Thrita. 2015 September; 4(3): e29441. DOI: 10.5812/thrita.29441
Published online 2015 September 7. **Research Article**

Anesthetic Experience of 1000 Cases During 10 Years in Renal Transplantation: A Retrospective Study

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Received: April 25, 2015; **Accepted:** May 2, 2015

Background: Since the first renal transplantation surgery, clinical studies have failed to ascertain the benefit of one anesthetic technique over another.
Objectives: This article provides an overview of the important issues to be considered in these patients, and also discusses several anesthetic challenges in these surgeries.
Patients and Methods: Through a retrospective study, we described our experience during 10 years, from 2002 until 2012, in 1000 cases of living and cadaveric transplants. We reviewed their medical history and noted age, sex, blood groups, cause of end stage renal disease, history of dialysis and the type of renal transplantation. Preoperative investigation and preparation, as well as details of anesthetic management, were also recorded.
Results: General anesthesia was performed in 82% of patients and for the rest of them, spinal, epidural and combined spinal and epidural were done. The age of the patients was in the range of 12 - 68 years, with the mean of 36 ± 11 years. The mean of surgery duration was 2.9 ± 1.1 hours. The most significant point during surgery is keeping the mean arterial pressure > 95 mmHg and maintaining fluid load with crystalloid.
Conclusions: The type and amount of fluid replacement therapy and optimizing hemodynamic status, before and during reperfusion of the transplanted kidney, are of particular importance during renal transplantation surgery.

Keywords: Anesthesia; Kidney Transplantation; Delayed Graft Function; Reperfusion; Blood Pressure

1. Background

Kidney transplantation is the preferred therapeutic option for patients with end-stage renal disease (ESRD). Patients undergoing renal transplant surgery have several high risk features, like cardiovascular diseases, diabetes mellitus, and need for hemodialysis.

The appropriate anesthesia for renal transplantation requires a thorough understanding of metabolic and systemic abnormalities induced by the ESRD. Being familiar with transplant medicine and having expertise in management and optimization of these patients, for the best possible outcome, is of great significance (1). Anesthetic methods, which are used in this operation, are dependent on knowledge, experience and familiarity of the anesthetist with the special conditions of this surgery.

2. Objectives

The aim of this study was to find the characteristics of patients, causes of ESRD, anesthetic management and the impact of pre-existing diseases on intraoperative or early postoperative complications of the recipients.

3. Patients and Methods

This retrospective study was conducted at Sina University Hospital affiliated to Tehran University of Medical Sciences, Tehran, Iran. All patients registered their names and completed their medical documentation in the Iranian Renal Disease Society and took an informed consent of their renal transplantation. We reviewed the medical history of 1000 cases of living and cadaveric renal transplants from 2002 to 2012, and noted age, sex, blood groups, cause of ESRD, history of dialysis and type of renal transplantation. Preoperative investigation and preparation, as well as details of anesthetic management, were also recorded.

4. Results

One thousand renal recipient patients were enrolled in this study with an age range of 12 - 68 years and a mean

of 36 ± 11 years. The male patients comprised 68.5% and the female 31.5% of the total. In 62.6% of the cases, patients had received the kidney from a living donor, whereas the source of kidney in 37.4% of the patients was a cadaver. The causes of ESRD are shown in the Table 1. Twenty six (2.6%) patients had repeated transplantation. A number of 930 (93%) patients had already been on hemodialysis, of which 11 (1.1%) were on peritoneal dialysis, and only 59 (5.9%) were primitive transplantation cases, without any history of dialysis. The mean of surgery duration was 2.9 ± 1.1 hours. Preoperatively, all patients had routinely undergone cardiovascular, upper and lower respiratory, gastrointestinal and hematologic work-up. A total of 948 (94.8%) of the patients had revealed a pre-existing problem (Table 2). The blood groups distribution among the patients is also shown in Table 2. Anemia was the most common co-existing problem. The average hemoglobin level before operation was 8.6 ± 0.7 mg/dL A proportion of 76% of the patients took iron supplements and only 18% received erythropoietin. The mean of total blood loss during operation was 340 ± 52 mL. Only in 43 patients, the volume of bleeding exceeded 500 mL. Therefore, one unit of packed red cells was transfused to these patients.

