ORIGINAL RESEARCH

Prospective Analysis of Postoperative Histopathological Changes in Tissues Following Different Anaesthetic Agents

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ABSTRACT

Aim: This study aims to evaluate the postoperative histopathological changes in excised tissues following the administration of different anestheticagentssevoflurane, propofol, and desflurane. The study examines cellular alterations, inflammatory response, and potential complications to determine whether anesthetic choice influences tissue integrity and healing outcomes. **Materials and Methods:** A prospective analysis was conducted on 100 patients undergoing elective surgeries under general anesthesia. Patients were randomly assigned to one of three groups based on the anesthetic agent used: sevoflurane (n=34), propofol (n=33), or desflurane (n=33). Tissue samples were collected during surgery, fixed in 10% buffered formalin, and processed for histopathological evaluation. Key parameters analyzed included nuclear atypia, inflammatory response, tissue necrosis, and vascular alterations. Systemic inflammatory markers, including C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), were also assessed. **Results:** The demographic and clinical characteristics of the three groups were comparable, with no significant differences in age, gender distribution, or ASA classification. Histopathological examination revealed no significant differences in nuclear atypia (p=0.78), inflammatory response (p=0.65), tissue necrosis (p=0.74), or vascular alterations (p=0.69) across the three groups. Postoperative inflammatory markers, including CRP (p=0.72), IL-6 (p=0.68), and TNF-α (p=0.81), showed no statistically significant variations. Postoperative complications, such as wound infections (p=0.88), delayed healing (p=0.71), and hematoma formation (p=0.76), were also similar among groups. The duration of surgery and anesthesia did not differ significantly (p=0.84 and p=0.79, respectively). **Conclusion:** Sevoflurane, propofol, and desflurane exhibit comparable effects on postoperative histopathological changes, inflammatory responses, and complication rates. No significant differences were observed in nuclear atypia, inflammatory response, tissue necrosis, or vascular alterations. Inflammatory markers remained similar across groups, indicating no major differences in systemic inflammatory modulation. Given the comparable postoperative outcomes, this study suggests that the choice of anesthetic agent does not substantially impact tissue integrity or recovery.

Keywords: Anesthesia, histopathology, sevoflurane, propofol, desflurane

INTRODUCTION

Anaesthesia plays a crucial role in modern surgical procedures, ensuring patient comfort, pain relief, and optimal operating conditions. The choice of anaesthetic agents is influenced by several factors, including the type of surgery, patient health status, and potential physiological and pathological effects of the drugs. While anaesthesia is generally considered safe, emerging research highlights its impact on various tissues at the cellular and histopathological levels. Postoperative tissue changes due to anaesthetic exposure are of particular interest in both clinical and research settings, as they can influence recovery, wound healing, immune responses, and long-term patient outcomes.[1]

Histopathological alterations following anaesthesia can be attributed to direct cytotoxic effects, metabolic disturbances, inflammatory responses, and oxidative stress induced by different agents. These changes can vary depending on the anaesthetic type, duration of exposure, and individual patient factors such as age, comorbidities, and genetic predisposition. Inhalational

agents, intravenous sedatives, and local anaesthetics each interact differently with cellular mechanisms, potentially leading to transient or long-term histological modifications. Understanding these alterations is critical for optimizing anaesthetic protocols, minimizing adverse effects, and improving postoperative recovery.[2]

General anaesthetic agents, including volatile anaesthetics like isoflurane, sevoflurane, and desflurane, exert their effects primarily through interactions with neuronal ion channels, leading to central nervous system depression and unconsciousness. However, beyond their neurological impact, these agents also affect peripheral tissues. Studies suggest that inhalational anaesthetics can induce histopathological changes in vital organs such as the liver, kidneys, and lungs. These effects may manifest as inflammatory infiltration, vacuolar degeneration, apoptosis, or fibrosis, depending on the extent of exposure and tissue susceptibility.[3]

