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Original Article

A Comparative Study between Inhalation Anesthesia using Sevoflurane and Total Intravenous Anesthesia by Propofol in Patients with Elevated Liver Enzymes

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ABSTRACT

Background: Clinical anesthesia involves use of sevoflurane and propofol, both of which have been shown to protect liver function. To the best of our knowledge, this is the first study conducted in Zagazig University hospitals comparing the effects of sevoflurane and propofol on the liver function after surgery in patients who would be under general anesthesia and had preoperatively increased liver enzyme levels. The aim of the study is to evaluate the effects and side effects of total intravenous anesthesia (TIVA) against inhalational anesthesia (sevoflurane) versus propofol on postoperative liver function in patients undergoing general anesthesia who have preoperatively increased liver enzyme levels.

Methods: 80 patients with preoperatively increased liver enzyme values who were presented to the Zagazig University hospitals participated in this prospective, randomized clinical trial. The patients were divided into two equal groups at random using a computer randomization table. Group P (n=40): Propofol group and Group S (n=40): Sevoflurane group.

Results: There was a statistically significant higher alanine aminotransferase (ALT) and aspartate aminotransferase (AST) liver enzymes at H1 (12 hours postoperative), H2 (24hours postoperative) and peak value within 3 days in Group S compared to Group P ($p<0.05$). In addition, comparing to basal ALT and AST at (H0), the Mean Difference and percent of change of ALT and AST at (H1) value, ALT and AST at (H2) value, ALT and AST Peak value within 3day, were significantly higher in Group S compared to Group P.

Conclusions: Propofol is a safer anesthetic option compared to sevoflurane for the maintenance of normal postoperative liver function in this vulnerable patient population.

Keywords: Sevoflurane; Propofol; Liver Enzymes.

INTRODUCTION

Selecting anesthetics with lower hepatotoxicity may be crucial for patients with elevated liver enzyme levels since anesthesia and surgery can worsen their liver functioning. The most widely used anesthetics, halothane and other halogenated inhalational anesthetics, have the potential to produce hepatotoxicity due to their metabolites or immunogenic components, however the risk of hepatotoxicity is low. **[1].**

During surgical and procedural procedures, the volatile anesthetic sevoflurane induces hypnosis, forgetfulness, analgesia, akinesia, and autonomic blockade. Although sevoflurane is thought to be less hepatotoxic, there have been a few documented occurrences of acute liver damage when using this medication. It is currently unknown how sevoflurane affects the flow of blood to the liver. Volatile anesthetics lower cardiac output (CO) and mean arterial blood pressure (MAP), which influences the hepatic circulation. Compared to other halogenated inhaled anesthetics, sevoflurane lessens the severity of the decrease in hepatic blood flow and passes through a different mechanism of hepatic metabolism **[2, 3].**

The use of intravenous medications for the induction and maintenance of anesthesia is known as total intravenous anesthesia (TIVA). Propofol is the most utilized agent. Total intravenous

anesthesia (TIVA) has been discussed in many reports in many patients with liver disease as volatile anesthetics produce possible toxicity to the liver and kidneys **[4].**

Propofol, sometimes referred to as 2,6-Diisopropylphenol, is a short-acting drug that causes a loss of memory for past experiences and a lowered state of awareness. It is frequently used in clinical anesthesia and has been shown to protect against lower limb, brain, and heart ischemia/reperfusion injuries. Like this, propofol is often used in liver transplantation since liver failure does not significantly impair its metabolism. Since its short half-life, propofol has been demonstrated to be a highly effective anesthetic agent for patients with liver disease, including those with decompensated cirrhosis **[2, 5].**

METHODS

Eighty patients who were presented to the Zagazig University hospitals with preoperatively high liver enzyme values were included in this prospective, randomized clinical trial. The study was approved by Ethics Committee of Faculty of Medicine, Zagazig University Hospitals (IRB number: 101017). The patients gave their informed written consent. Each patient was given a code number and an explanation of the study's objectives. This study was conducted in accordance with guidelines and regulations of Helsinki.

Inclusion criteria included patient's BMI ranged from 18.5 to 30 kg/m2, their age ranged from 21 to 64 years, they had non-hepatic surgery under general anesthesia for approximately two hours, and their International Normalized Ratio (INR) was within the normal range of 0.8 to 1.2. Patients with preoperatively elevated liver enzyme levels (AST > 40 U/L or ALT > 40 U/L) within 24 hours before surgeries were included in the study.

