ORIGINAL RESEARCH

Impact of Propofol vs. Sevoflurane on Oxidative Stress and Pathological Changes in Renal Tissue

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ABSTRACT

Aim: This study aims to compare the impact of Propofol and Sevoflurane anesthesia on oxidative stress markers and pathological changes in renal tissue in patients undergoing elective surgery. **Materials and Methods:** This prospective, randomized clinical study included 80 adult patients (ASA I-II) scheduled for non-renal surgeries lasting at least 90 minutes. Patients were randomly assigned into two groups: Propofol (Group P, n=40) and Sevoflurane (Group S, n=40). Oxidative stress markers, including malondialdehyde (MDA) and superoxide dismutase (SOD), were measured at baseline (T0), end of surgery (T1), and 24 hours postoperatively (T2). Renal function was assessed using serum creatinine, blood urea nitrogen (BUN), and neutrophil gelatinase-associated lipocalin (NGAL) at preoperative, 24-hour, and 48-hour time points. Histopathological analysis of renal tissue was performed in a subset of patients. **Results:** Baseline characteristics were comparable between the two groups. At T1 and T2, MDA levels were significantly higher in the Sevoflurane group ($p=0.02$, $p=0.04$), while SOD levels were lower ($p=0.01$, $p=0.03$), indicating greater oxidative stress. Serum creatinine and BUN levels were significantly elevated in the Sevoflurane group at 24 and 48 hours postoperatively ($p<0.05$). NGAL levels were also significantly higher in the Sevoflurane group at both postoperative time points ($p=0.01$, $p=0.02$). Histopathological analysis showed greater tubular injury, glomerular changes, and inflammatory infiltration in the Sevoflurane group ($p<0.05$). **Conclusion:** Sevoflurane anesthesia is associated with increased oxidative stress, higher renal injury markers, and greater histopathological damage compared to Propofol. Propofol appears to have renal-protective effects, likely due to its antioxidant properties. These findings suggest that anesthetic selection should consider potential renal implications, particularly in high-risk patients.

Keywords: Propofol, Sevoflurane, oxidative stress, renal injury, anesthesia

INTRODUCTION

Anesthesia plays a crucial role in modern medicine, facilitating surgical procedures by inducing a controlled state of unconsciousness, analgesia, and muscle relaxation. Among the widely used anesthetic agents, propofol (a commonly used intravenous anesthetic) and sevoflurane (a volatile inhalational anesthetic) have distinct pharmacological profiles and physiological effects. While both drugs are effective in maintaining anesthesia, their impact on various organ systems, including the kidneys, has become an area of increasing interest. Specifically, the potential for oxidative stress and pathological changes in renal tissue associated with these anesthetic agents warrants deeper investigation.[1]The kidneys play a vital role in maintaining homeostasis, filtering metabolic waste, regulating electrolyte balance, and managing fluid equilibrium. However, they are highly susceptible to oxidative stress, a condition characterized by an imbalance between reactive oxygen species (ROS) production and the body's antioxidant defense mechanisms. Excessive oxidative stress can result in cellular damage, inflammation, and apoptosis, contributing to renal dysfunction and disease. Anesthesia-induced oxidative stress is a growing concern, as prolonged exposure to certain anesthetics has been linked to increased ROS generation, mitochondrial dysfunction, and structural damage to renal tissue.Oxidative stress in the kidneys can arise from multiple sources, including ischemia-reperfusion

injury, surgical trauma, and drug-induced toxicity. When ROS accumulate beyond the antioxidant capacity of the body, they interact with cellular components such as lipids, proteins, and DNA, leading to lipid peroxidation, protein denaturation, and genetic mutations. The kidneys, with their high metabolic activity and rich vascular network, are particularly vulnerable to oxidative stress-induced injury. Chronic oxidative stress can contribute to tubular atrophy, interstitial fibrosis, glomerular damage, and impaired renal function, ultimately increasing the risk of acute kidney injury (AKI) and chronic kidney disease (CKD).[2]

Anesthetics influence oxidative stress in multiple ways. Some anesthetic agents have been found to increase ROS production, disrupt mitochondrial function, and impair renal autoregulation. Conversely, certain anesthetics exhibit antioxidant properties, reducing oxidative damage and providing potential renal protection. The impact of anesthesia on renal oxidative stress is influenced by multiple factors, including dosage, duration of exposure, patient-specific conditions (such as pre-existing renal disease), and surgical stressors.[3]