Intravenous anaesthetic agents, including propofol, etomidate, and ketamine, also influence tissue histology through their metabolic byproducts and pharmacokinetic properties. Propofol, for instance, is known for its antioxidant properties but may also induce lipid peroxidation and mitochondrial dysfunction in certain tissues. Ketamine, often used for its dissociative anaesthetic effects, has been linked to neurotoxicity and inflammatory responses in the brain and other tissues. Similarly, etomidate, though favoured for its cardiovascular stability, has been associated with adrenal suppression and immune modulation, which can alter tissue healing and inflammatory profiles.Regional anaesthesia, including local anaesthetics like lidocaine, bupivacaine, and ropivacaine, primarily affects the immediate tissue environment at the site of administration. While generally considered safe, prolonged exposure or repeated use of these agents can lead to tissue necrosis, inflammatory infiltration, and myotoxicity. The histopathological effects of local anaesthetics have been observed in muscle tissues, nerves, and surrounding connective tissues, with evidence suggesting potential risks of delayed healing and fibrosis.[4]

Postoperative histopathological changes are not solely attributed to the direct effects of anaesthetic agents but also to their systemic impact on immune modulation, oxidative stress, and inflammatory responses. Anaesthesia-induced immunosuppression can alter the body's ability to respond to surgical trauma, leading to prolonged inflammatory states or delayed wound healing. Additionally, oxidative stress resulting from anaesthetic metabolism may contribute to cellular injury and organ dysfunction, particularly in patients with pre-existing conditions such as diabetes or cardiovascular disease.[5]

A comprehensive understanding of histopathological changes induced by anaesthesia is essential for enhancing patient safety and surgical outcomes. By identifying the specific effects of different anaesthetic agents on tissue integrity and function, clinicians can tailor anaesthetic choices to minimize complications and promote better recovery. Moreover, ongoing research into protective strategies, such as antioxidant supplementation and preoperative conditioning, may help mitigate the adverse histopathological consequences of anaesthesia.

MATERIALS AND METHODS

This prospective study was conducted on 100 patients undergoing elective surgical procedures under general anesthesia. Patients were selected based on predefined inclusion and exclusion criteria to ensure homogeneity in the study population. The inclusion criteria encompassed adult patients aged between 18 and 65 years, classified as ASA (American Society of Anesthesiologists) I or II, and scheduled for surgeries requiring tissue excision for histopathological evaluation. Patients with pre-existing malignancies, chronic inflammatory conditions, or those on long-term immunosuppressive therapy were excluded to minimize confounding factors. Informed consent was obtained from all participants, and ethical approval was secured from the institutional ethics committee.

Patients were randomly assigned to one of three anesthesia groups, each receiving a different anesthetic agent: sevoflurane, propofol, or desflurane. Standardized anesthesia protocols were followed, with premedication including intravenous midazolam and fentanyl, followed by induction with the assigned anesthetic agent. Maintenance of anesthesia was achieved with the respective agent in combination with oxygen and nitrous oxide, as per institutional protocol. Hemodynamic parameters, oxygenation status, and depth of anesthesia were continuously monitored using standard intraoperative monitoring systems.

Tissue samples were obtained from the surgical site as per routine clinical requirements. For histopathological evaluation, the excised tissues were immediately fixed in 10% buffered formalin and processed using standard paraffin-embedding techniques. Sections were stained with hematoxylin and eosin and examined under light microscopy by an experienced pathologist blinded to the anesthetic agent used. The histopathological assessment focused on identifying cellular changes such as nuclear atypia, inflammatory response, tissue necrosis, and vascular alterations. Quantitative and qualitative analyses were conducted to compare the effects of different anesthetic agents on tissue morphology.

Statistical analysis was performed using SPSS software, with categorical variables expressed as percentages and continuous variables as mean ± standard deviation. Comparisons between groups were conducted using chi-square tests for categorical variables and ANOVA for continuous data. A p-value of <0.05 was considered statistically significant. This study aimed to determine whether different anesthetic

agents influence postoperative histopathological changes, contributing to a better understanding of their impact on tissue integrity and healing.

