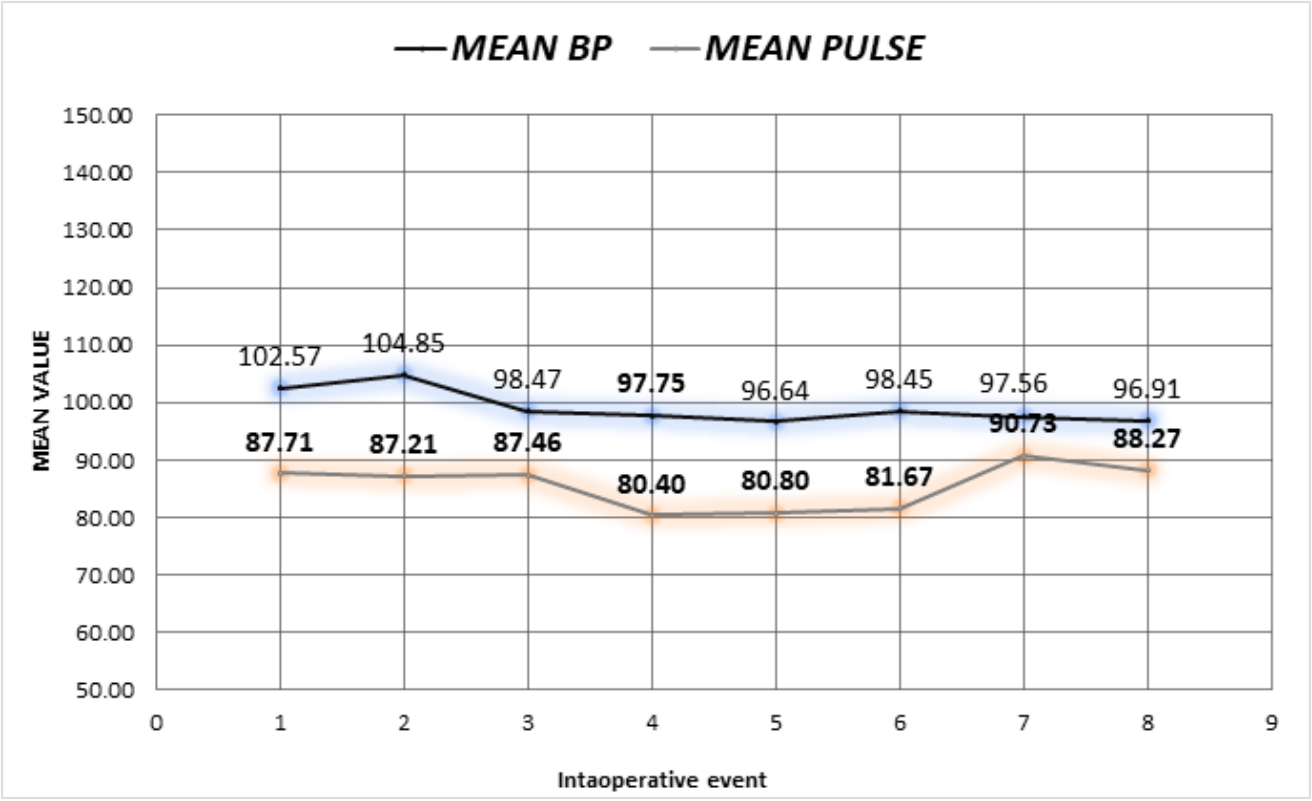

Fig. 3: Shows mean arterial blood pressure (Mean BP) & Mean pulse at various intraoperative events during renal transplantation. Intraoperative events – 1. Pre induction, 2. During induction, 3. Post induction, 4. During anastomosis, 5. Post anastomosis, 6. After release of clamps, 7. Extubation, 8. Post extubation

Table 2: Compares the mean recovery time amongst three inhalational agents (desflurane, sevoflurane & isoflurane). The p value obtained was <0.05, which was significant

Maintenance Agent	Number of patients	Mean recovery time (in mins)	SD	p- value
Desflurane	34	22.27	12.06	<0.05
Isoflurane	46	25.65	10.93	
Sevoflurane	20	31.25	12.97	
Overall	100	25.65	12.05	

outcomes. In patients with chronic kidney disease, any surgical procedure done would have significant increment in perioperative mortality and morbidity.[3,6]

