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COMPARISON OF POSTOPERATIVE INFLAMMATION, OXIDATIVE STRESS, PAIN AND COGNITIVE IMPAIRMENT IN PROPOFOL AND SEVOFLURANE: A RANDOMIZED CLINICAL TRIAL

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Background: *The choice of anesthetics is critical to guard brain functions, reduce complications associated with surgical operations, and provide superior-standard care and better patients' quality of life.* ***Objectives:*** *To compare postoperative inflammatory response, oxidative stress, cognitive dysfunction and pain index in patients undergoing elective, non-cardiac, abdominal surgery using propofol or sevoflurane anesthesia.* ***Methods:*** *A prospective, parallel, randomized, double-blinded clinical trial was conducted from December 2021 to April 2023 on 44 patients undergoing elective abdominal surgeries and anesthetized with either infusion of propofol or inhalational sevoflurane at Damanhour Teaching Hospital, El-Beheira, Egypt., Blood samples were drawn from the patients before surgery, 1 and 24 hours after surgery. Inflammatory response was measured by using matrix metalloproteinase-9 (MMP-9), oxidative stress by utilizing superoxide dismutase (SOD), cognitive dysfunction by using S100 calcium-binding protein β (S100-β), neuron-specific enolase (NSE) levels and Montreal Cognitive Assessment score (MoCA-B), pain by applying the numerical pain rating scale (NPRS).* ***Results:*** *Propofol group showed significantly higher SOD enzyme activities and lower MMP-9 levels 1hour, and 24 hours postoperatively compared to sevoflurane group, (P=0.03, 0.04) respectively. Time to emerge from anesthesia and NPRS scores were significantly lower in propofol compared to sevoflurane group, (P<0.001). Postoperative nausea and vomiting were significantly lower in propofol group compared to sevoflurane group.* ***Conclusion:*** *Propofol infusion lowered postoperative pain scores, inflammatory response, and oxidative stress, shortened the time to emerge from anesthesia, and decreased incidence rates of vomiting and nausea in patients scheduled for elective, abdominal operations under the effect of general anesthetics*

Keywords: *Cognitive dysfunction; Inflammatory response; Matrix metalloproteinase-9; Neuron-specific enolase; Superoxide dismutase*

INTRODUCTION

Choosing suitable anesthetics is crucial to guard brain function, reduce perioperative morbidity and mortality, provide high-standard care, and maintain better life quality[1]. Anesthesia and surgery have serious cognitive effects, especially on memory functions[2]. Many

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mechanisms are involved in the occurrence of postoperative cognitive disorders as it is a relatively complex process involving surgical trauma, anesthetic stimulation, and surgical duration[3]. Deterioration of the physiologic functions decreases the drug metabolism rate and raises the body's sensitivity to anesthetic drugs[4,5]. Residual anesthetic drugs affect the central nervous system (CNS) resulting in reduced respiratory function, delayed patient recovery, and cognitive dysfunction[4,5]. The development of postoperative cognitive dysfunction (POCD) is attributed to neuroinflammation that is induced by anesthesia and surgery and superimposed by oxidative stress resulting from surgical trauma, thus depleting the body of antioxidants[6].

Propofol is one of the most commonly used intravenous anesthetics due to its fast onset of action, rapid recovery, and fewer side effects[7]. Sevoflurane is the safest inhalational anesthetic with the advantage of having a reduced blood-gas partition coefficient. It allows precise concentration control, making it safe for the elderly and children[8]. Propofol exerts its effect by potentiating the inhibitory neurons through activation of type A-gamma-aminobutyric acid ($GABA_A$) receptors, while sevoflurane modulates the molecular targets, such as glutamate receptors, 2-pore domain potassium channels, and $GABA_A$ receptors[9]. The degree of postoperative pain control after propofol or sevoflurane anesthesia is a point of contention[10], as it can be inconvenient because acute postoperative pain might lead to the risk of chronic pain[11,12], delayed patient recovery, and functional limitation in patients undergoing major and ultra-major operations[13].

Cognitive dysfunction is a huge burden for both the patient and the hospital[14]. The impairment of cognitive functions could influence memory, language comprehension, attention, and concentration, interfering with postoperative treatment and prognosis[15]. Inflammation is a highly complex process as prolonged inflammation could disrupt immunity or cell dysfunction[16]. The relationship between inflammation and oxidative stress is bidirectional[17]. Persistent inflammation, that might occur after surgical procedures produces high amounts of inflammatory mediators that cause oxidative stress[18]. Oxidative stress occurs due to disequilibrium between producing and eliminating reactive oxygen species[19] which can cause inflammation by attracting immune cells to the damaged area[20].

S100 calcium-binding protein β (S100-β) is an acidic calcium-binding protein manufactured by astrocytes to provide better interaction between neurons and glial cells[21]. The (CNS) is rich in S100-β, but it has scarce serum concentration. The blood-brain barrier (BBB) becomes defective after brain damage and S-100β is released in the blood. Thus, serum S-100β concentrations can be used as a biomarker of (POCD) to evaluate brain injury[22]. Neuron-specific enolase (NSE) is a type of enolase involved in the glycolytic pathway, that is widely present in nerve tissue and neuroendocrine tissues, less in serum, cerebrospinal fluid, and other non-neurological tissues. When neurons are damaged or dysfunctional, NSE penetrates the blood-brain barrier into the blood[1], thus, the serum NSE concentration levels can be used as a biomarker of neuronal injury[23] and quantitative measures of brain damage[24]. Matrix metalloproteinase 9 (MMP-9) is considered a proteolytic enzyme manufactured by certain cell types, such as keratinocytes, monocytes, and tissue macrophages[25], and plays a significant role in the inflammatory process[26]. Oxidative stress is a degenerative process due to low levels of antioxidants or excessive synthesis of Free Radicals (FRs) such as reactive oxygen and nitrogen species. FRs encompass hydroxyl radicals, superoxide anion radicals, oxygen in the singlet form, and hydrogen peroxide (H_2O_2). These FRs damage lipids, proteins, and deoxyribonucleic acid (DNA), starting an organized cascade that leads to cell destruction[27]. Superoxide dismutase (SOD) is a major antioxidant enzyme that could destroy free superoxide radicals and other kinds of reactive oxygen species, that can protect the body cells from damage[28]. The Montreal Cognitive Assessment (MoCA) score is a validated scale used to determine mild cognitive dysfunction in highly educated patients[29]. It has some limitations in determining cognitive impairment in illiterate and limited-education individuals[30]. The Basic Montreal Cognitive Assessment score (MoCA-B) was developed by omitting literacy-

dependent tasks and substituting them with literacy-independent tasks to overcome this limitation and optimize the possibility of detecting cognitive impairment in illiterate elders or those with low levels of education[31]. The Numeric Pain Rating Scale (NPRS) is a reliable and valid scale used to identify a patient's level of pain. It consists of 11 points (from 0 to 10)[32,33] where 0 indicates no pain and 10 denotes the highest level of pain[34,35,36].

This study aimed to compare propofol and sevoflurane anesthetics regarding their effect on POCD, postoperative pain, inflammation, and oxidative stress in patients undergoing elective, abdominal, and non-cardiac surgery under the effect of general anesthetics. The study's primary outcome is the change in the cognitive function serum enzyme levels (NSE and S-100β) and Montreal Objective Cognitive Assessment (MoCA-B) scores. The secondary outcome is the change in MMP-9 levels, SOD enzyme activities, and NPRS scores.

MATERIALS AND METHODS

Study design

This was a single-center, parallel, randomized (1:1), double-blinded clinical trial conducted at a tertiary Hospital, from December 2021 to April 2023. Before the study, approvals were obtained from the committee of ethics of the Faculty of Pharmacy: -Damanhour University (08/11/2021- no: 1121PP44) and the General Organization for Teaching Hospitals and Institutes (01/12/2021- no: HD000154) Patients' consent to participate was also attained. The study was conducted according to The Declaration of Helsinki[37]. The current clinical trial was registered on www.ClinicalTrials.gov, (21/03/2022- no: NCT05289349) and was reported according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines[38] .

Patients characteristics

Inclusion criteria

Patients were considered eligible if they were aged 21 years old or above, undergoing elective, abdominal, non-cardiac surgery under general anesthesia, classified as physical status I or II according to the American Society of Anesthesiologists (ASA), with a body mass index (BMI) ranging from 25 to 35 kg/m^2.

Exclusion criteria

Patients who suffer from chronic inflammatory, cardiovascular, cerebrovascular, liver, endocrine, blood, respiratory, immune diseases, visual or auditory abnormalities, infections, abnormal conscious level, cognitive function abnormalities, or dementia. Patients with (MoCA-B) score < 24 points. Patients who have abnormal serum creatinine levels. Chronic users of sedatives or steroids, alcohol and drug abusers, and those who were allergic to any of the study materials and drugs were also excluded.

Patient assessment

Full history was recorded, clinical examination, airway function, complete blood count (CBC), coagulation factors, liver and kidney enzymes, and blood glucose level (BGL). Electrocardiogram and Echocardiography (Echo) were also evaluated.

Randomization and blinding

Randomization was executed using the online application (https://www.randomizer.org), which generated a random sequence to allocate patients into 2 groups (1:1 ratio), to receive either sevoflurane (Group S) or propofol (Group P) through a random number order. The allocation sequence was concealed using sealed opaque envelopes which were arranged sequentially by a trial-independent individual. The patients were blinded to the type of anesthesia.