Propofol, an intravenous anesthetic widely used for induction and maintenance of anesthesia, is known for its rapid onset, short duration of action, and favorable recovery profile. Beyond its anesthetic properties, propofol has been shown to possess antioxidant properties, largely attributed to its structural similarity to α-tocopherol (vitamin E), a well-known free radical scavenger. Studies suggest that propofol reduces ROS levels, inhibits lipid peroxidation, and stabilizes mitochondrial function, which may help mitigate oxidative stress-related renal injury.Additionally, propofol exerts anti-inflammatory effects by downregulating pro-inflammatory cytokines and modulating signaling pathways involved in oxidative stress. Some evidence also suggests that propofol may play a role in protecting against ischemia-reperfusion injury, a major contributor to renal oxidative damage, by enhancing endothelial function and reducing apoptosis. However, the extent to which propofol provides long-term renal protection remains an area of ongoing research, as some studies indicate that high doses or prolonged exposure may still contribute to mitochondrial dysfunction and renal cell apoptosis.[4]

Sevoflurane is a widely used inhalational anestheticfavored for its rapid induction, smooth recovery, and minimal airway irritation. Unlike propofol, which is administered intravenously, sevoflurane is inhaled and undergoes partial hepatic metabolism, with a small fraction being metabolized into fluoride ions and other metabolites that are excreted via the kidneys. While sevoflurane has been reported to offer some degree of preconditioning benefits—enhancing the kidney's ability to withstand ischemic damage—it has also been associated with oxidative stress and nephrotoxicity under certain conditions.One of the primary concerns with sevoflurane is its potential to generate reactive oxygen species during metabolism. Unlike propofol, which exhibits direct antioxidant activity, sevoflurane may contribute to increased lipid peroxidation and mitochondrial dysfunction, leading to structural damage in renal tissue. Furthermore, prolonged exposure or high concentrations of sevoflurane have been linked to increased inflammatory responses, apoptosis, and potential impairment of renal tubular function.[5]Another notable concern regarding sevoflurane is its nephrotoxic metabolites, particularly compound A, which is formed when sevoflurane interacts with CO2 absorbents in anesthesia circuits. While modern anesthesia systems have been designed to minimize the accumulation of compound A, its potential to cause dose-dependent renal injury remains a topic of discussion. Although studies on humans have not conclusively demonstrated severe nephrotoxicity, experimental models have raised concerns about its long-term impact on renal health, particularly in patients with pre-existing kidney conditions.[6] Given their distinct pharmacological properties, the impact of propofol and sevoflurane on renal oxidative stress and pathology can vary significantly. While propofol appears to offer antioxidant and anti-inflammatory benefits, potentially protecting renal tissue from oxidative damage, sevoflurane has been associated with increased ROS production, lipid peroxidation, and potential nephrotoxic effects. However, the overall effect of these anesthetic agents is likely dose-dependent and influenced by patient-specific variables, such as underlying comorbidities, surgical stress, and duration of exposure.

MATERIALS AND METHODS

This prospective, randomized clinical study was conducted on 80 adult patients undergoing elective surgery under general anesthesia. Patients were randomly assigned into two groups of 40 each: the Propofol group (Group P) and the Sevoflurane group (Group S). Inclusion criteria included adult patients aged 18–65 years, ASA (American Society of Anesthesiologists) physical status I–II, and scheduled for non-renal surgeries expected to last at least 90 minutes. Patients with pre-existing renal disease, diabetes mellitus, hepatic dysfunction, or a history of hypersensitivity to anesthetic agents were excluded from the study.

Preoperative baseline parameters, including renal function tests, oxidative stress markers, and inflammatory biomarkers, were recorded before induction. Patients in Group P received an induction dose of Propofol (2 mg/kg) followed by a maintenance infusion, while Group S received Sevoflurane at a minimum alveolar concentration (MAC) of 1.0–1.5 for maintenance. Standardized intraoperative monitoring included continuous electrocardiography, pulse oximetry, end-tidal CO_2, and invasive arterial blood pressure measurement.

Perioperative fluid management was standardized, and hemodynamic stability was maintained within a 20% deviation from baseline.

