Comparison of Two Different Inhalation Anesthetics on Grafted Kidney Function in Patients Undergoing Renal Transplantation Surgery: Desflurane or Sevoflurane?

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ABSTRACT

Background. Anesthetic management of patients during renal transplantation is vitally important for ensuring proper functioning of kidneys that have undergone ischemia-reperfusion damage. The goal of this prospective study was to compare the effects of 2 different inhalation agents (sevoflurane and desflurane) on grafted kidney function in renal transplantation surgery.

Methods. Sixty-five patients who were scheduled for living donor renal transplantation were enrolled in the study. General anesthesia was performed on all patients. Thirty-five pairs of recipients and donors were anesthetized with sevoflurane (group S) and 30 pairs of recipients and donors were anesthetized with desflurane (group D). Each patient's demographic characteristics, immunologic and clinical data, and hemodynamic parameters were recorded. The estimated glomerular filtration rate was calculated in the preoperative period and on postoperative days 1 and 7. The blood samples were collected before the operation and on postoperative days 1 and 7 for measurement of serum creatinine, neutrophil gelatinase-associated lipocalin, and interleukin 18.

Results. There were no significant differences in demographic characteristics or immunologic data between group D and group S. Intraoperative heart rate and mean arterial blood pressure were the same between groups. Creatinine, estimated glomerular filtration rate, neutrophil gelatinase-associated lipocalin, and interleukin 18 values did not differ between groups ($P > .05$) in the preoperative period and postoperative days 1 and 7.

Conclusions. Sevoflurane and desflurane had no adverse effects on grafted kidney functions according to short-term graft outcomes in patients undergoing living donor renal transplantation.

ANESTHETIC management of patients during renal transplant surgeries is vitally important for ensuring proper functioning of kidneys that have undergone ischemia-reperfusion damage. Intraoperative hemodynamic stabilization must be maintained, and anesthetic agents that have adverse effects on kidneys are to be avoided. Sevoflurane and desflurane are the most frequently used inhalation agents in modern anesthesia [1]. It is well known that neither of these drugs has toxic effects on the kidneys unless the safe dose range is exceeded. However, some studies

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have suggested that compound A, which emerges with the interaction of carbon dioxide absorbents and inorganic fluoride ions as the byproduct of sevoflurane metabolism, causes nephrotoxic effects in rats [2–4].

In renal transplantation surgery, a limited number of studies have emphasized the effects of inhalation agents on transplanted kidney function [5,6]. Blood urea nitrogen (BUN), serum creatinine, and creatinine clearance were used in the evaluation of kidney function in these studies. However, those parameters are affected by several factors (eg, diet, sex, body mass index), and they take at least 24 to 48 hours to increase in the event of kidney dysfunction; thus, diagnosis may be delayed. Currently, interleukin 18 (IL-18) and neutrophil gelatinase-associated lipocalin (NGAL), which increase within a few hours of ischemic kidney damage, are used for early diagnosis of acute renal injury.

The goal of the present prospective study was to compare the effects of 2 different inhalation agents (sevoflurane and desflurane) on grafted kidney function in renal transplantation recipients by measuring serum NGAL, IL-18, and creatinine levels and estimated glomerular filtration rate (eGFR) in the perioperative period.

PATIENTS AND METHODS

We enrolled 70 patients between 18 and 45 years of age who were diagnosed with end-stage renal disease and scheduled for living donor kidney transplant. This prospective, randomized clinical study was conducted between April 2013 and October 2015. Approval for the study was obtained from the Ethics Committee of Istanbul Medical Faculty (2013/1073), and written informed consent was obtained from the patients 1 day before the surgery. Before renal transplantation, immunologic factors (eg, a number of matched [HLA]-A, -B, -DR, crossmatch test, pretransplant and posttransplant HLA antibodies) that affect grafted kidney function were analyzed in all patients.