Sample size calculation

Based on the findings of previous studies[7,39-42], sample size was estimated assuming an 80% study power and 95% confidence level. The sample size was calculated to be 20 patients in each group, increased to 22 to make up for the 10% loss to follow-up[43]. MedCalc Statistical Software version 19.0.5 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2019).

Patient preparation before anesthesia

Before operation day, participants were taught how to report their postoperative pain level using (NPRS) which is a scale consisting

of 11 points, where 0 equals no pain and 10 equals maximum unbearable pain. Participants were fasting overnight for 6 to 8 hours for solid meals and 2 hours for any clear fluids before operation day. Patients were given crystalloid solutions infused at a rate of 5ml/kg/h and monitored until the morning of the operation.

Anesthesia protocol and drugs

All patients received their anesthetic technique that involved; preoxygenation using 100% oxygen for 3 minutes, anesthesia induction using intravenous propofol (2 mg/kg) Medium Chian Triglycerides (MCT) 1%, 200 mg/20ml ampoule, Fresenius Kabi, Bad Hamburg, Germany), IV fentanyl citrate (1 μg/kg), and intravenous atracurium besylate (0.5 mg/kg) was given to help in tracheal intubation process.

Anesthesia maintenance was carried out with either IV propofol infusion 4-6 mg/kg/h in (group P)[44,45] or with 1-3% sevoflurane inhalation in (group S)[45] (Sevoflurane, 250 ml bottle, Kahira Pharmaceuticals & Chemical Industries Company, Cairo, Egypt under license of AbbVie, Berkshire, UK). The depth of anesthesia of patients was monitored with entropy which was maintained between 40 and 60 by titrating the respective anesthetic agents. Continuous infusion of IV fentanyl citrate (0.5 ug/kg/h) was given till surgery ended and neuromuscular blockade was maintained by administering intermittent boluses of IV atracurium besylate (0.1 mg/kg) if needed. To manage postoperative pain, all patients were given IV paracetamol (15 mg/kg) thirty minutes before the operation ended.

By the end of the surgery, anesthetic agents were stopped, and muscle relaxation reversal was carried out by giving intravenous neostigmine methyl sulfate (0.04 mg/kg) plus IV atropine sulfate (0.02 mg/kg). Following extubating, patients were moved to the post-anesthesia care unit (PACU). Each patient was given paracetamol 1 g IV infusion every 6 hours to manage postoperative pain. Ketorolac tromethamine 30 mg IV was administered as a single dose which was increased to 15-30 mg IV/6h as needed for patients who reported unbearable pain.

Demographic and clinical data collection

Age, sex, weight, height, body mass index (BMI), (ASA) physical status classification system, duration of anesthesia (the time from anesthesia beginning till ending in minutes), surgical operative duration (the time from starting skin incision till finally skin closure in minutes), and emergence time from anesthesia (the time from ending anesthetics use to patients replaying to the doctor's questions in minutes) were recorded.

Perioperative hemodynamic parameters

Heart rate (HR) (beats/min.), peripheral oxygen saturation (SPO_2%), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MBP) (mmHg) were recorded; before the induction of anesthesia (T0) and 1 hour after the end of the operation (T1).

Assessment of pain, cognitive function, inflammatory response, and oxidative stress

The NPRS was used to evaluate patients' pain before the operation (T0), 1h (T1), and 24 hours (T2) after the end of the operation. Arabic version of the (MoCA-B) test, (a test with a maximum score of 30 and a cut-off score of < 24/30), https://mocacognition.com/paper) was used to help assess the cognitive function before the operation (T0), 24h (T2) after the end of the operation, and seven days later (D7). It is designed to detect Mild Cognitive Impairment (MCI) in individuals with limited education or illiterate patients. A single assessor (H.H.E) was trained to the NPRS and MoCA-B scales and was blinded to the type of anesthesia.

Blood sampling and serum biomarker measurement

Three venous blood samples (4 ml each) were drawn from each patient of the two studied groups by a sterile syringe and placed in dark yellow vacutainer tubes (gel + blood clot activator); before operation (T0), 1h (T1) and 24h (T2) after the end of the operation. Vacutainer tubes were centrifugated at 2.400 x g for (20 min.) and patients' serum was collected into several Eppendorf tubes. Tubes were stored at -80°C freezer until the analysis of samples. Certain enzyme-linked immunosorbent assay (ELISA) kits were

obtained for estimating serum levels of; Human S100-β (catalog no: 201-12-4851, SunRed, China), and Human NSE (catalog no: 201-12-0938, SunRed, China) to evaluate the cognitive function, MMP-9 (catalog no: 201-12-0937, SunRed, China) to determine the inflammatory response, and colorimetric assay of SOD (catalog no: 221114, Biodiagnostic, Egypt) to evaluate the effect of anesthetics on oxidative stress.

Postoperative adverse effects monitoring and management

Perioperative adverse events were recorded during the procedure as; tachycardia (Heart rate > 100 beats/minute), bradycardia (Heart rate < 60 beats/minute), hypertension (MBP > 25% from baseline), hypotension (MBP < 25% from baseline), hypoxemia (O_2 saturation < 90%), bleeding, and postoperative nausea and vomiting. Tachycardia and hypertension were managed by increasing the depth of anesthesia. Bradycardia was managed using atropine sulfate (0.5 mg IV), and hypotension was treated by temporarily decreasing anesthesia depth, and increasing the rate of crystalloid infusion. If hypotension persisted, ephedrine hydrochloride (5 mg IV) was given. Post Operative Nausea and Vomiting (PONV) were treated using intravenous ondansetron (0.15 mg/kg). The researcher recorded all study outcomes and data while being completely blinded to each group assignment.

Statistical analysis

Statistical analysis of the data was done using the IBM SPSS Version 23 for Windows (SPSS Inc., Chicago, USA). The normality of continuous data was tested using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Continuous data were described by the mean, standard deviation (SD), median, and interquartile range (IQR). Categorical data were described by frequency and percentage. The difference in HR, O2 saturation, SBP, DBP, and MBP between propofol and sevoflurane was assessed by independent t-test and the difference between T0 and T1 was assessed by dependent t-test. Perioperative adverse events were evaluated by the Chi-square test. Differences in the change in NPRS score, MoCA-B score, S100-β, NSE, MMP-9, and SOD across time were assessed using repeated measures of ANOVA, as well as the between-groups effect and interaction of time and groups. The Greenhouse-Geisser and Hyunh-Feldt corrections were used when necessary. Post-hoc analysis of the change across time was assessed using the Bonferroni test. The significance level was set at a *P*-value < 0. 05.

RESULTS AND DISCUSSION

Results

Demographic and laboratory data

Fifty-six candidate patients undergoing elective, abdominal, non-cardiac surgery under the effect of general anesthetics were assessed for enrolment; 44 patients were eligible for randomization and 12 were excluded as follows: three patients with ASA physical status III, two patients with BMI more than 35 kg/m^2, two patients with liver cirrhosis, two patients with end-stage kidney dysfunction, one patient with dilated cardiomyopathy, one patient with ischemic stroke, and one patient with systemic lupus erythematosus on long-term use of steroids. As shown in the consort flow diagram **(Fig. 1)** All 44 patients successfully managed to complete the study and were considered for the analysis.

Table 1 shows that both groups were comparable regarding age, weight, height, BMI, sex, ASA PS, anesthesia duration, operative duration, hospital stay duration, preoperative laboratory investigations, and preoperative comorbidities. (p >0.05).

The time to emerge from anesthesia was significantly shorter in (group P) (9.50±1.626 min. vs 15.05±4.029 min.) and the ketorolac dose was lower (36.14±9.99 vs 48.41±20.67 mg) in (group P) compared to (group S) respectively with statistically significant differences between the two groups, P = 0.03 **(Table 1).**

There were no statistically significant differences between groups being studied in HR, SPO_2, SBP, DBP, and MBP at different time points as shown in **(Table 2)**.