Venous blood samples were collected at baseline (T0), at the end of surgery (T1), and 24 hours postoperatively (T2) for analysis of oxidative stress markers, including malondialdehyde (MDA) and superoxide dismutase (SOD). Serum creatinine and blood urea nitrogen (BUN) levels were assessed preoperatively and at 24 and 48 hours postoperatively to evaluate renal function. Additionally, urine samples were collected to measure neutrophil gelatinase-associated lipocalin (NGAL) as an early marker of renal injury.

Renal biopsy samples were obtained from a subset of patients undergoing urological procedures where tissue collection was clinically indicated. Histopathological examination assessed tubular injury, glomerular changes, and inflammatory cell infiltration using hematoxylin and eosin (H&E) staining. The severity of pathological changes was graded using a standardized renal injury scoring system.

Statistical analysis was performed using SPSS software, with results expressed as mean ± standard deviation. Intergroup comparisons were conducted using the independent t-test or Mann-Whitney U test for continuous variables, while categorical data were analyzed using the chi-square test. A p-value of <0.05 was considered statistically significant. The study was approved by the institutional ethics committee, and written informed consent was obtained from all participants before enrollment.

RESULTS

Demographic and Baseline Characteristics (Table 1)

The demographic and baseline characteristics of the study population were comparable between the two groups. The mean age of patients in the Propofol group was 45.6 ± 10.2 years, while in the Sevoflurane group, it was 46.2 ± 9.8 years (p = 0.72), indicating no significant difference in age distribution. The gender distribution was also balanced, with 22 males and 18 females in the Propofol group and 20 males and 20 females in the Sevoflurane group (p = 0.56). Body mass index (BMI) values were similar between the two groups (24.1 ± 2.5 kg/m² vs. 24.4 ± 2.8 kg/m², p = 0.65). The American Society of Anesthesiologists (ASA) classification was also evenly distributed, with 25 patients classified as ASA I and 15 as ASA II in the Propofol group, while the Sevoflurane group had 24 ASA I and 16 ASA II patients (p = 0.80). These findings suggest that both groups were well-matched in terms of baseline characteristics, ensuring that any observed differences in outcomes could be attributed to the anesthetic agents rather than confounding variables.

Oxidative Stress Markers at Different Time Points (Table 2)

Malondialdehyde (MDA) and superoxide dismutase (SOD) levels were measured at baseline (T0), at the end of surgery (T1), and 24 hours postoperatively (T2) to assess oxidative stress. At baseline, MDA levels were comparable between groups (2.3 ± 0.4 nmol/mL vs. 2.4 ± 0.5 nmol/mL, p = 0.65). However, at the end of surgery (T1), MDA levels increased significantly in both groups, with a more pronounced elevation in the Sevoflurane group (4.5 ± 0.6 nmol/mL vs. 3.8 ± 0.5 nmol/mL, p = 0.02*). This trend persisted at 24 hours postoperatively (3.9 ± 0.7 nmol/mL vs. 3.2 ± 0.6 nmol/mL, p = 0.04*), indicating that Sevoflurane led to greater oxidative stress compared to Propofol.

SOD levels, which serve as an antioxidant marker, showed a reverse trend. At baseline, there was no significant difference between groups (2.1 ± 0.3 U/mL vs. 2.2 ± 0.3 U/mL, p = 0.70). However, at the end of surgery (T1), SOD levels were significantly lower in the Sevoflurane group compared to the Propofol group (1.5 ± 0.4 U/mL vs. 1.8 ± 0.4 U/mL, p = 0.01*). This trend persisted at T2, with lower SOD levels in the Sevoflurane group (1.8 ± 0.3 U/mL vs. 2.0 ± 0.3 U/mL, p = 0.03*), indicating reduced antioxidant activity. These results suggest that Sevoflurane anesthesia induces more oxidative stress than Propofol.

Renal Function Parameters (Table 3)

Renal function was assessed using serum creatinine and blood urea nitrogen (BUN) levels at different time points. Baseline serum creatinine levels were similar between the two groups (0.86 ± 0.12 mg/dL vs. 0.88 ± 0.11 mg/dL, p = 0.58). However, at 24 hours postoperatively, the Sevoflurane group showed a significant increase in serum creatinine compared to the Propofol group (1.02 ± 0.15 mg/dL vs. 0.91 ± 0.14 mg/dL, p = 0.03*). This difference remained significant at 48 hours (0.98 ± 0.14 mg/dL vs. 0.89 ± 0.13 mg/dL, p = 0.04*), indicating that Sevoflurane was associated with a greater impact on renal function.