Co-morbidities in patients with end stage renal disease are quite common and frequently severe.[3,6] Special attention should be given to presence of anemia, hypertension and assessment of intravascular volume status. Anemia has been found to be associated with cardiovascular morbidity and mortality.[6] Harnett et al.[9] observed independent risk of mortality in patient with dialysis to be 1.18 per one gram/dl fall in hemoglobin level.[9]

In our study, 15% patients who required intraoperative blood transfusion had a preoperative mean hemoglobin value of 9.01g% (+/-1.16), while the value was 10.41g% (+/-1.82) in 85% of patients who did not require intraoperative blood transfusion. The value was statistically significant (P value <0.01). Hence, preoperative iron supplements and hemoglobin levels are crucial in renal transplantation.

All the 100 cases in our study were done under general anesthesia and 27 were also given epidural. Epidural blockade is considered in high risk cases for general anesthesia, however epidural is considered in otherwise normal patients too. There are studies in which cases are done under continuous epidural blockade with intravenous sedation. In a study done by Anand Jain et al.[3] they used continuous epidural anesthesia with intermittent sedation in 5 cases, with no major complication recorded. Combined spinal-epidural is also gaining importance in renal transplantation. In an article by G. Bhosale et al.[10] it was concluded that, combined spinal-epidural is useful reginal technique in kidney transplant surgeries. In another study by N. Hadimioglu et al. they concluded that regional

(combined spinal and epidural) is an important alternative to general anesthesia.[11]

It had been observed that recipients' hemodynamic variables during renal transplantation have a great influence on early diuresis of graft. The most important measure intraoperatively is to maintain an optimum intravascular fluid volume to enhance early graft function.[5,12,13] Some studies has shown that in recipients of renal transplantation, intravascular volume must be high to counteract various immunological and physiological insults.[12,13] Central venous pressure between 10 and 15 mmHg is still widely accepted and recommended in anesthesia management of renal transplantation.[5,12,13] However, according to some authors intraoperative hydration might not be compulsory.[13,14] In our study, mean central venous pressure was maintained between 12.89 mmHg in post induction period to 17.30 mmHg at the time of release of clamps. These patients have a narrow margin of safety and may oscillate between hypo and hypervolemia.[15]

In graft dysfunction, hypotension is a significant factor. In our study mean arterial blood pressure after the release of clamps was 98.45 mmHg. In the study by Aulakh NK et al.[13] mean arterial pressure more than 95 mmHg with optimum perioperative hydration was found to have better early graft function. According to another study by Campos L et al.[14] mean arterial blood pressure >/= 93 mmHg and less than 2.5 liters perioperative fluid administration was related to better graft survival.

In perioperative medicine and organ transplantation, fluid management remains a controversial topic. Large volume of fluids used during intraoperative management of transplant patients had shown to improve graft function. Classically administration of more potassium containing solutions like lactated Ringer's can lead to hyperpotassemia and therefore Normal Saline has been used instead.

Crystalloid solutions are preferred usually to correct fluid and electrolyte disturbances.[3] However, colloids may be used in conditions like severe hypovolemia in emergency situation.[3] Over the few decades, anesthesiologists are bending towards the use of synthetic colloids instead of natural colloids such as albumin, blood and fresh frozen plasma. In a study by Cittanova ML et al.[16] nephrosis like lesions were observed in transplanted kidney obtained from deceased donor who received HES200/0.62.[17] In our study both crystalloid and colloid have been used for fluid replacement. 40% patients received crystalloid while 24% received both crystalloid and colloid with colloid being mainly gelatin based. Drub effect can be exerted by some fluids that could change organ preservation and reperfusion, however low molecular weight hydroxyl ethyl starch (HES) seems to be less harmful in renal transplantation than first thought, especially when free water requirements are taken into account by clinicians in these settings.[3]

Albumin, a normal endogenous colloid having wide safety margin can be used in patients with large fluid volume deficit. In our study 36% patients received a combination of crystalloid and albumin. In studies done by Shah RB et al.[18] and Schnuelle P et al.[17] it was concluded that albumin should be used in selective patients rather than routine protocol.