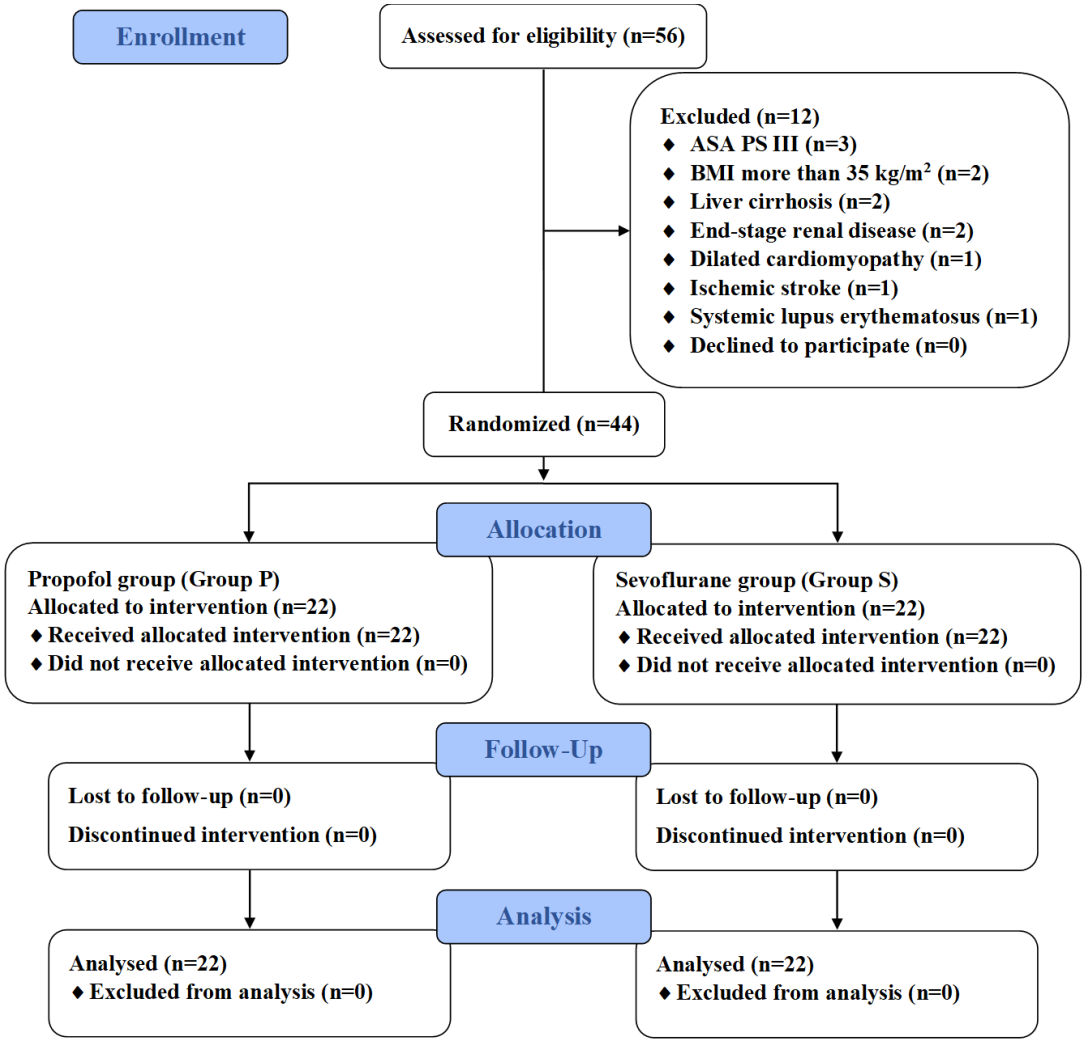

Fig. 1:CONSORT flow diagram showing the flow of patients throughout the study.

Table 1: Baseline characteristics, preoperative laboratory investigations, and preoperative comorbidities of the study groups (N = 44) **.**

Variables		Group P (*n*=22)	Group S (*n*=22)	*p*
Age (years)	**Mean ±SD**	48.00±11.309	51.09±12.524	0.395 [a]
Weight (kg)	**Mean ±SD**	82.14±9.508	83.64±11.345	0.637 [a]
Height (m)	**Mean ±SD**	168.727±5.624	166.818±6.374	0.298 [a]
BMI (kg/m^2)	**Mean ±SD**	28.853±2.792	29.982±3.012	0.198 [a]
Sex (F/M) [*n* (%)]	***n* (%)**	13 (59.1) / 9 (40.9)	12 (54.5) / 10 (45.5)	0.761 [b]
ASA PS (I/II) [*n* (%)]	***n* (%)**	10 (45.5) / 12 (54.5)	7 (31.8) / 15 (68.2)	0.353 [b]
Anesthesia duration (min.)	**Mean ±SD**	195.91±63.105	190.82±54.357	0.776 [a]
Operative duration (min.)	**Mean ±SD**	184.68±62.454	179.95±54.621	0.791 [a]
Time to emerge (min.)	**Mean ±SD**	9.50±1.626	15.05±4.029	<0.001[a]*
Hospital duration stay (day)	**Median (min-max)**	2.00 (5)	2 (6)	0.694†
Ketorolac Dose (mg)	**Mean ±SD**	36.14±9.99	48,41±20.67	0.030 [a]*

Table 1: Continued.

Preoperative laboratory investigations				
Hb (g/dl)	**Mean ±SD**	12.318±1.710	12.673±1.675	0.491 [a]
Hct (%)	**Mean ±SD**	39.141±12.151	38.505±4.276	0.818 [a]
Platelets/µl	**Median (Min-Max)**	243500.00 (63000-534000)	233000.00 (50000-409000)	0.549†
Leucocytes/ µl	**Median (Min-Max)**	7050 (4500-14400)	6150 (4300-11000)	0.227†
Prothrombin time (sec.)	**Mean ±SD**	13.105±1.333	13.118±0.885	0.970 [a]
Prothrombin activity (%)	**Mean ±SD**	87.647±10.227	87.172±10.408	0.879 [a]
INR	**Mean ±SD**	1.118±0.128	1.131±0.113	0.712 [a]
Urea (mg/dl)	**Mean ±SD**	30.395±6.887	27.757±6.808	0.302 [a]
Creatinine (mg/dl)	**Mean ±SD**	0.802±0.168	0.807±0.241	0.943 [a]
ALT (U/L)	**Mean ±SD**	21.278±7.983	20.186±15.836	0.793 [a]
AST (U/L)	**Mean ±SD**	23.489±8.713	21.289±12.815	0.551 [a]
Blood glucose (mg/dl)	**Mean ±SD**	101.938±21.831	98.200±22.463	0.678 [a]
Preoperative comorbidities:				
Smoking	***n* (%)**	3 (13.6)	7 (31.8)	0.150 [b]
Type II DM	***n* (%)**	2 (9.1)	2 (9.1)	1.000 [b]
Hypertension	***n* (%)**	1 (4.5)	2 (9.1)	0.550 [b]
Bronchial asthma	***n* (%)**	2 (9.1)	0 (0)	0.148 [b]
Thrombocytopenia	***n* (%)**	1 (4.5)	1 (4.5)	1.000 [b]
Thalassemia	***n* (%)**	1 (4.5)	0 (0)	0.312 [b]
Hyperbilirubinemia	***n* (%)**	1 (0)	0 (0)	0.312 [b]

Group P: patients received propofol infusion; Group S: patients received sevoflurane inhalation. BMI: body mass index; ASA PS: American Society of Anesthesiologists / physical status classification; Hb: hemoglobin; Hct: hematocrit; INR: international normalized ratio; ALT: alanine transaminase; AST: aspartate transaminase; mg: milligram.

[a]Independent t-Test, [b]Chi-square test or †Mann–Whitney U test

*Significance set at $p < 0.05$.

Table 2: Difference in heart rate, oxygen saturation, systolic, diastolic, and mean blood pressure between the study groups across time (N = 44).

Variables	Time	Group P (*n*=22) (Mean ±SD)	Group S (*n*=22) (Mean ±SD)	*p*
HR (beats/min.)	**T0**	84.14±19.290	83.55±11.181	0.902 [a]
	T1	81.00±18.840	80.05±15.783	0.856 [a]
	P	0.47 [b]	0.40 [b]	
O_2 saturation (%)	**T0**	98.32±1.615	97.50±1.739	0.113 [a]
	T1	97.23±2.654	97.09±1.849	0.844 [a]
	P	0.04 [b]	0.30 [b]	
SBP (mmHg)	**T0**	137.95±14.911	140.41±13.831	0.574 [a]
	T1	132.86±14.287	140.09±19.751	0.172 [a]
	P	0.15 [b]	0.95 [b]	
DBP (mmHg)	**T0**	79.77±10.071	83.23±8.389	0.223 [a]
	T1	86.85±9.568	89.23±13.505	0.507 [a]
	P	0.001 [b]	0.09 [b]	
MBP (mmHg)	**T0**	101.82±11.939	105.41±9.659	0.279 [a]
	T1	103.14±12.202	107.14±15.419	0.345 [a]
	P	0.58 [b]	0.64 [b]	

Group P: patients received propofol infusion; Group S: patients received sevoflurane inhalation; T0: at baseline. T1: 1 hour after surgery; HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure**.**
[a]Independent t-test. [b]Paired t-Test.

Pain, cognitive function, inflammatory response, and oxidative stress

Table 3 shows that NPRS scores were significantly lower in (group P) at T1 and T2 (Mean± SD= 4.05± 1.362 and 1.82± 0.664) than (group S) (Mean ± SD = 6.41 ± 0.590 and 2.95±0.213), respectively *(P*= <0.001).

There was no significant difference between (group P) and (group S) in the MoCA-B scores, S100-β, and NSE enzyme levels, (*p*=0.85, 0.63, and 0.60, respectively).

MMP-9 levels were significantly lower in (group P) at T1 and T2 (Mean±SD = 108.736 ± 16.298 and 98.014±14.437 ng/ml) than (group S) (Mean ± SD= 125.155±20.151 and111.291 ± 19.826 ng/ml), (*p*=0.04).

SOD enzyme activities were significantly higher in (group P) at T1 and T2 (Mean±SD= 28.078±8.601 and 21.206 ± 6.554 U/L) than (group S) (Mean ± SD =19.408±9.116 and 14.257± 8.157 U/L), (*p*= 0.03).

There was a significant difference in the NPRS score, MoCA-B score, and NSE. S100-β, MMP-9 levels, and SOD enzyme activities across time in each group (*p*=<0.001) (Figure 2), (Supplementary **Table 1**). There was a significant interaction between time and type of group in each group (*p*=<0.001).