Table 1. Frequency of the Causes of End-Stage Renal Disease

Etiology	Number
Systemic hypertension	346
Diabetes mellitus	168
Congenital kidney malformation	23
Autoimmune disease	125
Polycystic kidney	68
Kidney stone	54
Infection	48
Unknown	168

Table 2. Frequency of the Co-Existing Diseases and Blood Groups of the Recipients

Variables	Percent
Co-existing disease	
Anemia	78.3
Diabetes mellitus	15.4
Systemic hypertension	42.7
Heart failure	7.6
Pulmonary hypertension	3.2
Pleural effusion	7.9
Hypothyroidism	8.3
Blood groups	
O	37.6
A	30.3
B	26.4
AB	5.7

4.1. Intra-Operative Anesthesia Management

The anesthetic choice, in most of the cases (820), was general anesthesia. For the rest of them, we administered spinal anesthesia (55), continuous epidural (60) and combined spinal and epidural technique (65). We chose regional technique for patients with heights higher than 155 cm and BMI < 30, who consented to this procedure.

In our center, all living related renal transplants were done electively, early in the morning, while the cadaveric renal transplants were done in emergency situations. Perioperative immunosuppressive therapies were administered to all patients, according to our institutional protocol: 1. Mycophenolate mofetil (Cellcept, Roche, Basel, Switzerland): 1 g; 2. Cyclosporine (Neoral, Novartis AG, Basel, Switzerland): 5 - 6 mg/kg, 3. Methylprednisolone: 6 - 7 mg/kg.

In elective cases, for reducing the risk of volume overload, hyperkalemia and achievement of a better hemostasis, hemodialysis was performed for all recipients, within 24 hours before surgery. Peripheral intravenous access was secured in the hand opposite to the functioning fistula. Central venous line was inserted for all patients. Radial artery catheterization was performed in 225 patients for obtaining blood gas analysis and hemodynamic monitoring, in unstable patients. The induction of anesthesia was performed with a combination of midazolam (0.03 - 0.06 mg/kg) and fentanyl (1 - 3 μg/kg) and 1 mg/kg lidocaine, as premedication, thiopental sodium (3 - 5mg/kg) as a hypnotic drug. For preparing muscle relaxation, atracurium (0.5 mg/kg) was employed. Anesthesia was maintained with isoflurane 1% - 1.5%, atracurium 10 mg/40 minute, fentanyl 50 - 75 μg/h. The nitrous oxide supplementation with oxygen was maintained for all patients, except in those with O_2 saturation of less than 95% or in the case of bowel expansion that bulged into the surgical filed.

In the regional technique, spinal anesthesia was induced by hyperbaric bupivacaine (15 - 20 mg) plus 25 μg fentanyl and 0.2 mg adrenaline, in the lateral position, according to the surgical side and the level of anesthesia was kept at T6 level. In epidural anesthesia, the procedure was done at L2 - L3 or L3 - L4 level, with Tuohy needle and the catheter was advanced five to eight cm in the epidural space. At first, bupivacaine (0.5%) 10 mg was injected and then bupivacaine (0.5%) 8 - 10 mg/h was infused, during the surgery. For intraoperative sedation, midazolam and fentanyl were administrated, based on the needs of the patients.