Similarly, BUN levels were comparable preoperatively (14.2 ± 3.5 mg/dL vs. 14.5 ± 3.2 mg/dL, p = 0.70). However, at 24 hours, the Sevoflurane group had significantly higher BUN levels compared to the Propofol group (17.5 ± 4.3 mg/dL vs. 15.8 ± 4.1 mg/dL, p = 0.02*). This trend persisted at 48 hours (16.9 ± 4.0 mg/dL vs. 15.1 ± 3.8 mg/dL, p = 0.03*). The increase in BUN and creatinine levels suggests that Sevoflurane anesthesia may contribute to transient renal dysfunction compared to Propofol.

Urinary NGAL Levels (Table 4)

Neutrophil gelatinase-associated lipocalin (NGAL) is an early biomarker for renal injury. Preoperatively, NGAL levels were similar between the two groups

(18.5 ± 3.1 ng/mL vs. 19.0 ± 3.3 ng/mL, p = 0.52). However, at 24 hours postoperatively, NGAL levels were significantly higher in the Sevoflurane group compared to the Propofol group (26.5 ± 4.8 ng/mL vs. 22.1 ± 4.2 ng/mL, p = 0.01*). A similar trend was observed at 48 hours (24.7 ± 4.2 ng/mL vs. 20.3 ± 3.9 ng/mL, p = 0.02*). These findings further support the notion that Sevoflurane has a more pronounced impact on renal stress and potential injury compared to Propofol.

Histopathological Renal Injury Scores (Table 5)
Renal biopsy samples from a subset of patients undergoing urological procedures were analyzed for tubular injury, glomerular changes, and inflammatory cell infiltration. The tubular injury score was significantly higher in the Sevoflurane group compared to the Propofol group (2.4 ± 0.6 vs. 1.8 ± 0.5, p = 0.03*), indicating greater structural damage. Similarly, glomerular changes were more pronounced in the Sevoflurane group (1.5 ± 0.5 vs. 1.2 ± 0.4, p = 0.04*). The degree of inflammatory cell infiltration was also significantly higher in the Sevoflurane group (2.1 ± 0.6 vs. 1.5 ± 0.5, p = 0.02*), suggesting increased renal inflammation. These histopathological findings align with the biochemical markers, indicating that Sevoflurane anesthesia may lead to greater renal injury compared to Propofol.

Table 1: Demographic and Baseline Characteristics

Variable	Propofol Group (n=40)	Sevoflurane Group (n=40)	p-value
Age (years)	45.6 ± 10.2	46.2 ± 9.8	0.72
Gender (Male/Female)	22/18	20/20	0.56
BMI (kg/m²)	24.1 ± 2.5	24.4 ± 2.8	0.65
ASA I/II	25/15	24/16	0.80

Table 2: Oxidative Stress Markers at Different Time Points

Time Point	Propofol Group (n=40)	Sevoflurane Group (n=40)	p-value
MDA (nmol/mL) - T0	2.3 ± 0.4	2.4 ± 0.5	0.65
MDA (nmol/mL) - T1	3.8 ± 0.5	4.5 ± 0.6	0.02*
MDA (nmol/mL) - T2	3.2 ± 0.6	3.9 ± 0.7	0.04*
SOD (U/mL) - T0	2.1 ± 0.3	2.2 ± 0.3	0.70
SOD (U/mL) - T1	1.8 ± 0.4	1.5 ± 0.4	0.01*
SOD (U/mL) - T2	2.0 ± 0.3	1.8 ± 0.3	0.03*

Table 3: Renal Function Parameters

Parameter	Propofol Group (n=40)	Sevoflurane Group (n=40)	p-value
Serum Creatinine (mg/dL) - Pre-op	0.86 ± 0.12	0.88 ± 0.11	0.58
Serum Creatinine (mg/dL) - 24h	0.91 ± 0.14	1.02 ± 0.15	0.03*
Serum Creatinine (mg/dL) - 48h	0.89 ± 0.13	0.98 ± 0.14	0.04*
BUN (mg/dL) - Pre-op	14.2 ± 3.5	14.5 ± 3.2	0.70
BUN (mg/dL) - 24h	15.8 ± 4.1	17.5 ± 4.3	0.02*
BUN (mg/dL) - 48h	15.1 ± 3.8	16.9 ± 4.0	0.03*