Supplementary Table 1: Pairwise comparison of the difference in the changes across time in the study groups (N=44)**.**

Variables	Group	Time points	*P*
NPRS score	**P (n = 22)**	**T0 and T1**	<0.001*
		T1 and T2	<0.001*
		T0 and T2	<0.001*
	S (n = 22)	**T0 and T1**	<0.001*
		T1 and T2	<0.001*
		T0 and T2	<0.001*
MoCA-B score	**P (n = 22)**	**T0 and T2**	0.01*
		T2 and D7	0.25
		T0 and D7	<0.001*
	S (n = 22)	**T0 and T2**	<0.001*
		T2 and D7	0.06
		T0 and D7	<0.001*
S100-β (pg/Ml)	**P (n = 22)**	**T0 and T1**	<0.001*
		T1 and T2	<0.001*
		T0 and T2	<0.001*
	S (n = 22)	**T0 and T1**	<0.001*
		T1 and T2	<0.001*
		T0 and T2	<0.001*
NSE (µg/L)	**P (n = 22)**	**T0 and T1**	<0.001*
		T1 and T2	<0.001*
		T0 and T2	<0.001*
	S (n = 22)	**T0 and T1**	<0.001*
		T1 and T2	<0.001*
		T0 and T2	<0.001*
MMP-9 (ng/Ml)	**P (n = 22)**	**T0 and T1**	<0.001*
		T1 and T2	<0.001*
		T0 and T2	<0.001*
	S (n = 22)	**T0 and T1**	<0.001*
		T1 and T2	<0.001*
		T0 and T2	<0.001*
SOD (U/L)	**P (n = 22)**	**T0 and T1**	<0.001*
		T1 and T2	<0.001*
		T0 and T2	<0.001*
	S (n = 22)	**T0 and T1**	<0.001*
		T1 and T2	<0.001*
		T0 and T2	<0.001*

S100-β: S100 calcium-binding protein β; NSE, neuron-specific enolase; MMP-9: Matrix metalloproteinase-9; SOD: superoxide dismutase. Group P: patients received propofol infusion; Group S: patients received sevoflurane inhalation; T0: at baseline. T1: 1 hour after surgery; T2: 2 hours after surgery; D7: 7 days after surgery.
Post-hoc Bonferroni test.
*Significance level was set at $p < 0.05$.

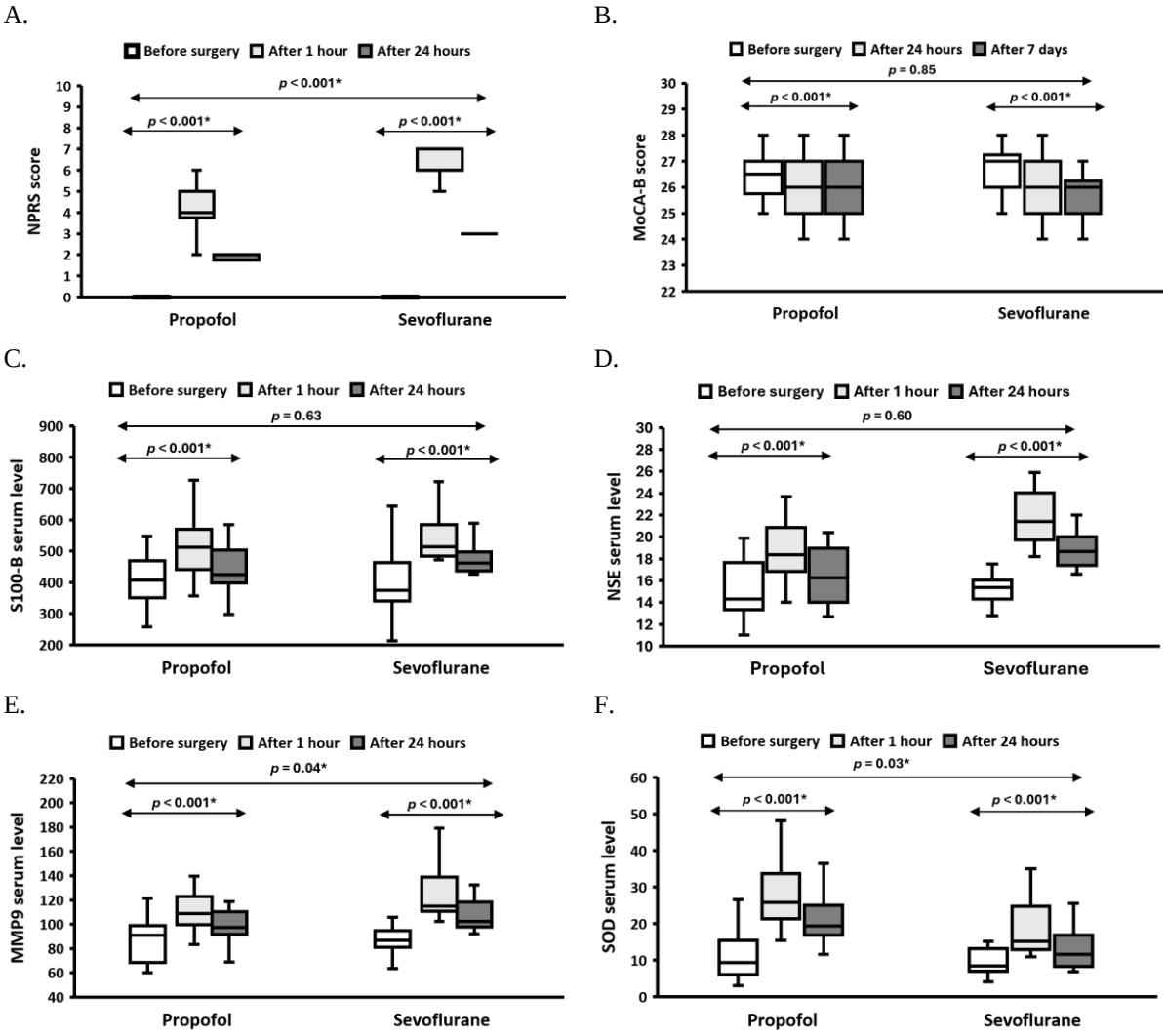

Fig. 2: Change of serum enzyme levels of measured parameters [A. NPRS score, B. MoCA-B score, C. S100-β (pg/ml), D. NSE (µg/L), E. MMP-9 (ng/ml), F. SOD (U/L)] at different time points while using propofol or sevoflurane anesthetics.

S100-β: S100 calcium-binding protein β; NSE, neuron-specific enolase; MMP-9: Matrix metalloproteinase-9; SOD: superoxide dismutase. Group P: patients received propofol infusion; Group S: patients received sevoflurane inhalation; T0: at baseline. T1: 1 hour after surgery; T2: 24 hours after surgery. D7: 7 days after surgery.
*Significance level was set at $p < 0.05$.

Adverse effects

Table 4 shows the perioperative adverse events of the two studied groups. Four patients (18.2%) in (group P) and two patients (9.1%) in group S experienced tachycardia which was managed by increasing the depth of anesthesia, no statistically significant differences were found between the two studied groups. Four patients (18.2%) in (group P) and five patients (22.7%) in (group S) experienced bradycardia which was managed using IV atropine sulfate 0.5 mg, with no statistically significant differences between both studied groups. Five patients (22.7%) in (group P) and seven patients in group S (31.8%) experienced hypertension which was managed by increasing the depth of anesthesia, with no statistically significant differences between either group. Three patients (13.5%) in (group P) experienced hypotension; two of them were managed by decreasing the rate of propofol infusion, and the other one was managed by

using IV ephedrine hydrochloride 5 mg. Two patients (9.1%) in (group S) experienced hypotension which was managed by decreasing sevoflurane concentration, with no statistically significant differences between both groups. Three patients (13.6%) in (group P) and one patient (4.5%) in (group S) experienced intraoperative bleeding, which was managed by ligation and electrosurgery, with no statistically significant differences between both groups. One patient (4.5%) in group P and ten patients (45.5%) in group S experienced postoperative nausea with six of them (27.3%) experiencing postoperative vomiting that was managed with ondansetron 4 mg IV, with statistically significant differences between the two groups. No patient experienced hypoxemia in either group **(Table 4).**

Table 3: Difference in NPRS score, MoCA-B score, NSE, S100-β, MMP-9, and SOD between the study groups across time (N=44).

Variables	Time	Group P (n = 22) Mean ± SD	Group S (n = 22) Mean ± SD	*p*
NPRS score	**T0**	0	0	<0.001*
	T1	4.05±1.36	6.41±.59	
	T2	1.82±0.66	2.95±0.21	
P		<0.001[a]*	<0.001[a]*	-
MoCA-B score	**T0**	26.45±1.057	26.73±0.935	0.85
	T1	26.09±1.151	25.91±1.065	
	T2	25.95±1.090	25.68±0.995	
P		<0.001*	<0.001*	-
S100-β (pg/mL)	**T0**	420.186±111.431	406.027±107.776	0.63
	T1	522.791±106.566	551.336±88.731	
	T2	456.055±112.714	485.255±71.749	
P		<0.001[a]*	<0.001[a]*	-
NSE (µg/L)	**T0**	16.650±6.570	15.864±3.889	0.60
	T1	20.591±7.191	22.750±5.750	
	T2	18.168±7.027	19.645±4.556	
P		<0.001[a]*	<0.001[a]*	-
MMP-9 (ng/mL)	**T0**	87.209±19.006	88.832±14.570	0.04*
	T1	108.736±16.299	125.155±20.151	
	T2	98.014±14.437	111.291±19.826	
P		<0.001[a]*	<0.001[a]*	-
SOD (U/L)	**T0**	10.831±6.093	11.594±7.570	0.03*
	T1	28.078±8.601	19.408±9.116	
	T2	21.206±6.554	14.257±8.157	
P		<0.001[a]*	<0.001[a]*	-

S100-β: S100 calcium-binding protein β; NSE: neuron-specific enolase; MMP-9: Matrix metalloproteinase-9; SOD: superoxide dismutase. Group P: patients received propofol infusion; Group S: patients received sevoflurane inhalation; T0: at baseline. T1: 1 hour after surgery; T2: 24 hours after surgery.