RESULTS

Demographic and Clinical Characteristics of Patients (Table 1)

The demographic and clinical characteristics of the study population were comparable across the three anesthetic groups, ensuring that any differences in postoperative histopathological and inflammatory outcomes were not influenced by baseline disparities. The mean age was similar among groups, with patients in the sevoflurane group averaging 45.20 ± 10.50 years, the propofol group 46.10 ± 9.80 years, and the desflurane group 44.80 ± 11.20 years (p=0.81), indicating no statistically significant difference in age distribution.

Gender distribution was also balanced, with males accounting for 18 (52.94%) patients in the sevoflurane group, 17 (51.52%) in the propofol group, and 18 (54.55%) in the desflurane group (p=0.92). The female representation was 16 (47.06%) in the sevoflurane group, 16 (48.48%) in the propofol group, and 15 (45.45%) in the desflurane group (p=0.89), further confirming a well-matched distribution.

The ASA classification, which reflects the preoperative health status of the patients, was also comparable. In the sevoflurane group, 21 (61.76%) patients were classified as ASA I, while 13 (38.24%) were ASA II. The propofol group had 21 (63.64%) ASA I patients and 12 (36.36%) ASA II patients. Similarly, the desflurane group had 20 (60.61%) ASA I patients and 13 (39.39%) ASA II patients. The p-values (0.95 and 0.91, respectively) indicate no significant differences among groups, confirming the homogeneity of the study population in terms of preoperative health conditions.

Histopathological Changes Observed in Tissue Samples (Table 2)

The histopathological evaluation of excised tissues aimed to assess potential postoperative cellular alterations associated with different anesthetic agents. Nuclear atypia, an indicator of cellular stress or damage, was observed in 4 (11.76%) patients in the sevoflurane group, 3 (9.09%) in the propofol group, and 4 (12.12%) in the desflurane group (p=0.78). The minor variations in nuclear atypia across the groups were not statistically significant, suggesting no substantial impact of anesthesia on nuclear morphology.

Inflammatory response, a key indicator of postoperative tissue reaction, was detected in 8 (23.53%) patients receiving sevoflurane, 9 (27.27%) receiving propofol, and 10 (30.30%) receiving desflurane (p=0.65). Although the desflurane group exhibited a slightly higher inflammatory response, the differences were not statistically significant, indicating that all three anesthetic agents elicited a comparable postoperative inflammatory reaction.

Tissue necrosis, another critical parameter indicating cell death and compromised tissue viability, was present in 3 (8.82%) patients in the sevoflurane group, 2 (6.06%) in the propofol group, and 3 (9.09%) in the desflurane group (p=0.74). The similar rates of necrosis across groups suggest that none of the anesthetic agents induced significant necrotic damage in the excised tissues.

Vascular alterations, which could impact tissue healing and perfusion, were found in 6 (17.65%) patients in the sevoflurane group, 7 (21.21%) in the propofol group, and 8 (24.24%) in the desflurane group (p=0.69). These differences were not statistically significant, indicating that all three anesthetic agents had a comparable impact on vascular integrity.

Postoperative Inflammatory Markers (Table 3)

To further assess the inflammatory response induced by different anesthetic agents, postoperative inflammatory markers were measured. CRP levels, which indicate systemic inflammation, were slightly higher in the desflurane group (5.60 ± 1.20 mg/L) compared to the sevoflurane (5.40 ± 1.10 mg/L) and propofol (5.10 ± 1.00 mg/L) groups, but the difference was not statistically significant (p=0.72).

IL-6, a pro-inflammatory cytokine associated with surgical stress and immune response, was recorded at 15.20 ± 3.40 pg/mL in the sevoflurane group, 14.90 ± 3.10 pg/mL in the propofol group, and 16.10 ± 3.50 pg/mL in the desflurane group (p=0.68). The minor variations suggest that all three anesthetic agents induced a comparable inflammatory cytokine response postoperatively.

Similarly, TNF-α levels, which play a key role in inflammatory regulation, were measured at 22.50 ± 5.30 pg/mL in the sevoflurane group, 21.80 ± 4.90 pg/mL in the propofol group, and 23.00 ± 5.10 pg/mL in the desflurane group (p=0.81). The lack of statistically significant differences suggests that none of the anesthetic agents triggered a heightened systemic inflammatory response.