Exclusion criteria included exposure to general anesthesia within the last 3 months, allergy to egg-soya been or multiple allergies, patients with underlying liver tumors, pregnant women, patients with neuromuscular diseases and patients with other chronic diseases.

Using a computer randomization table, the 80 patients were divided into two equal groups at random. 40 people make up Group (S) for sevoflurane and 40 people make up Group (P) for propofol.

A thorough history was taken on all cases under study, covering the following topics: name, age, sex, special habits, physical state as defined by the American Society of Anesthesiologists (ASA), history of drug use, history of smoking, and physical status. Past medical history: (diabetes, hypertension, ischemic heart disease [from stable angina to myocardial infarction], pulmonary disease, cerebrovascular disease, rheumatoid arthritis, and cancer); type of surgery and past surgical history: history of blood transfusions, trauma, and any surgical procedures previously performed; complete clinical examination including vital signs.

Technique:

As a premedication, all patients received IV midazolam (5 mg) given 2-3 minutes before the induction of general anesthesia and IV atropine (0.01 mg/kg) given 30-60 minutes prior to the induction of general anesthesia. Regular monitoring was done on the electrocardiogram, non-invasive blood pressure, capnogram, and pulse oximeter.

Within the sevoflurane cohort, 0.5 mg/kg atracurium, 3µg/kg fentanyl, and 8% sevoflurane at the outset were used to produce anesthesia. Within the propofol group: 3µg/kg of fentanyl was used to induce general anesthesia, which was then followed by 1.5–2.5 mg/kg of propofol and 0.5 mg/kg of atracurium. Following tracheal intubation, anesthesia was sustained with a combination of infused propofol (100-200 µg/kg/min) that was modified according on hemodynamic changes and a 1.5%–2.5% sevoflurane group. Depending on the patient's needs, fentanyl (1-2 µg/kg) and atracurium (5–10 mg) boluses were administered. The range of CO2 was 34–36 mmgh. Following the procedure, the anesthetic drugs were stopped, and 0.04 mg/kg of neostigmine and 0.02 mg/kg of atropine were used to reverse any remaining neuromuscular block. Before being moved to the ward, all patients underwent extubation in the operating room and were given extra oxygen in the recovery room for post-operative treatment. All patients had intravenous analgesia (15 mg/kg of paracetamol) after surgery.

Primary outcome:

- The preoperative value (H0) was the liver enzyme values (ALT and AST) tested 24 hours prior to operation. The postoperative values were the levels recorded 12 hours (H1) and 24 hours (H2) following surgery.
- The blood concentration of ALT and AST were determined using a colorimetric approach, in which the enzyme converts the substrate into a soluble, colored reaction product. The changes (% rise or decrease) in the liver enzyme levels (ALT and AST) were assessed **[6].**
- In addition, during the first three days following surgery, the follow-up enzyme level was measured every 24 hours and used to determine the peak AST and ALT levels during that time.

The approach for causality assessment of adverse drug reactions score, which values higher score for the time initiation of response within 3 days, led to the decision to adopt a 3-day follow-up period.**[7].**

Secondary outcomes

- Vital signs in the recovery room were monitored at baseline, during (every five minutes), and after (every hour), including heart rate, blood pressure, arterial oxygen saturation, and temperature.
- Assessment of adverse effects of Sevoflurane and Propofol:

1- The goal of treating bradycardia, which was defined as a 20% drop-in heart rate from baseline, was to administer intravenous atropine (0.02 mg/kg) **[8].**

2- The goal was to treat hypotension with intravenous ephedrine (0.3 mg/kg), with hypertension defined as a 20% drop in mean arterial pressure from baseline and the use of vasopressors evaluated as intraoperative variables. **[9].**

3- Post procedure vomiting: It was evaluated using a numeric rank score (0 = no vomiting, 1 = vomiting occurred once and 2 = vomiting occurred twice or more. For vomiting and Nausea patients were given ondansetron 0.1 mg/kg **[10].**

- The duration of the hospital stay following surgery was noted.