Intraoperative monitoring included heart rate, noninvasive blood pressure, central venous pressure, electrocardiogram, oxygen saturation and end tidal CO_2, in all patients. Intraoperative hypertension was controlled with bolus IV injection of 5 - 10 mg labetalol (65 cases) or nitroglycerin infusion (25 cases), to keep the mean arterial pressure (MAP) in the range of 95 - 105 mmHg. Hypotension was managed with dopamine infusion (42 patients) to keep the MAP > 90 mmHg. In all patients with the diagnosis of severe pulmonary hypertension (seven cases), we started infusing norepinephrine drip, before

injection of anesthetic drugs, to avoid decreasing systemic vascular resistance and blood pressure during the induction of anesthesia (2, 3). Regarding the intraoperative replacement fluid that was used, it must be mentioned that during 2002 - 2008, normal saline (65 - 75 mL/kg) was the intraoperative replacement fluid of choice (534 cases). Gradually, our experience led us toward a combination of ringer lactate and normal saline, administered in equal amounts, to avoid increasing metabolic acidosis. In all cases, before artery clamping, heparin 3 - 4 unit/kg was intravenously injected. The mean time of vessel grafting was 25 ± 7.5 minutes, the renal artery was usually grafted to common iliac artery (780 cases), and external iliac artery graft was less common. In all patients, before reperfusion of the kidney, 5 mg verapamil was injected into the renal artery by the surgeon, using an insulin needle. After reperfusion of the kidney, in all patients, intravenous furosemide (150 - 200 mg) was slowly given. In this period, according to color, stiffness and turgidity of the transplanted kidney in the hand of the surgeon, we tried to optimize the blood pressure (MAP > 95 mmHg), using rapid crystalloid infusion, lower the level of anesthesia or perform dopamine infusion.

In cadaveric renal transplant, 0.5 g/kg of mannitol were continuously infused from skin incision to the end of the operation.

At the end of the operation, neuromuscular blockade was reversed with IV injection of neostigmine (0.05 mg/kg) combined with atropine (0.025 mg/kg). Postoperatively, most of the patients were extubated immediately, without any complication. However, in 46 patients, reversal of muscle relaxation was delayed and undergoing ventilator support for about 1 - 2 hours was necessary. Five patients were sent to the intensive care unit because of developing low blood pressure and pulmonary edema. Eighty-eight percent of the patients had a good early renal graft function and the creatinine serum level decreased within the first 2 postoperative days. In 10% of the patients, renal graft function within 3 - 5 days came back to near normal level, while in 2% of the cases, the serum creatinine level did not decrease and, eventually, three patients needed to undergo hemodialysis.

4.2. Postoperative Care

The most common problem in the recovery unit was pain. The rescue analgesia was provided with IV morphine (4 - 6 mg) for 492 cases, IV pethidine (25 - 30 mg) for 158, IV tramadol (50 mg) for 75 and IV infusion of paracetamol for 150 patients. Epidural analgesia was also used in 125 patients to relive the postoperative pain. Catheter bladder discomfort (CRBD) was the next common problem in recovery that presented as the urge to pass urine or discomfort in the suprapubic region. This problem was more significant in general anesthesia patients and in several instances became a confounding factor to assess the pain in the surgical site. In 35% of the patients, it was so severe that resulted in agitation and pulling the catheter. These patients needed IV ketamine 25 mg one or two times plus 2 - 3 mg morphine, for treatment. Postoperative nausea and vomiting were seen in 23% of the patients, especially after opioid injection, requiring IV injection of ondansetron or metoclopramide. Only 20 (2%) patients had profound hypotension (MAP ≤ 50 mmHg) that needed crystalloid and dopamine infusion. Because of excessive blood drainage, five patients came back to the operating room. Totally, 32 cases of pulmonary hypertension existed. Sixteen of them had mild and nine of them had moderate pulmonary hypertension, while seven cases had severe pulmonary hypertension.

5. Discussion

The kidneys are essential for adjusting body fluid volumes, electrolyte composition, acid base balance, and hemoglobin concentration (4). Absence of the physiologic function of the kidneys leads to uremia. Effective and safe anesthesia for renal transplantation depends on an understanding of the pathophysiology and biochemistry of uremia and its effect on the pharmacokinetics and metabolism of drugs used (5). In addition, comorbid conditions represent a common problem and, frequently, are very severe, leading to complications of the anesthesia and surgical process (6, 7).