Repeated measures of ANOVA

[a]post-hoc Bonferroni test was significant across the three time points (p = <0.001).

p value of interaction of groups* time = <0.001.

*Significance level was set at $p < 0.05$.

Table 4: Perioperative adverse events of study groups.

Variables	Group P (*n*=22) [*n* (%)]	Group S (*n*=22) [*n* (%)]	*P*
Tachycardia	4 (18.2)	2 (9.1)	0.380
Bradycardia	4 (18.2)	5 (22.7)	0.709
Hypertension	5 (22.7)	7 (31.8)	0.498
Hypotension	3 (13.6)	2 (9.1)	0.635
Hypoxemia	0 (0)	0 (0)	-
Bleeding	3 (13.6)	1 (4.5)	0.294
Nausea	1 (4.5)	10 (45.5)	0.002
Vomiting	0 (0)	6 (27.3)	0.008

P-values were obtained by a chi-square test with significance set at $p < 0.05$. Group P: patients received propofol infusion; Group S: patients received sevoflurane inhalation.

Discussion

The current study showed that propofol could significantly reduce perioperative inflammation, oxidative stress, and pain sensation among patients undergoing elective, abdominal, and non-cardiac surgeries. Propofol was significantly associated with a shorter time of emergence after the operation ended. It also significantly decreased postoperative nausea and vomiting as compared to sevoflurane. No statistically significant difference could be detected between propofol and sevoflurane regarding cognitive dysfunction, thus the null hypothesis can be partially rejected.

Anesthetic modality and type of surgical operation have been argued in the contribution of postoperative inflammation occurrence, suggesting that Propofol has both antioxidant and anti-inflammatory advantages[46], while sevoflurane is thought to be able to reduce inflammatory mediators and leukocyte count in patients undergoing cardiopulmonary bypass (CPB) cardiac surgery[47]. Our results found that propofol could decrease the risk of the inflammatory response, as shown by lower levels of MMP-9, than sevoflurane at both 1hr and 24h postoperatively. This was in line with Tian et al.[48], Zhao et al.[8] and Zhou et al.[49] who demonstrated significantly lower levels of MMP-9 in propofol than in the sevoflurane group at 24h postoperatively. Furthermore, Wang et al.[50] reported significantly lower levels of MMP-9 in patients undergoing cancer resection operations in propofol than sevoflurane group. Additionally, Ding et al.[22], Zhou et al.[49], Liu et al.[1], and Zhao et al.[8] showed significantly lower levels of inflammatory cytokines at 24h postoperatively in the propofol than the sevoflurane group. Tang et al.[51] showed significantly higher MMP-9 levels at 0 h, 6 h, and 12 hours after cardiopulmonary bypass cardiac surgery in the sevoflurane than in the propofol group. Franzen et al.[52] showed augmented interleukin 6 levels in the sevoflurane than the propofol group, suggesting a higher possibility of postoperative inflammation.

On the contrary, Yang et al.[53] suggested significantly lower inflammatory response in patients undergoing uni-valve replacement surgery under CPB and anesthetized with sevoflurane. Moreover, Shen et al.[54] mentioned that the combined use of propofol and sevoflurane decreased inflammatory cytokines at 3h and 12h postoperatively than sevoflurane alone in elderly patients who underwent cholecystectomy operation, while Bettex et al.[55] demonstrated no significant difference between propofol and sevoflurane regarding postoperative inflammation on cyanotic and

cyanotic children and so did Lindholm et al.[56] who reported no significant difference between both anesthetics concerning inflammatory response.

In the present study, propofol could decrease the risk of oxidative stress more than sevoflurane at both 1hr and 24h postoperatively, as shown by higher enzyme activities of SOD. Propofol's structure is similar to phenol-based antioxidants which look like the endogenously secreted vitamin E, thus, propofol acts as a free radical scavenging agent[46]. Similar to our findings, Liu et al.[1] reported significantly higher SOD enzyme activities at 24h postoperative in the propofol than the sevoflurane group, conversely Li et al.[28] revealed no significant difference in SOD enzyme activities at 24h postoperative between the two anesthetic drugs in pediatric patients undergoing liver transplantation. This could be attributed to the difference in age group (5 months–2 years) as compared to (30-77 years) in our study. Nashibi et al.[57] reported no significant results regarding SOD levels in the propofol group as compared to isoflurane inhalational anesthetic agent in patients who experienced craniotomy due to supratentorial tumor.

Propofol was significantly associated with a shorter emergence time from anesthesia and a lower ketorolac dose as compared to sevoflurane. This was in accordance with Tian HT et al.[7] who reported a significant reduction in postoperative recovery time in propofol than sevoflurane group in patients who underwent lung cancer resection operation. This agrees with Zhao et al.[8] who confirmed lower pain index results in propofol than sevoflurane group at both 24 and 48h after spine fracture operations and Zhou et al.[49] who showed significantly longer awaking times and higher pain scores in lung cancer patient undergoing thoracoscopic surgery.

The short emergence time in propofol is likely due to its lipophilicity and short context-sensitive half-time. Even though some amount of propofol stays in body compartments that aren't adequately perfused, propofol slowly returns from those compartments contributing little to the amount of propofol in the central compartment, which is rapidly cleared, so its concentration in the main central compartment decreases below the hypnotic threshold after stopping its infusion rapidly[58,59]. On the other hand, Cohen et al.[60] reported no significant difference in emergence time between propofol and sevoflurane in children, aged 2–36 months, who underwent ambulatory surgery. This could be because Cohen performed shorter duration operations that lasted for about 30 minutes, unlike our selected operations that lasted for around 3 hours. Alternatively, Parida et al.[58] showed no significant difference in emergence time in patients undergoing daycare surgeries. Singh et al.[59] showed significantly shorter emergence and response times in sevoflurane than propofol group in patients who underwent elective daycare surgical procedures under general anesthesia, which might be attributed to the stoppage of the studied drugs at the initiation of skin closure with the maintenance of anesthesia with nitrous oxide till the end of skin closure and also the short anesthesia duration in these studies (<1h). Conversely, Orhon et al.[61] found shorter recovery times in the sevoflurane than in the propofol group, which could be because the operators reduced the sevoflurane concentration and propofol infusion rate 15 minutes before the entire operation was completed. Shah et al.[62] also reported a significantly shorter emergence time in sevoflurane than in the propofol group during laparoscopic surgery.

There was no notable significant difference in perioperative hemodynamic parameters between propofol and sevoflurane across time. This was consistent with previous studies conducted on elderly patients undergoing major surgeries[21], laparoscopic cholecystectomy[63], percutaneous nephrolithotomy[61], radical gastrectomy procedures[64], tumor resection operations[65] and endoscopic lumbar discectomy[66]. On the contrary, Bharti et al.[67] reported significantly lower MBP after anesthesia induction in the propofol as compared to the sevoflurane group in patients undergoing laryngoscope.

The present study assumed that propofol could reduce pain scores as the results show at both 1h and 24h postoperatively and consequently postoperative analgesic doses in comparison with sevoflurane, which agreed with the results of many previous clinical trials[49,64,68-70]. A systematic review and meta-analysis[71] confirmed higher odds of needed

rescue analgesia and postoperative pain in the sevoflurane group more than in the propofol group in pediatric surgeries. Propofol exerts its antinociceptive effect through activation of $GABA_A$ receptors, and its antioxidant and anti-inflammatory action[64,69]. Propofol antinociception is also mediated by a spinal delta opioid receptor[69]. In comparison, an elevation of pain perception was reported to occur due to hyperalgesic effects of volatile anesthetics such as sevoflurane at a minimum alveolar concentration (MAC) of 0.1%. These effects could be mediated by the adjustment of serotonin 5-hydroxytryptamine 3 (5-HT3) receptor-mediated currents and also by central cholinergic and adrenergic conductance[64,68]. However, preceding studies concluded no significant difference in pain and analgesic consumption between propofol and sevoflurane, which could be because previous studies treated postoperative pain using patient-controlled analgesia (PCA) with oxycodone and IV paracetamol/6h[72], PCA with morphine sulfate, wound infiltration with levobupivacaine, and oral dihydrocodeine/8h[73], and PCA with fentanyl[74] which agreed with Choi et al.[75] who found no significant difference in postoperative pain intensity and postoperative analgesic need between propofol and sevoflurane groups both combined with remifentanil in the first 24 hours after surgery.

The incidence of PODC is attributed to intraoperative trauma and anesthesia in surgical patients[67]. Our results demonstrated no significant difference between propofol and sevoflurane regarding the biomarkers investigating the cognitive impairment of patients. This agrees with Verma et al.[66], who reported no significant differences in cognitive scores at 1h postoperatively, Geng et al.[63] who reported no significant changes in S100-β levels at 1h and 24h postoperatively between propofol and sevoflurane group, El-Hadi et al.[77] who showed insignificant S100-β levels changes and Mini-Mental State Examination (MMSE) scores between the propofol and sevoflurane groups before and 120 minutes after lumbar disc surgery, and Guo et al.[78] who reported no significant difference in MMSE and MoCA scores between propofol and sevoflurane group. On the contrary, several clinical trials found significantly lower cognitive scores[7, 8, 21, 22, 49, 50, 63], and higher S100-β levels[7, 8, 21, 22, 49] at 24h postoperative in sevoflurane compared to propofol group. This might be because those studies were conducted on an older age group than our study. Tang et al.[51] reported significantly higher NSE, S100β serum levels at 0 hours, 6 hours, and 12 hours after surgery in the propofol than sevoflurane group. He also reported lower POCD incidence at 12 hours and 24 hours after operation in propofol than sevoflurane group using MMSE score which might be because patients were undergoing cardiopulmonary bypass cardiac surgery.