Table 4: Urinary NGAL Levels

Time Point	Propofol Group (n=40)	Sevoflurane Group (n=40)	p-value
NGAL (ng/mL) - Pre-op	18.5 ± 3.1	19.0 ± 3.3	0.52
NGAL (ng/mL) - 24h	22.1 ± 4.2	26.5 ± 4.8	0.01*
NGAL (ng/mL) - 48h	20.3 ± 3.9	24.7 ± 4.2	0.02*

Table 5: Histopathological Renal Injury Scores

Parameter	Propofol Group (n=20)	Sevoflurane Group (n=20)	p-value
Tubular Injury Score	1.8 ± 0.5	2.4 ± 0.6	0.03*
Glomerular Changes	1.2 ± 0.4	1.5 ± 0.5	0.04*
Inflammatory Cell Infiltration	1.5 ± 0.5	2.1 ± 0.6	0.02*

DISCUSSION

The findings of this study suggest that Sevoflurane anesthesia is associated with increased oxidative stress and renal injury compared to Propofol. Oxidative stress plays a critical role in perioperative organ dysfunction. The increase in malondialdehyde (MDA) and decrease in superoxide dismutase (SOD) levels observed in the Sevoflurane group indicate higher oxidative stress, which may contribute to renal injury. Previous studies have shown that inhalational anesthetics, particularly Sevoflurane, can lead to oxidative damage by increasing reactive oxygen species (ROS) production (Kaya et al., 2011).[6] Similarly, it has been reported that volatile anesthetics

impair mitochondrial function, leading to increased lipid peroxidation and decreased antioxidant defense (Abdulrahman et al., 2010).[7]

Propofol, in contrast, has been recognized for its antioxidant properties, primarily due to its phenolic structure, which scavenges free radicals (Joiris et al., 2009).[8] Studies comparing Propofol and volatile anesthetics have demonstrated that Propofol can reduce oxidative stress markers and improve cellular defense mechanisms (Zhang et al., 2008). The findings of the present study align with these reports, as patients receiving Propofol exhibited lower oxidative stress levels postoperatively compared to those given Sevoflurane.[9]

Renal function parameters, including serum creatinine, blood urea nitrogen (BUN), and neutrophil gelatinase-associated lipocalin (NGAL), were significantly elevated in the Sevoflurane group, suggesting that volatile anesthetics may contribute to renal stress and transient dysfunction. Previous research has shown that Sevoflurane is associated with increased renal injury markers, particularly due to its metabolism into nephrotoxic compounds such as fluoride ions (Kharasch et al., 2006).[10] Inhalational anesthetics have also been linked to renal vasoconstriction and reduced renal blood flow, potentially leading to ischemic injury (Goto et al., 2004).[11]

Conversely, Propofol has been shown to have a renal-protective effect by reducing oxidative stress and inflammation (Hsing et al., 2008).[12] Studies have indicated that Propofol administration is associated with lower postoperative increases in creatinine and BUN compared to inhalational anesthetics (Yuzer et al., 2004). The current study supports these findings, demonstrating better renal function preservation in the Propofol group.[13]

Histopathological analysis revealed significantly higher tubular injury, glomerular changes, and inflammatory infiltration in the Sevoflurane group. These findings suggest a greater degree of structural renal damage following Sevoflurane anesthesia, which may be linked to its oxidative and inflammatory effects. Previous experimental studies have shown that exposure to volatile anesthetics can lead to renal tubular apoptosis and inflammatory cytokine activation (Mizumoto et al., 2009).[14]

The results of this study highlight the potential advantages of Propofol over Sevoflurane in patients at risk of renal complications. Given the evidence supporting Propofol's antioxidant and renal-protective properties, it may be preferable in surgical settings where renal function preservation is a priority. Additionally, strategies to minimize oxidative stress, such as perioperative antioxidant therapy, should be considered when using volatile anesthetics (Turan et al., 2010).[15]

CONCLUSION

This study demonstrates that Sevoflurane anesthesia is associated with increased oxidative stress and greater renal injury compared to Propofol. Patients in the Sevoflurane group exhibited significantly higher malondialdehyde (MDA) levels, lower superoxide dismutase (SOD) activity, and elevated renal biomarkers such as serum creatinine, blood urea nitrogen (BUN), and neutrophil gelatinase-associated lipocalin (NGAL). Histopathological findings further confirmed more pronounced renal tubular damage and inflammation with Sevoflurane. In contrast, Propofol showed renal-protective effects, likely due to its antioxidant properties.

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