During the early years, the number of living donor transplants, in comparison to cadaveric transplants, was high (up to 65% of total cases per year). However, by increasing facilities of cadaveric donor during recent years, cadaveric donor transplantation has increased to 85% - 90% of the total cases of renal transplant per year. In this review, the anesthetic choice was general anesthesia that is in congruence with the other studies (8). The successful use of regional anesthesia has been reported by several researchers (9). We used epidural anesthesia in selected patients. We assumed that postoperative pain would be better controlled by this technique (10). We performed spinal anesthesia for tall and non-obese patients, especially those with hypertension or lung or endocrine disorders, to keep the minimal toxicity for the patient and transplanted kidney, in addition to sufficient pain relief and maintenance of vital functions (11).

The American Society of Anesthesiologists standard monitoring recommendation is usually followed. Patients with more advanced comorbid conditions, like heart failure, may require more extensive monitoring, such as invasive blood pressure (1).

The autoregulation of renal blood flow, which is caused by the myogenic response and tubuloglomerular feedback, enables the kidney to maintain solute and water regulation independent of wide fluctuations of arterial blood pressure (12). However, in the kidney transplant recipients, in whom kidneys were already considered functionally denervated and ischemic, the autoregulation is, at a certain degree, impaired. Therefore, this issue forced

us to maintain normal to high blood pressure, hoping that the kidney preserves its perfusion (13).

It is noteworthy that urinary flow rate is not subject to autoregulation. Tubular water reabsorption determines urinary flow rate and is closely related to the hydrostatic pressure in the peritubular capillaries (14). Care should be taken to maintain normovolemia and normotension, to evade decreases in renal perfusion. Avoiding intraoperative renal insults and maintaining isovolemia, adequate cardiac output, and renal perfusion pressure are the best interventions to prevent postoperative kidney injury and are more important than the choice of a specific anesthetic technique (15). In our experience, the color, stiffness and turgidity of kidney, under the hand of the surgeon, were the best indicators of adequacy of renal perfusion and predictors of graft functionality in the postoperative period.

Fluid management remains a controversial subject, in organ transplantation (16). To keep the intravascular volume, crystalloid solutions are usually preferred. At the beginning of our experience, normal saline was the crystalloid of choice, although it might make the underlying acidosis worse and may eventually aggravate hyperkalemia. Therefore, after our study regarding the use of Ringer lactate, as a safe intraoperative fluid replacement therapy, we changed our policy to use a combination of normal saline and Ringer lactate in equal amounts (17). In another study, it has been shown that intraoperative tight control of metabolic acidosis. by infusion of sodium bicarbonate, improves early post-operative renal function in renal transplant recipients (18).

Finally, in the postoperative period, control of pain and agitation were the other challenges of the anesthesiologists. In regional techniques, we observed these problems in a small proportion of the patients. However, in general anesthesia patients, to reduce the intensity of surgical pain and agitation, resulting from CRBD, we had to use IV narcotics or paracetamol at the end of surgery (19). In addition, IV ketamine, prior to intraoperative bladder catheterization, was used to reduce the incidence of CRBD in the postoperative period (20).

Regarding the distribution of blood groups in recipients, it was similar to the normal blood groups distribution in the Iranian population (21).

Anesthesia for renal transplant surgery poses a challenge for the attending anesthesiologist. According to the general status of the patient and the underlying problem, each patient needs an individualized intra- and postoperative anesthetic regimen. The type and amount of fluid replacement therapy and optimizing hemodynamic status before and during reperfusion of the transplanted kidney are of particular importance during renal transplantation surgery. Therefore, performing an appropriate anesthesia management and not a particular anesthetic regime can improve renal outcome, after renal transplant surgery.

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