Kalimeris et al.[79] observed significantly higher S100-β levels at 24h postoperatively in the sevoflurane than in the propofol group, this might be because the study involved the carotid endarterectomy operation which was associated with cerebral ischemia. On the contrary, Qin et al.[80] denoted significantly lower cognitive scores and higher S100-β levels at the end of the surgery and 24h postoperatively in the propofol than the sevoflurane group. The authors pointed out that radical surgery for lung cancer could easily induce cerebral hypoxia and sevoflurane could better inhibit pulmonary vasoconstriction and reduce pulmonary shunt as compared to propofol. Thus, better relieving patients' cerebral hypoxia and reducing neuronal damage. Yan et al.[1] recognized significantly higher NSE levels at 24h postoperatively in the sevoflurane than in the propofol group which matched our results. This could be because the study patients were exposed to craniocerebral trauma. Yao et al.[81] investigated post-operative cognitive dysfunction in geriatric patients who underwent laparoscopic surgery, by conducting an MMSE test and found that it was insignificantly higher in propofol than sevoflurane group on the first day postoperative, unlike Tang et al.[51] who reported significantly higher MMSE scores in the propofol than sevoflurane group 24h postoperatively.

In the current study, nausea and vomiting following an operation were the most predominant adverse effects, more frequently in (group S) than in (group P). This was in line with earlier clinical trials[7, 61, 72]. Similarly, preceding studies documented a higher probability of occurrence of nausea[49] and vomiting[58] in the sevoflurane than in the

propofol group. In comparison, numerous clinical trials suggested no significant difference in incidence rates of PONV between both anesthetics This could be because patients were sedated for a shorter period and were given prophylactic antiemetics[59,70]. Shah et al.[62] reported no significant difference between the propofol and sevoflurane group regarding postoperative nausea and vomiting which might be attributed to the shorter operative duration (76 minutes) as compared to (250 minutes) in the current study. Oppositely, Matsuura et al.[82] reported that PONV occurrence in propofol was higher than in sevoflurane group, which might be attributed to imbalanced groups with a greater number of risk factors of nausea and vomiting in the propofol group. Although the two groups were not significantly different from each other regarding S100 B, NSE levels, and MoCA-B scores, the interaction between time and groups was significant. This highlights the importance of the time factor for the establishment of the effect of anesthetics on the biomarkers.

This study has some points of strength as it compared two of the most commonly used anesthetics in surgical operations. Assessment of cognitive function together with inflammation, oxidative stress, and pain gives an overall view of the possible advantages of using propofol rather than sevoflurane anesthesia and how the use of propofol could affect the safety profile of patients undergoing surgical operations. Pain assessment and cognitive dysfunction were done using validated tools. S100B, MMP-9, NSE, and SOD enzyme levels were assessed at different time points (before the operation, 1 hour, and 24 hours after operation), which allowed for a comparison of the influence of the anesthetics across time.

However, there were some limitations in the recent study. Firstly, it was a single-center trial, and the time required to follow-up patients was not quite long. Secondly, pain assessment was patient-reported, so it was affected by the patient's emotional status. Thirdly, the study was not a clear comparison between sevoflurane and propofol anesthesia, because propofol was given for induction of anesthesia to all patients as inducing anesthesia using inhalational sevoflurane is not commonly used with adult patients. Fourthly, the study was conducted in the same site which might restrict the generalizability of the outcomes to other settings, so further multicenter trials and larger and longer duration studies are needed to investigate the concluded association.

Further studies should be applied to investigate the difference between propofol and sevoflurane in a wider context while considering neuroendocrine stress response factors, and genetic polymorphisms. Enrollment of patients from different ASA physical statuses other than class I and II should be considered in future studies.

Conclusion

Propofol infusion could be more effective than sevoflurane inhalation anesthesia during elective, noncardiac, and abdominal surgeries. Propofol could shorten the time to emerge from anesthesia, modify inflammatory response, give better analgesic outcomes, decrease oxidative stress, and reduce incidences of nausea and vomiting.

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REFERENCES

1. Y. Liu, J. Xia, Z.-J. Peng, and Y.-F. Ma, "Effects of propofol anesthesia on oxidative stress, neurological function and inflammatory cytokines in patients with craniocerebral trauma", ***J Hainan Med Univ***, 23(24), 151-154 (2017).
2. N. Caza, R. Taha, Y. Qi, and G. Blaise, "The effects of surgery and anesthesia on memory and cognition", ***Prog Brain Res***, 169, 409-422 (2008).
3. J. E. Cottrell and J. Hartung, "Developmental disability in the young and postoperative cognitive dysfunction in the elderly after anesthesia and surgery: do data justify changing clinical practice?", ***Mt Sinai J Med,*** 79 (1), 75-94 (2012).
4. J. E. Cottrell and J. Hartung, "Anesthesia and cognitive outcome in

elderly patients: a narrative viewpoint", ***J Neurosurg Anesthesiol***, 32(1), 9-17 (2020).
5. Z.-Y. Yao, Z Jia, Y-H Xie, L-L Zhang, *et al.*, "Analgesic effect of dezocine in different doses on elderly patients undergoing abdominal operation under general anesthesia and its influence on stress response to postoperative tracheal extubation", ***Eur Rev Med Pharmacol Sci***, 21(22), 5223-5229 (2017).
6. S. A. Safavynia and P. A. Goldstein, "The role of neuroinflammation in postoperative cognitive dysfunction: moving from hypothesis to treatment", ***Front Psychiatry***, 9, 752 (2019).
7. H. Tian, X. Duan, Y. Yang, Y. Wang, Q. Bai, and X. Zhang, "Effects of propofol or sevoflurane anesthesia on the perioperative inflammatory response, pulmonary function and cognitive function in patients receiving lung cancer resection", ***Eur Rev Med Pharmacol Sci***, 21(23), 5515-5522 (2017).
8. Y. Zhao and H. Zhang, "Propofol and sevoflurane combined with remifentanil on the pain index, inflammatory factors and postoperative cognitive function of spine fracture patients", ***Exp Ther Med***, 15 (4), 3775-3780 (2018).
9. Z. Liang *et al.*, "Tracking the effects of propofol, sevoflurane and (S)-ketamine anesthesia using an unscented Kalman filter-based neural mass model", ***J Neural Eng***, 20 (2), (2023).
10. C. L. Wu and S. N. Raja, "Treatment of acute postoperative pain", ***Lancet***, 377 (9784), 2215-2225 (2011).
11. H. Kehlet, T. S. Jensen, and C. J. Woolf, "Persistent postsurgical pain: risk factors and prevention", ***lancet***, 367 (9522), 1618-1625 (2006).
12. H.-Y. Liu, Hsiao-Ping Wang, Chen-June Seak, *et al.*, "Influences of Cognitive Function and Depressive Symptoms on Pain Trajectories During the First Year Following Hip Fracture Surgery: A Prospective Cohort Study", ***J Am Med Dir Assoc***, 25 (1), 104-111 (2024).
13. M. Admiraal, Mark L van Zuylen, Henning Hermanns, *et al.*, "The Effect of Preoperative Disability, Cognitive Impairment, Frailty and Opioid Use on Acute Postoperative Pain in Older Patients Undergoing Surgery A Prospective Cohort Study", ***J Pain***, 24(10), 1886-1895 (2023).
14. J. Ma, J. Williams, D. Eastwood, *et al.*, "High-dose Propofol Anesthesia Reduces the Occurrence of Postoperative Cognitive Dysfunction via Maintaining Cytoskeleton", ***Neuroscience***, 421, 136-143 (2019).
15. W.-X. Li, *R.-Y. Luo, C. Chen, et al.*, "Effects of propofol, dexmedetomidine, and midazolam on postoperative cognitive dysfunction in elderly patients: a randomized controlled preliminary trial", ***Chin Med J***, 132 (4), 437-445 (2019).
16. Y. Wu, S. Antony, J. L. Meitzler, and J. H. Doroshow, "Molecular mechanisms underlying chronic inflammation-associated cancers", ***Cancer Lett***, 345(2), 164-173 (2014).
17. G. Baskaran, *R. H. Heo, M. K. Wang, et al.*, "Associations of inflammatory biomarkers with morbidity and mortality after noncardiac surgery: A systematic review and meta-analysis", ***J Clin Anesth***, 97,111540 (2024).
18. S. A. Jones, "Directing transition from innate to acquired immunity: defining a role for IL-6", ***Jimmunol***, 175 (6), 3463-3468 (2005).
19. S. P. Hussain, L. J. Hofseth, and C. C. Harris, "Radical causes of cancer", ***Nat Rev Cancer***, 3 (4), 276-285 (2003).
20. F. J. Pashkow, "Oxidative stress and inflammation in heart disease: do antioxidants have a role in treatment and/or prevention?", ***Int J Inflam***, 2011 (2011).
21. Y. Qiao, H. Feng, T. Zhao, H. Yan, H. Zhang, and X. Zhao, "Postoperative cognitive dysfunction after inhalational anesthesia in elderly patients undergoing major surgery: the influence of anesthetic technique,