Among crystalloids, general consensus is to use Normal Saline and restrict use of potassium containing fluids like lactated Ringer's solution because of the potential risk of hyperkalemia. However, recent studies showed that use of large volume of normal saline found to be associated with hyperchloremic metabolic acidosis that can potentiate pre-existing acidosis, resulting hyperkalemia.[19–21] In our study majority of patients (67%) were given Normal saline while 31% patients received both lactated ringer's and normal saline, and 2% received only Ringer's lactate. In recent studies done by O'Malley CM et al.[22] and Manisha P. Modi et al.,[20] they concluded that lactated ringer's may be a safer choice in live related renal transplantation as it avoids the chances of metabolic acidosis and significant hyperkalemia.[19,22] In another study by Jorge Alejandro Trujillo Zea et al.[23] the authors found that lactated ringer's used in the perioperative period of renal transplant surgeries, resulted in similar potassium levels during the postoperative period, higher bicarbonate and pH levels, and also lower chlorides, despite using the similar infusion volume in comparison to normal saline solutions.[23]

Cardiovascular disease is an important comorbidity in patients with chronic renal failure.[24] Perioperative cardiovascular complication rate is 6% in renal transplant procedures.[20] One of the poor predictors of prognosis in such patients is ejection fraction <25%.[21] In our study one patient has ejection fraction of 25%, the patient was posted electively after preoperative optimization. Induced with titrated doses of injection fentanyl & injection Propofol. Anesthesia was maintained with Nitrous Oxide, Oxygen and Desflurane. Intraoperatively preload was maintained, we avoid increase in afterload and hypotension, fluid was titrated to maintain CVP of 12 to 15 mmHg, Patient was extubated uneventfully. In a study done by Divya Srivastava et al.[24] they published anesthesia management of 8 Renal transplant patients with Dilated Cardiomyopathy having ejection fraction < 40%. They preferred combined spinal epidural over GA in such patients and concluded that careful preoperative optimization, vigilant intraoperative monitoring, modification of anesthetic plan to patient's specific needs, optimization of fluid volume status, and postoperative care is crucial in success of renal transplant in such patients.[24]

In our study, neuromuscular blockade was maintained with Atracurium (96%), Vecuronium (1%) or Rocuronium (3%). Prolong neuromuscular blockade with delayed recovery was seen in 3 patients and needed postoperative

ventilator support. Mean recovery time was significantly less ($p<0.05$) in patients with desflurane (22.27 mins) as compared to sevoflurane (31.25 mins) or isoflurane (25.65 mins). (Table 2) In a study by Ergönenç J. et al.[25] it was concluded that desflurane provides better quality and more rapid recovery than sevoflurane, and the return of cognitive functions in the early postoperative period was faster, as was found in our study. In another recent study by Arpa Chutipongtanate et al.[26] it was observed that desflurane induces peripheral blood Tregs (regulatory T cells) increment after 24-h exposure, which could be beneficial in the context of kidney transplantation.

Postoperative care of renal transplant recipients is also crucial. Postoperative complications should be diagnosed and treated as soon as possible. Postoperative mortality was noted in one patient (weight 104 kgs), as the transplant was done in emergency without preoperative optimization.

5. Limitation of Study

Major limitation of study is missing data as the study is retrospective in nature. The other is that, the experience of the study is six year ago so a lot of advancement in technique and management of renal transplantation has happened.

6. Conclusion

Transplant anesthesia is a specialized field, which requires a good understanding of the abnormalities in patients with renal failure, familiarity with transplant medicine and expertise in management of these patients. With improvement in anesthetic and surgical techniques as well as immunosuppressive drugs, many patients are being accepted for transplantation who would have been considered unsuitable earlier. Proper patient selection, preoperative patient preparation and intraoperative physiological stability with close association between nephrologists, urosurgeons and anesthesiologists was found to be crucial in the management of our renal transplant patients and had given us good results. Further large scales studies are desired.

7. Source of Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

8. Conflicts of Interest

None

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