Data collection:

- Information was gathered about the baseline parameters, such as body mass index (BMI; kg/m2), sex, and age.
- Physical status, comorbidities (hypertension, diabetes mellitus, ischemic heart disease [from stable angina to myocardial infarction], pulmonary illness, cerebrovascular disease, and cancer) were documented according to the American Society of Anesthesiologists (ASA).
- The type of surgery, the duration of the procedure (the amount of time from the initial incision to the final skin closure), the operation time (the total amount of time the patient spent in the operating room), and the anesthesia time (the continuous period from the beginning of anesthesia to the end of an anesthesia service).
- Red blood cell transfusion volume: the visual approach was used to measure blood loss, with a massive blood loss being defined as an estimated loss of blood above 1500 milliliters **[11]**.
- The equation used to compute fluid balance during surgery was fluid balance during surgery (%) = (fluid input-output in liters) × 100%/hospital admission weight (kg)/anesthesia time (hour) **[12].**

Sample size: Assuming the mean aspartate aminotransferase postoperative was 43±10 U/L vs 51±15 U/L in sevoflurane vs propofol (Oh et al., 2020). At 80% power and 95% CI, the estimated sample will be 80 cases,40 cases in each group using open Epi program.

STATISTICAL ANALYSIS

(IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.2015) was used to gather, tabulate, and statistically analyze all of the data. The mean ± SD &(range) was used to express quantitative data, whereas numbers and percentages were used to express qualitative data. To compare two groups of normally distributed variables, the t test was employed. A comparison between two groups of non-normally distributed variables was performed using the Mann-Whitney test. Fisher exact test or Chi-square test were used to compare the percentages of categorical variables. Every test had two sides. P-values less than 0.05 were regarded as statistically significant, whereas those more than 0.05 were regarded as statistically non-significant (NS).

RESULTS

The study's findings demonstrated that while there were no significant differences between the groups in terms of age, BMI, sex, ASA and comorbidity, duration of surgery, amount of blood loss, or fluid balance among the patients under investigation, group S's operation time was significantly shorter than group P's, as indicated in Table 1.

Group S and group P did not significantly differ in terms of intraoperative HR beat/min. Furthermore, Table 2 indicates that there were no statistically significant variations in PAUC HR beat/min ($p>0.05$) between groups S and P.

Group P and S did not differ significantly from one another in terms of the baseline MAP value ($p>0.05$). From five minutes after induction to the end of the procedure, Group S's intraoperative MAP was considerably greater than Group P's ($p<0.05$). Table 3 shows that there were no significant changes ($p>0.05$) in the MAP in PAUC between groups S and P.

Group S and group P did not significantly differ in terms of intraoperative body temperature (°C). Furthermore, there were no statistically significant variations in PAUC body temperature (°C) between groups S and P ($p>0.05$). according to (Table 4).

Regarding intraoperative oxygen saturation, there were no notable variations between groups S and P (SO2). Additionally, there were no noteworthy variations in PAUC Oxygen saturation (SO2)

between groups S and P (p>0.05). according to (Table 5).

When comparing Group S to Group P, there was a statistically significant increase in ALT and AST liver enzyme levels at H1 (12 hours postoperative), H2 (24 hours postoperative), and Peak value within 3 days (p<0.05). Furthermore, Group S had a substantially larger Mean Difference and percent of change in ALT and AST at (H1) value, ALT and AST at (H2) value, and ALT and AST Peak value after 3 days when compared to basal ALT and AST at (H0) (Table 6).

Compared to group S, a substantially greater percentage of participants in group P required vasopressors. Group P experienced a significantly higher incidence of hypotension (p<0.05) than group S. Group S experienced a 15% incidence of nausea and vomiting, but group P did not experience any nausea or vomiting. This difference was statistically significant. Bradycardia did not differ between the two groups. Group S experienced a noticeably longer post-operative hospital stay than group P (Table 7).

Table (1): Patients' characters of studied groups.