Two different inhalation anesthetic agents were administered to the recipients. The patients were divided into group S (sevoflurane) and group D (desflurane) using a computerized single block randomization. Similarly, the same volatile anesthetic agents were administered to donors. Routine motorization was provided by using electrocardiograms, invasive blood pressure, and pulse oximetry. An intravenous 5 mL/kg/h 0.9% NaCl infusion was started in the operating room. Anesthesia was induced using 0.03 mg/kg of midazolam, 2 mg/kg of propofol, 0.2 μg/kg of remifentanil, and 0.5 mg/kg of rocuronium. After insertion of an endotracheal tube, mechanical ventilation was started with a tidal volume of 8 mL/kg, a respiratory rate of 10 to 12 breaths/min, and a positive end-expiratory pressure of 4 cm H_2O; it was then targeted to achieve an end-tidal carbon dioxide concentration of 32 to 35 mm Hg throughout the operation. General anesthesia was maintained with 4% to 6% desflurane in group D and 2% to 3% sevoflurane in group S with a mixture of 50% oxygen and 50% air with 2 L of fresh gas flow.

We aimed to keep the end-tidal volatile anesthetic concentration of 1.2 to 1.4 MAC for anesthesia maintenance. The goal was to maintain intraoperative blood pressure within 20% of preoperative values. If hypotension occurred, the patients were treated with volume replacement and incremental ephedrine doses of 5 mg. Bradycardia (heart rate [HR] <50 beats/min) was treated with 0.01 mg/kg of atropine. All patients received continuous infusion of remifentanil (0.1–0.2 μg/kg) throughout the operation. Soda lime was used as a carbon dioxide absorbent. An anesthetics gas analyzer (Datex-Ohmeda, Helsinki, Finland) was used to measure the end-tidal volatile anesthetic concentration. After induction of anesthesia, invasive arterial and central venous pressure monitorization was applied to all patients. We administered 0.9% NaCl to maintain central venous pressure at 12 to 15 mm Hg throughout the operation, and 15 mg/kg of methylprednisolone was administered to patients before reperfusion. All surgeries were performed by the same surgical team.

At the end of surgery, residual muscle relaxants were reversed with neostigmine, and all patients were extubated. The recipients were transported to the postanesthesia care unit after endotracheal extubation, and 1.5 mg/kg of intravenous tramadol and 1 g of paracetamol were administered for postoperative pain control. The patients were transferred to a transplantation ward when the discharge criteria were met. Immunosuppressive therapy for renal transplant patients in the postoperative period consisted of a combination of tacrolimus with mycophenolate mofetil/mycophenolate sodium and prednisolone.

Demographic characteristics of all patients, duration of surgery and anesthesia, warm and cold ischemia time, intraoperative hemodynamic data (eg, HR, mean arterial pressure), and the amount of intravenous fluids were recorded. eGFR were calculated by using the Modification Diet in Renal Disease Study equation in the preoperative period and postoperative days 1 and 7. Acute rejection and graft loss within 1 month of transplantation were also documented.

Collection of the Samples

Blood samples were obtained for the measurement of serum creatinine, NGAL, and IL-18. The samples were collected before the operation and on postoperative days 1 and 7. Specimens were centrifuged at 2600*g* for 10 minutes to remove the sediment. Serum samples were frozen in 1-mL aliquots at −20°C.

Determination of Serum NGAL and IL-18 Levels

Serum levels of NGAL and IL-8 were evaluated by using a commercial enzyme-linked immunosorbent assay kit (Bioassay Technology Laboratory, Korean Biotech Co, Ltd) by following the manufacturer's instructions.

Statistical Methods

The creatinine level was 1.5 ± 0.5 mg/dL on postoperative day 7 with desflurane in this pilot study. We calculated that a minimum of 27 patients would be required for each group to obtain an SD of 0.4 with α and β errors of 0.05 and 0.2, respectively. We therefore chose to include 35 patients in each group in case of dropouts. All statistical analyses were performed by using SPSS version 21.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, United States), and P values $< .05$ were considered significant. The Kolmogorov-Smirnov test was performed to assess the deviation from normal distribution. Quantitative variables were summarized as mean ± SD. The Student t test was used for parametric data in the comparison of groups, and the Wilcoxon signed-rank test was used for paired data. The χ^2 test and the Fisher exact test were used to identify the frequency and rate in categorical variables and to calculate variations between the groups.