cerebral injury and systemic inflammation", ***BMC Anesthesiol***,15, 1-7 (2015).
22. F. Ding, X. Wang, L. Zhang, J. Li, F. Liu, and L. Wang, "Effect of propofol-based total intravenous anaesthesia on postoperative cognitive function and sleep quality in elderly patients", ***Int J Clin Pract***,75(7), e14266 (2021).
23. S.-H. Park and S.-K. Hwang, "Prognostic Value of Serum Levels of S100 Calcium-Binding Protein B, Neuron-Specific Enolase, and Interleukin-6 in Pediatric Patients with Traumatic Brain Injury", ***World Neurosurg***, 118, e534-e542 (2018).
24. M. A. Isgrò, P. Bottoni, and R. Scatena, "Neuron-specific enolase as a biomarker: biochemical and clinical aspects", ***Adv Exp Med Biol***, 125-143 (2015).
25. M. Ram, Y. Sherer, and Y. Shoenfeld, "Matrix Metalloproteinase-9 and Autoimmune Diseases", ***J Clin Immunol***, 26(4), 299-307 (2006).
26. A. Yabluchanskiy, Y. Ma, R. P. Iyer, M. E. Hall, and M. L. Lindsey, "Matrix metalloproteinase-9: Many shades of function in cardiovascular disease", ***Physiology (Bethesda)***, 28(6), 391-403 (2013).
27. M. L. Tataranno, S. Perrone, M. Longini, and G. Buonocore, "New antioxidant drugs for neonatal brain injury", ***Oxid Med Cell Longev,*** 2015 (2015).
28. H. Li, Y. Weng, S. Yuan, W. Liu, H. Yu, and W. Yu, "Effect of sevoflurane and propofol on acute kidney injury in pediatric living donor liver transplantation", ***Ann Transl Med***, 7 (14), 340 (2019).
29. Z. S. Nasreddine, N. A. Phillips, V. Bédirian, *et al.*, "The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment", ***J Am Geriatr Soc***, 53(4), 695-699 (2005).
30. S. Zhou, J. Zhu , N. Zhang, *et al.*, "The influence of education on Chinese version of Montreal cognitive assessment in detecting amnesic mild cognitive impairment among older people in a Beijing rural community", ***ScientificWorldJournal***, 2014, 689456 (2014).
31. P. Julayanont, S. Tangwongchai, S. Hemrungrojn, *et al.*, "The montreal cognitive assessment—basic: a screening tool for mild cognitive impairment in illiterate and low-educated elderly adults", ***J Am Geriatr Soc***, 63(12), 2550-2554 (2015).
32. P. E. Mintken, P. Glynn, and J. A. Cleland, "Psychometric properties of the shortened disabilities of the Arm, Shoulder, and Hand Questionnaire (QuickDASH) and Numeric Pain Rating Scale in patients with shoulder pain", ***J Shoulder Elbow Surg***, 18 (6), 920-926 (2009).
33. J. Katz and R. Melzack, "Measurement of Pain", ***Surg Clin North Am***, 79(2), 231-252 (1999).
34. K.-Y. Moon and D. Shin, "Correlation between psychosocial stresses, stress coping ability, pain intensity and degree of disability in patients with non-specific neck pain", ***Physiol Behav***, 275, 114433 (2024).
35. I. López-de-Uralde-Villanueva *et al.*, "Minimal Clinically Important Differences in Hand Pain Intensity (Numerical Pain Rate Scale) and Related-Function (Boston Carpal Tunnel Questionnaire) in Women With Carpal Tunnel Syndrome", ***Arch Phys Med Rehabil***, 105 (1), 67-74 (2024).
36. M. K. Sharma, S. Chaudhary, and S. Shenoy, "Short-term effect of frequency specific intramuscular electrical stimulation on post dry needling soreness of upper fibers of trapezius: A randomized controlled trial", ***J Bodyw Mov Ther***, 40, 217-223 (2024).
37. M. D. Goodyear, K. Krleza-Jeric, and T. Lemmens, "The Declaration of Helsinki", ***BMJ***, 335 (7621), 624-5 (2007).
38. K. F. Schulz, D. G. Altman, and D. Moher, "CONSORT 2010 statement: updated guidelines for reporting

parallel group randomised trials", ***BMJ***, 340, c332 (2010).
39. C. Han *et al.*, "A comparison of the effects of midazolam, propofol and dexmedetomidine on the antioxidant system: A randomized trial", ***Exp Ther Med***, 9(6), 2293-2298 (2015).
40. G. Koksal, C. Sayilgan, S. Aydin, H. Uzun, and H. Oz, "The effects of sevoflurane and desflurane on lipid peroxidation during laparoscopic cholecystectomy", ***Eur J Anaesthesiol***, 21(3), 217-220 (2004).
41. D. Rohan *D. Buggy, et al.*, "Increased incidence of postoperative cognitive dysfunction 24 hr after minor surgery in the elderly", ***Can J Anaesth***, 52 (2), 137-142 (2005).
42. J. Ortiz, L. C. Chang, D. A. Tolpin, C. G. Minard, B. G. Scott, and J. M. Rivers, "Randomized, controlled trial comparing the effects of anesthesia with propofol, isoflurane, desflurane and sevoflurane on pain after laparoscopic cholecystectomy", ***Braz J Anesthesiol***, 64, 145-151 (2014).
43. A. Petrie and C. Sabin, *Medical statistics at a glance*, ***John Wiley & Sons*** (2019).
44. S. M. Khorsand. Maintenance of general anesthesia: Overview, ***UpToDate*** (2022)
45. J. F. Butterworth Iv, D. C. Mackey, and J. D. Wasnick, in ***Morgan & Mikhail's Clinical Anesthesiology***, *7e*. New York, NY: McGraw-Hill Education, (2022).
46. F. Karacaer, E. Biricik , M. Ilgınel , *et al.*, "The anti-inflammatory and antioxidant effects of propofol and sevoflurane in children with cyanotic congenital heart disease", ***J Cardiothorac Vasc Anesth***, 37(1), 65-72 (2023).
47. E. J. Cho, J. H. Yoon, S. J. Hong, S. H. Lee, and S. B. Sim, "The effects of sevoflurane on systemic and pulmonary inflammatory responses after cardiopulmonary bypass", ***J Cardiothorac Vasc Anesth***, 23 (5), 639-645 (2009).
48. H.-T. Tian, X.-H. Duan, Y.-F. Yang, Y. Wang, Q.-L. Bai, and X. Zhang, "Effects of propofol or sevoflurane anesthesia on the perioperative inflammatory response, pulmonary function and cognitive function in patients receiving lung cancer resection", ***Eur Rev Med Pharmacol Sci***, 21(23), 5515-5522 (2017).
49. Y. Zhou and T. Xu, "Effect of propofol and sevoflurane on perioperative and postoperative outcomes in lung cancer patients after thoracoscopic surgery", ***Trop J Pharm Res***, 20 (4), 873-879 (2021).
50. G. Wang, J. Liu, J. Gao, and X. Zheng, "Comparison of the effects of sevoflurane and propofol anesthesia on pulmonary function, MMP‐9 and postoperative cognition in patients receiving lung cancer resection", ***Oncol Lett***, 17(3), 3399-3405 (2019).
51. S. Tang, W. Huang, K. Zhang, W. Chen, and T. Xie, "Comparison of effects of propofol versus sevoflurane for patients undergoing cardiopulmonary bypass cardiac surgery", ***Pak J Med Sci***, 35(4), 1072 (2019).
52. S. Franzén, E. Semenas, A. Larsson, M. Hultström, and R. Frithiof, "Plasma cytokine levels in spinal surgery with sevoflurane or total intravenous propofol anesthesia–A post hoc analysis of a randomized controlled trial", ***Cytokine***, 169, 156290 (2023).
53. X.-L. Yang, D. Wang, G.-Y. Zhang, and X.-L. Guo, "Comparison of the myocardial protective effect of sevoflurane versus propofol in patients undergoing heart valve replacement surgery with cardiopulmonary bypass", ***BMC Anesthesiol***, 17, 1-7 (2017).
54. Y. Shen, Y. Liu, Y. Wu, and J. He, "Changes of recovery quality and early cognitive function after treatment of sevoflurane combined with propofol in the elderly undergoing cholecystectomy", ***Am J Transl Res***, 13 (10), 11868 (2021).
55. D. A. Bettex, *P. M. Wanner, M. Bosshart, et al.*, "Role of sevoflurane