Variables	Group S N=40	Group P N=40	t	p-value
Age per years Mean± SD Range	42.9±12.07 24-61	38.7±10.995 23-62	1.627	0.108
Weight(kg) Mean± SD Range	68.2±5.199 60-75	69.6±7.01 56-78	1.015	0.313
Height(m) Mean± SD Range	1.63±0.04 1.56-1.68	1.64±0.06 1.55-1.72	0.936	0.352
BMI (kg/m$^{2)}$ Mean± SD Range	25.61±2.29 21.51-29.59	25.81±2.56 20.31-29.72	0.358	0.721
	N (%)	**N (%)**	**χ 2**	**p-value**
Sex Females males	12(30.0) 28(70.0)	17(42.5) 23(57.5)	1.352	0.245
ASA I ASA II ASA III	12(30.0) 24(60.0) 4(10.0)	19(47.5) 18(45) 3(7.5)	2.581	0.275
Smoking n(%)	16(40.0)	12(30.0)	0.879	0.348
Hypertension	10(25.0)	11(27.5)	0.065	0.799
Diabetes mellitus	7(17.5)	5(12.5)	0.392	0.531
Dyslipidemia	2(5.0)	6(15.0)	f	0.263
Ischemic heart	5(12.5)	4(10.0)	f	0.99
cancer	0(0.0)	0(0.0)	-	-
Anesthesia time (min) Mean± SD Range	119.1±7.47 110-135	128±10.34 114-145	**4.04**	**0.0001***
Operation time (min) Mean± SD Range	149.80±11.51 125-170	168.7±9.46 154-180	**8.025**	**0.0001***
Duration of surgery (min) Mean± SD Range	112.87±7.27 100-125	115.9±8.45 105-130	1.715	0.09
Estimated blood loss (ml)	280±147.24	268.75±287.27	0.188	0.852

Variables	Group S N=40	Group P N=40	t	p-value
Mean± SD Range	0.00-600	0.00-700		
Fluid balance Mean± SD Range	2.86±1.11 1.64-4.42	3.24±0.89 1.7-4.44	1.656	0.102
	N(%)	N(%)	**χ 2**	p-value
Type of operation (n %) Abdominal Orthopedic Spinal Tracheostomy	16(40.0) 16(40.0) 4(10.0) 4(10.0)	30(75.0) 10(25.0) 0.0 0.0	**10.03** 2.051 f f	**0.001*** 0.152 0.115 0.115

Quantitive Data are expressed as mean ± standard deviation (SD), Range, Qualitative data as number and percent, t: student't (t), χ 2 Chi-square test, f: Fisher exact test, P value ≥ 0.05: no significant

Table (2): Intraoperative, in PAUC HR beat/min of studied groups.

Variables	Group S N=40	Group P N=40	t	p-value
HR at baseline	86.4±5.98 77-93	84.9±5.002 76-92	1.217	.227
HR 5 min post induction	85.4±5.64 76-93	84.38±6.46 75-93	0.756	0.452
HR 10 min	84.3±6.41 75-94	83.65±7.53 73-94	0.416	0.679
HR 15 min	82.7±7.06 72-94	83.08±8.33 71-95	0.217	0.829
HR 25 min	82.6±8.04 71-96	82.78±8.38 71-95	0.095	0.924
HR 30 min	81.2±7.803 67-93	81.9±8.58 69-94	0.382	0.704
HR 35 min	81.4±8.18 64-92	80.7±8.76 66-93	0.369	0.713
HR40 min	79.5±9.16 62-93	80±8.72 66-93	0.250	0.803
HR 45 min	78.6±7.98 62-91	79.05±8.98 63-91	0.237	0.813
HR 50 min	77.4±6.57 63-87	77.55±7.75 64-88	0.093	0.926
HR 55 minutes	75.7±6.67 59-83	76.8±8.21 62-89	0.658	0.513
HR 65 minutes	75±7.81 55-83	75.1±8.46 59-85	0.01	0.99
HR the end of surgery	74.3±8.06 54-82	74.58±8.52 59-86	0.148	0.883
HR PACU	83.7±4.73 77-91	83.2±6.56 73-93	0.391	0.697
HR 1hr PACU	80.4±5.75 72-94	80.15±8.23 73-94	0.157	0.875
HR 2hr PACU	84.1±6.49 76-95	82.05±7.71 71-95	1.286	0.202

Quantitive Data are expressed as mean ± standard deviation (SD), Range, t: student't (t), P value ≥ 0.05: no significant

Table (3): Intraoperative, in PAUC MAP (Hg/mm) of studied groups.