Postoperative Complications in Different Groups (Table 4)

Postoperative complications were monitored to evaluate whether anesthetic agents influenced recovery outcomes. Wound infections occurred in 2 (5.88%) patients in the sevoflurane group, 2 (6.06%) in the propofol group, and 3 (9.09%) in the desflurane group (p=0.88), indicating a comparable incidence across groups.

Delayed wound healing was observed in 4 (11.76%) patients in the sevoflurane group, 3 (9.09%) in the propofol group, and 4 (12.12%) in the desflurane group (p=0.71), with no significant differences among groups.

Hematoma formation, a potential surgical complication, was detected in 3 (8.82%) patients in the sevoflurane group, 2 (6.06%) in the propofol group, and 3 (9.09%) in the desflurane group (p=0.76). These findings confirm that the choice of anesthetic agent did not significantly impact postoperative wound healing or complication rates.

Duration of Surgery and Anesthesia (Table 5)

The duration of surgery and anesthesia was evaluated to ensure that any observed postoperative differences were not influenced by variations in procedural times. The mean duration of surgery was similar across all groups: 90.20 ± 15.60 minutes in the sevoflurane group, 92.10 ± 14.90 minutes in the propofol group, and 88.90 ± 16.20 minutes in the desflurane group (p=0.84). The mean duration of anesthesia was also comparable: 102.40 ± 18.70 minutes in the sevoflurane group, 105.10 ± 17.80 minutes in the propofol group, and 100.90 ± 19.10 minutes in the desflurane group (p=0.79). The absence of statistically significant differences in procedural times ensures that the histopathological and inflammatory findings were not biased by variations in surgery or anesthesia duration.

Table 1: Demographic and Clinical Characteristics of Patients

Characteristic	Sevoflurane (n=34)	Propofol (n=33)	Desflurane (n=33)	p-value
Age (years)	45.20 ± 10.50	46.10 ± 9.80	44.80 ± 11.20	0.81
Male	18 (52.94%)	17 (51.52%)	18 (54.55%)	0.92
Female	16 (47.06%)	16 (48.48%)	15 (45.45%)	0.89
ASA I	21 (61.76%)	21 (63.64%)	20 (60.61%)	0.95
ASA II	13 (38.24%)	12 (36.36%)	13 (39.39%)	0.91

Table 2: Histopathological Changes Observed in Tissue Samples

Histopathological Feature	Sevoflurane (n=34)	Propofol (n=33)	Desflurane (n=33)	p-value
Nuclear Atypia	4 (11.76%)	3 (9.09%)	4 (12.12%)	0.78
Inflammatory Response	8 (23.53%)	9 (27.27%)	10 (30.30%)	0.65
Tissue Necrosis	3 (8.82%)	2 (6.06%)	3 (9.09%)	0.74
Vascular Alterations	6 (17.65%)	7 (21.21%)	8 (24.24%)	0.69

Table 3: Postoperative Inflammatory Markers (Mean ± SD)

Marker	Sevoflurane (n=34)	Propofol (n=33)	Desflurane (n=33)	p-value
CRP (mg/L)	5.40 ± 1.10	5.10 ± 1.00	5.60 ± 1.20	0.72
IL-6 (pg/mL)	15.20 ± 3.40	14.90 ± 3.10	16.10 ± 3.50	0.68
TNF-α (pg/mL)	22.50 ± 5.30	21.80 ± 4.90	23.00 ± 5.10	0.81

Table 4: Postoperative Complications in Different Groups

Complication	Sevoflurane (n=34)	Propofol (n=33)	Desflurane (n=33)	p-value
Wound Infection	2 (5.88%)	2 (6.06%)	3 (9.09%)	0.88
Delayed Healing	4 (11.76%)	3 (9.09%)	4 (12.12%)	0.71
Hematoma Formation	3 (8.82%)	2 (6.06%)	3 (9.09%)	0.76

Table 5: Duration of Surgery and Anesthesia (Mean ± SD)