in organ protection during cardiac surgery in children: a randomized controlled trial", ***Interact Cardiovasc Thorac Surg***, 20(2), 157-165 (2015).
56. E. Lindholm, E. Aune, I. Seljeflot, J. Otterstad, and K. Kirkebøen, "Biomarkers of inflammation in major vascular surgery: a prospective randomised trial", ***Acta Anaesthesiol Scand***, 59 (6), 773-787 (2015).
57. M. Nashibi, P. Sezari, K. Mottaghi, S. Yeganeh-Khah, and F. Safari, "Antioxidative effects of isoflurane and propofol on serum levels of catalase, glutathione and superoxide dismutase in craniotomy for supratentorial tumor", ***J Cell Mol Anesth***, 4 (2) (2019).
58. S. Parida and A. S. Badhe, "Comparison of cognitive, ambulatory, and psychomotor recovery profiles after day care anesthesia with propofol and sevoflurane", ***J Anesth***, 28, 833-838 (2014).
59. G. SInGh, H. Kaur, S, Kumar, *et al.*, "Propofol vs Sevoflurane in General and Cognitive Recovery from Anaesthesia in Day Care Surgery-A Randomised Clinical Trial", ***J Clin Diagn Res***, 14(12), (2020).
60. I. T. Cohen, J. C. Finkel, R. S. Hannallah, K. A. Hummer, and K. M. Patel, "Rapid emergence does not explain agitation following sevoflurane anaesthesia in infants and children: a comparison with propofol", ***Paediatr Anaesth***, 13(1), 63-67 (2003).
61. Z. N. Orhon, S. Devrim, M. Celik, Y. Dogan, A. Yildirim, and E. K. Basok, "Comparison of recovery profiles of propofol and sevoflurane anesthesia with bispectral index monitoring in percutaneous nephrolithotomy", ***Korean J Anesthesiol***, 64 (3), 223-228 (2013).
62. A. Shah and R. Adaroja, "Comparison of haemodynamic changes with propofol and sevoflurane anaesthesia during laparoscopic surgery", ***Natl J Med Res***, 1(2), 76-79 (2011).
63. Y.-j. Geng, Q.-h. Wu, and R.-q. Zhang, "Effect of propofol, sevoflurane, and isoflurane on postoperative cognitive dysfunction following laparoscopic cholecystectomy in elderly patients: a randomized controlled trial", ***J Clin Anesth***, 38, 165-171 (2017).
64. F.-h. Ji, D. Wang, J. Zhang, H.-y. Liu, and K. Peng, "Effects of propofol anesthesia versus sevoflurane anesthesia on postoperative pain after radical gastrectomy: a randomized controlled trial", ***J Pain Res***, 11, 1247 (2018).
65. L. Guo, F. Lin , H. Dai, *et al.*, "Impact of sevoflurane versus propofol anesthesia on post-operative cognitive dysfunction in elderly cancer patients: a double-blinded randomized controlled trial", ***Med Sci Monit***, 26, e919293 (2020).
66. A. K. Verma, R. Haldar, S. Srivastava, K. K. Das, and P. Mishra, "Comparison of Recovery Profiles of Patients Undergoing Endoscopic Lumbar Discectomy under Desflurane, Propofol, or Sevoflurane Anesthesia: A Randomized, Prospective, Clinical, Comparative Study", ***J Neurosci Rural Pract***, 13 (2), 226-235 (2022).
67. N. Bharti, P. Chari, and P. Kumar, "Effect of sevoflurane versus propofol-based anesthesia on the hemodynamic response and recovery characteristics in patients undergoing microlaryngeal surgery", ***Saudi J Anaesth***, 6 (4), 380-384 (2012).
68. M. Li, W. MEI, P. WANG, et *al.*, "Propofol reduces early post-operative pain after gynecological laparoscopy", ***Acta Anaesthesiol Scand***, 56(3), 368-375 (2012).
69. A. C. S. Chan, Q. Qiu, S. W. Choi , *et al.*, "Effects of intra-operative total intravenous anaesthesia with propofol versus inhalational anaesthesia with sevoflurane on post-operative pain in liver surgery: a retrospective case-control study", ***PloS One***, 11(2), e0149753 (2016).
70. T. Tan, R. Bhinder, M. Carey, and L. Briggs, "Day-surgery patients anesthetized with propofol have less postoperative pain than those

anesthetized with sevoflurane", ***Anesth Analg***, 111 (1), 83-85 (2010).
71. B. M. Abdallah, A. M. Elshoeibi, N. ElTantawi, *et al.*, "Comparison of postoperative pain in children after maintenance anaesthesia with propofol or sevoflurane: a systematic review and meta-analysis", ***Br J Anaesth***, 133(1), 93-102 (2024).
72. S. Pokkinen, A. Yli-Hankala, and M. L. Kalliomäki, "The effects of propofol vs. sevoflurane on post-operative pain and need of opioid", ***Acta Anaesthesiol Scand***, 58(8), 980-985 (2014).
73. S. S. Wong, F. Wang, T. C. Chan, and C. W. Cheung, "The analgesic effect of total intravenous anaesthesia with propofol versus inhalational anaesthesia for acute postoperative pain after hepatectomy: a randomized controlled trial", ***BMC Anesthesiol***, 23 (1), 1-11 (2023).
74. J.-E. Chang, S.-W. Min, H. Kim, *et al.*, "Association Between Anesthetics and Postoperative Delirium in Elderly Patients Undergoing Spine Surgery: Propofol Versus Sevoflurane", ***Global Spine J***, 14(2), 478-484 (2024).
75. E. K. Choi and S. Kim, "Effects of propofol-remifentanil versus sevoflurane-remifentanil on acute postoperative pain after total shoulder arthroplasty: a randomized trial", ***J Yeungnam Med Sci***, 40 (3), 247-251 (2023).
76. W. Dabrowski, Z. Rzecki, J. Pilat, and M. Czajkowski, "Brain damage in cardiac surgery patients", ***Curr Opin Pharmacol***, 12 (2), 189-194 (2012).
77. S. M. El-Hadi, A. A. Z. Abd Alkader, R. A. H. Abo Elwafa, E. Darwish Mohamed, and R. A. E. Abdel Azim, "Effect of sevoflurane versus propofol on early cognitive functions in elderly patients after lumbar disc surgery", ***Egypt J Anaesth***, 40 (1), 61-68 (2024).
78. J.-y. Guo, J.-y. Fang, S.-r. Xu, M. Wei, and W.-q. Huang, "Effects of propofol versus sevoflurane on cerebral oxygenation and cognitive outcome in patients with impaired cerebral oxygenation", ***Ther Clin Risk Manag***, 12, 81-85 (2016).
79. K. Kalimeris, S. Kouni, G. Kostopanagiotou, *et al.*, "Cognitive function and oxidative stress after carotid endarterectomy: comparison of propofol to sevoflurane anesthesia", ***J Cardiothorac Vasc Anesth***, 27(6), 1246-1252 (2013).
80. Y. Qin, J. Ni, L. Kang, Z. Zhong, L. Wang, and S. Yin, "Sevoflurane effect on cognitive function and the expression of oxidative stress response proteins in elderly patients undergoing radical surgery for lung cancer", ***J Coll Physicians Surg Pak***, 29(1), 12-15 (2019).
81. J. Yao, Z. Gao, W. Qu, and J. Li, "Propofol total intravenous anesthesia vs. sevoflurane inhalation anesthesia: Effects on post-operative cognitive dysfunction and inflammation in geriatric patients undergoing laparoscopic surgery", ***Exp Ther Med***, 28(3), 343 (2024).
82. H. Matsuura, S. Inoue, and M. Kawaguchi, "The risk of postoperative nausea and vomiting between surgical patients received propofol and sevoflurane anesthesia: A matched study", ***Acta Anaesthesiol Taiwan***, 54(4), 114-120 (2016).

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مقارنة التأثير الإلتهابى، الإجهاد التأكسدى، معامل الألم، والإعتلال الإدراكى اللاحق للعمليات بين عقارى البروبوفول والسيفوفلوران : تجربة سريرية عشوائية

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الخلفيـــة: إن إختيارأدوية التخدير يلعب دوراً حاسماً فى حماية الوظيفة العقلية للمخ، وتقليل المضاعفات المصاحبة للعمليات الجراحية ، وتوفير رعاية بجودة عالية وتحسين جودة حياة المرضى.

الأهداف: مقارنة الاستجابة الالتهابية ، والإجهاد التأكسدي، والإختلال المعرفي، ومؤشـر الألـم بعـد الجراحة لدى المرضى الذين يخضعون لجراحة اختيارية غير قلبية في منطقة البطن بإستخدام التخـدير الكلى بالبروبوفول أو السيفوفلوران.

المنهجية : تم إجراء تجربة سريرية مستقبلية، متوازية، عشوائية، مزدوجة التعميه فـي الفتـرة مـن ديسمبر ٢٠٢١ إلى أبريل ٢٠٢٣ على ٤٤ مريضًا والذين خضعوا لعمليات جراحية إختيارية في البطن و قد تم تخديرهم إما عن طريق تسريب البروبوفـول أو بإستنشـاق السـيفوفلوران فـي مستشـفى متخصص. تم أخذ عينات دم من المرضى قبل الجراحة وبعدها بساعة و٢٤ ساعة. تم قياس الاستجابة الالتهابية باستخدام إنزيم **Matrix Metalloproteinase-9 (MMP-9)**، والإجهاد التأكسـدي باسـتخدام **Superoxide Dismutase (SOD)**، والإختلال المعرفي بقياس مستويات **S100-β**، و **Neuron-Specific Enolase (NSE)**، ودرجة تقييم الإدراك المعرفي **(MoCA-B)**، والألم باسـتخدام مقيـاس التصـنيف الرقمي للألم .**(NPRS)**.

النتائج: لقد اظهرت مستويات MMP-9 انخفاضاً واضحاً و بينت أنشطة إنزيم (SOD) إرتفاعاً ملحوظاً فى مجموعة البروبوفول وذلك بعد ساعة و ٢٤ من انتهـاء العمليـة الجراحيـة مقارنـة بمجموعـة السيفوفلوران ($P< 0.05$). كان وقت الإفاقة من التخدير ودرجات (NPRS) أقـل بشـكلٍ ملحـوظٍ فـي مجموعة البروبوفول مقارنة بمجموعة السيفوفلوران ($P<0.001$) . كانت حالات الغثيان والقـيء بعـد الجراحة أقل بشكل ملحوظ في مجموعة البروبوفول مقارنة بمجموعة السيفوفلوران.

الاستنتاج: إن التسريب الوريدى للبروبوفول فى العمليات الجراحية يقلل درجات الألم بعد الجراحة، ويخفض الاستجابة الالتهابية، والاجهاد التأكسدى، ويقلل من الوقت اللازم للافاقه من التخدير، ويعمل على خفض معدلات القيء والغثيان لدى المرضى الذين خضعوا لعمليات جراحية اختيارية في البطن تحت تأثير التخدير العام.