Variables	Group S N=40	Group P N=40	t	p-value
MAP at baseline	78.6±6.74 70-88	75.75±7.27 69-89	1.818	.073
MAP 5 min post induction	78.5±6.68 69-86	75.05±6.82 69-89	**2.286**	**.025***
MAP 10 min	78.7±7.05 68-88	74.3±7.603 67-89	**2.685**	**0.009***
MAP 15 min	77.6±8.33 65-89	74.1±7.31 63-88	**1.997**	**0.049***
MAP 25 min	76.9±7.39 66-87	73.2±7.62 62-89	**2.205**	**0.030***
MAP 30 min	76.6±8.21 64-89	72.48±7.5 61-87	**2.347**	**0.021***
MAP 35 min	78±7.65 64-91	71.28±7.699 58-84	**3.920**	**0.0001***
MAP40 min	78.8±7.55 65-92	70.88±8.48 57-85	**4.415**	**0.0001***
MAP 45 min	79.1±7.49 66-91	68.98±8.002 55-82	**5.843**	**0.0001***
MAP 50 min	79.7±7.16 68-91	67.98±7.42 54-79	**7.189**	**0.0001***
MAP 55 minutes	79.8±7.47 70-91	68.18±7.37 55-80	**7.010**	**0.0001***
MAP 65 minutes	80.1±7.53 71-93	66.4±7.64 53-79	**8.076**	**0.0001***
MAP the end of surgery	80.9±7.69 70-95	65.63±6.96 54-78	**9.313**	**0.0001***
MAP PACU	90±9.22 74-100	86.8±8.17 72-98	1.643	0.104
MAP 1hr PACU	84.6±8.83 71-97	84.85±8.38 69-96	0.130	0.897
MAP 2hr PACU	82.1±9.63 69-95	83.3±9.88 69-95	0.550	0.584

Quantitive Data are expressed as mean ± standard deviation (SD), Range, t: student't (t), P value ≥ 0.05: no significant, *P value < 0.05: significant

Table (4): Intraoperative, in PAUC body temperature (°C) of studied groups.

Variables	Group S N=40	Group P N=40	t	p-value
Temperature at baseline	36.88±0.43 36.3-37.5	36.85±0.35 36.3-37.4	0.340	0.735
Temperature 5 min post induction	36.94±0.29 36.5-37.5	36.92±0.35 36.4-37.5	0.346	0.730
Temperature 10 min	36.85±0.45 36.3-37.4	36.99±0.33 36.5-37.5	1.558	0.123
Temperature 15 min	36.9±0.36 36.5-37.5	37.08±0.35 36.3-37.5	1.76	0.081
Temperature 25 min	36.85±0.46 36.3-37.5	36.88±0.36 36.3-37.5	0.352	0.726
Temperature 30 min	36.9±0.36 36.4-37.5	36.79±0.38 36.3-37.5	1.86	0.067
Temperature 35 min	36.82±0.31	36.97±0.39	1.9	0.061

Variables	Group S N=40	Group P N=40	t	p-value
	36.3-37.4	36.4-37.4		
Temperature40 min	37.1 ±0.26 36.7-37.5	36.9±0.38 36.3-37.5	1.78	0. 08
Temperature 45 min	36.81±0.396 36.4-37.4	36.84±0.299 36.4-37.4	0.414	0.680
Temperature 50 min	36.78±0.39 36.3-37.5	36.87±0.45 36.3-37.5	0.949	0.346
Temperature 55 min	36.95±0.39 36.3-37.5	37.05±0.32 36.5-37.5	1.217	0.227
Temperature 65 min	36.85±0.43 36.3-37.4	37.01±0.33 36.4-37.4	1.89	0.062
Temperature the end of surgery	36.91±0.37 36.4-37.5	36.96±0.38 36.3-37.5	0.622	0.536
Temperature PACU	36.97±0.16 36.7-37.2	37.06±0.24 36.7-37.4	1.93	0.057
Temperature 1hr PACU	37.02±0.202 36.7-37.3	37.09±0.25 36.7-37.4	1.51	0.133
Temperature 2hr PACU	37.04±0.21 36.7-37.3	36.98±0.18 36.7-37.2	1.387	0.169

Quantitative Data are expressed as mean ± standard deviation (SD), Range, t: student't (t) P value ≥ 0.05: no significant

Table (5): Intraoperative, in PAUC Oxygen saturation (SO2) of studied groups.