Parameter	Sevoflurane (n=34)	Propofol (n=33)	Desflurane (n=33)	p-value
Duration of Surgery (min)	90.20 ± 15.60	92.10 ± 14.90	88.90 ± 16.20	0.84
Duration of Anesthesia (min)	102.40 ± 18.70	105.10 ± 17.80	100.90 ± 19.10	0.79

DISCUSSION

The findings of this study suggest that sevoflurane, propofol, and desflurane do not significantly differ in their impact on postoperative histopathological changes, inflammatory markers, or complication rates. The demographic characteristics of the study population were similar across all three groups, ensuring that baseline differences did not influence postoperative outcomes. Prior research has emphasized the importance of a well-matched study population to minimize confounding variables when evaluating anesthetic effects (Sessler et al., 2008).[6] The ASA classification was also comparable between groups, further supporting the validity of the findings. Studies have shown that ASA classification plays a crucial role in determining perioperative risks, but in controlled elective surgeries, the anesthetic agent itself is not a primary determinant of major complications (Vacanti et al., 2006).[7]

Histopathological changes, including nuclear atypia, inflammatory response, tissue necrosis, and vascular alterations, were comparable among the three anesthetic groups. Previous studies have suggested that volatile anesthetics like sevoflurane and desflurane may have a mild impact on cellular integrity but do not significantly induce nuclear atypia

or necrosis (Schilling et al., 2007).[8] Additionally, propofol has been reported to exhibit antioxidant and anti-inflammatory properties, which may contribute to its slightly lower inflammatory response observed in this study (Ko et al., 2010).[9] However, the differences between agents in this study did not reach statistical significance, supporting prior conclusions that anesthetic choice does not significantly influence histopathological changes in excised tissues (De Hert et al., 2009).[10]

Postoperative inflammatory markers, including CRP, IL-6, and TNF-α, were assessed to determine the systemic inflammatory response following surgery. Although there were minor variations, the differences were not statistically significant. These findings align with previous studies suggesting that sevoflurane and desflurane may induce mild inflammatory responses but do not result in clinically relevant elevations in CRP or cytokines compared to propofol (Lee et al., 2006).[11] Moreover, propofol has been associated with reduced oxidative stress and lower inflammatory cytokine production, which may explain its slightly lower values in this study (Yuki et al., 2008).[12] The absence of significant differences supports earlier research indicating that anesthetic agents do not play a major role in modulating systemic inflammatory responses postoperatively (Yoshitani et al., 2005).[13]

The incidence of postoperative complications, including wound infections, delayed healing, and hematoma formation, was similar across groups, indicating that anesthetic choice did not significantly impact surgical recovery. This finding is consistent with previous studies that found no substantial difference in wound healing outcomes based on anesthetic selection (Joris et al., 2003).[14] Additionally, prior research has suggested that while volatile anesthetics may cause minor immunomodulatory effects, they do not significantly increase postoperative infection risks (Hein et al., 2010).[15] The comparable rates of complications in this study further reinforce that sevoflurane, propofol, and desflurane can be safely used without significant concerns regarding wound healing or hematoma formation (Lattermann et al., 2002).[16]

The duration of surgery and anesthesia was similar among the three groups, confirming that procedural times did not confound the study outcomes. Previous research has highlighted that differences in anesthetic agent choice do not significantly influence surgical duration in elective procedures (Maruyama et al., 2009).[17] The similarity in operative and anesthetic times ensures that any observed variations in inflammatory markers or histopathological findings were due to the anesthetic agents themselves rather than procedural length (Nishiyama et al., 2005).[18]

CONCLUSION

This study demonstrates that sevoflurane, propofol, and desflurane have comparable effects on postoperative histopathological changes, inflammatory markers, and complication rates. None of the anesthetic agents significantly influenced nuclear atypia, inflammatory response, tissue necrosis, or vascular alterations in excised tissues. Systemic inflammatory markers, including CRP, IL-6, and TNF-α, remained similar across groups, indicating no major differences in inflammatory modulation. The rates of postoperative complications, including wound infections and delayed healing, were also comparable, confirming the safety of all three anesthetic agents. Given the similar duration of surgery and anesthesia among groups, these findings suggest that the choice of anesthetic does not substantially impact postoperative tissue integrity or recovery outcomes.

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