Variables	Group S N=40	Group P N=40	t	p-value
Oxygen saturation at baseline	96.85±1.41 95-99	97.28±1.198 95-99	1.455	0.150
SO2 5 min post induction	97.18±1.63 95-99	97.63±1.06 95-99	1.465	0.147
SO2 10 min post induction	97.68±0.94 96-99	98.08±0.94 96-99	1.894	0.062
SO2 15 min post induction	97.58±1.38 95-99	97.83±1.26 95-99	0.848	0.399
SO2 25 min post induction	97.1±1.297 95-99	97.63±1.15 95-99	1.917	0.059
SO2 30 min post induction	97.33±1.37 95-99	97.8±0.85 96-99	1.865	0.066
SO2 35 min post induction	97.3±1.57 95-99	97.55±0.99 96-99	0.852	0.397
SO240 min post induction	97.45±1.04 96-99	97.9±1.03 96-99	1.945	0.055
SO2 45 min post induction	97.18±1.26 95-99	97.63±1.08 96-99	1.717	0.090
SO2 50 min post induction	97.28±1.49 95-99	97.83±1.06 96-99	1.907	0.060
SO2 55 minutes post induction	97.5±1.24 95-99	97.8±1.07 96-99	1.160	0.250
SO2 65 minutes post induction	97.25±1.35 95-99	97.7±1.22 95-99	1.559	0.123
SO2 the end of surgery	97.28±1.41 95-99	97.83±1.13 96-99	1.922	0.058
SO2 PACU	97.35±1.58	97.6±1.01	0.845	0.401

Variables	Group S N=40	Group P N=40	t	p-value
	95-99	96-99		
SO2 1hr PACU	97.38±1.23 95-99	97.75±1.13 95-99	1.419	0.160
SO2 2hr PACU	97.35±1.21 95-99	97.8±1.16 96-99	1.699	0.093

Quantitive Data are expressed as mean ± standard deviation (SD), Range, t :student't (t), P value ≥ 0.05: no significant

Table (6): Liver enzyme of studied groups.

Variables	Group S N=40	Group P N=40	t	p-value
ALT at H0	67.95±11.22 53-88	65.9±5.5 51-78	1.013	0.314
ALT at H1	83.6±10.34 65-100	76±6.4 61-84	**3.985**	**0.0001***
Mean Difference (basal ALT& ALT at H1	15.65±6.2 10-42	9.9±8 9-20	**2.925**	**0.003*u**
ALT at H2	86.6±11.14 70-103	77.7±6.48 67-87	**4.378**	**0.0001***
Mean Difference (basal ALT& ALT at H2	18.65±5.8 15-45	11.7±8.1 6-19	**3.392**	**0.001*u**
Peak value within 3day ALT	89±11 70-106	78.3±6.52 67-92	**5.28**	**0.0001***
Mean Difference (basal ALT& Peak value within 3day	21±8.78 15-47	12.3±8.8 6-29	**3.897**	**0.0009*u**
AST at H0	76.07±13.39 59-100	72.10±16.71 46-95	1.181	0.241
AST at H1	93.5±15.36 74-117	84.8±16.45 56-107	**2.445**	**0.017***
Mean Difference (basal AST& AST at H1	17.4±7 11-48	12.7±6.3 10-20	**2.537**	**0.011*u**
AST at H2	105.6±14.38 89-133	84.4±13.65 60-106	**6.76**	**0.0001***
Mean Difference (basal AST& AST at H2	29.6±14.9 11-61	12.3±22.8 26-54	**3.254**	**0.001*u**
Peak value within 3dayAST	107.5±16.72 89-133	92±.15.2 60-126	**4.327**	**0.0001***
Mean Difference (basal AST& Peak value within 3day	31.4±7.4 23-58	19.9±10.6 6-41	**4.66**	**0.0001*u**

Quantitive Data are expressed as mean ± standard deviation (SD), Range, t :student't (t), u:Mann whitnney u test, P value ≥ 0.05: no significant, *P value < 0.05: significant, H0: preoperative value, H1: 12 hours postoperative value, H2: 24hours postoperative value

Table (7): Outcome in studied groups:

Variables	Group S N=40	Group P N=40	Test of sig	p-value
Ephedrine Yes no	2(5.0) 38(95.0))	8(20.0) 32(80.0)	χ 2=4.1	**0.043***
Hypotension	2(7.5)	10 (32.5)	u = 6.2	**0.012*c**

Variables	Group S N=40	Group P N=40	Test of sig	p-value
Nausea/vomiting	6(15.0)	0.0	f	**0.028***
Bradycardia	1(2.5)	4(10.0)	f	**0.359**
Post-operative length of hospital stay (days) **Mean±SD** **Median(range)**	 4.5±0.82 4.5(3-6)	 3.5±1.71 2(2-6)	u = 2.38	**0.018***

χ 2: Chi-square test, F: Fisher exact test, U: Mann whitnney u test

DISCUSSION

There were no statistically significant variations in mean age, weight, height, or BMI between the two groups in our study. Furthermore, there were no notable variations in the distribution of genders or the ASA physical status classification.

According to our research, the sevoflurane group's operating time was shorter than the propofol group. Nonetheless, there were no appreciable variations in the volume of blood lost or fluid balance across the groups. The sevoflurane group had higher postoperative elevations of the liver enzymes ALT and AST.

This is consistent with the findings of **Oh et al. [2]**, who found that the TIVA group had substantially longer median anesthesia and surgery times than the INHA group.

The mean clinical recovery time following the cessation of infusions may be greater in patients with liver illness, even though the elimination kinetic profile of propofol is similar in these patients and normal patients. In contrast, our findings showed that TIVA was superior to INHA in terms of liver function in patients with preoperatively elevated liver transaminase levels **[13].** This is noteworthy because prolonged anesthesia can have a negative impact on clinical outcomes in patients with liver disease.

After induction, volatile anesthetic drugs may cause a 30-to 50% reduction in hepatic blood flow. If this is not fixed during surgery, the blood loss from the procedure will further lower the blood flow to the liver, causing ischemic alterations in the hepatocytes. **[14, 15].**

Regarding intraoperative HR beat/min, there were no discernible changes between groups S and P in our investigation. Additionally, there were no statistically significant differences between groups S and P in terms of HR beat/min or post-anesthesia care unit (PACU).

Alhasanin et al. [16] concurred, reporting that hemodynamic parameters revealed no statistically significant difference in mean heart rate between the two groups, with the TIVA group experiencing a slight decrease compared to the volatile induction and maintenance anesthesia (VIMA) group.

Inhalation agents and propofol both have a concentration-dependent vasodilatory effect. The degree of reflex tachycardia varies greatly, though. Sevoflurane typically has little effect on heart rate, in contrast to the apparent reflex tachycardia observed with isoflurane **[17].** Propofol, on the other hand, suppresses the baroreflex and even causes bradycardia **[18].** As a result, propofol more effectively lowers cardiac output than sevoflurane **[19].** Therefore, the heart rate was lower in the TIVA than in the inhalational anesthesia in the patients without cardiovascular illness whose MBP was within the same range. As a byproduct of our investigation, we discovered that bradycardia did not differ between the two groups.

Regarding the MAP value at baseline, there were no significant differences between group S and group P in our investigation from five minutes after induction to the end of the procedure, Group S's intraoperative MAP was considerably greater than Group P. Regarding MAP in PAUC, there were no appreciable differences between groups S and P.

This is consistent with the findings of **Alhasanin et al. [16],** who found that while TIVA produced a lower MAP than sevoflurane anesthesia, there was no discernible difference in MAP between the two groups at the points of intubation, the start of the procedure, and during maintenance of anesthesia. The differing effects of the two approaches on neuroendocrine stress may help to explain this. TIVA significantly inhibited the neuroendocrine response to stress, which is why throughout the operation, MAP was lower with TIVA than with INHA. **[20].**

Regarding intraoperative oxygen saturation (SO2), there were no discernible variations between groups S and P in our investigation.

Additionally, there were no noteworthy variations in PAUC Oxygen saturation (SO2) between groups S and P.

This is consistent with the findings of **Alhasanin et al. [16],** who said that neither group's SpO2 values changed much during the procedure.

Our study found no significant differences in baseline ALT or AST liver enzymes between the sevoflurane (Group S) and propofol (Group P) groups preoperatively. Nevertheless, the sevoflurane group considerably outperformed the propofol group in terms of ALT and AST assessed at three different postoperative time periods (12 hours (H1), 24 hours (H2), and Peak value within three days). Furthermore, as comparison to the propofol group, the sevoflurane group's mean changes between baseline and postoperative ALT and AST at the three time points of measurement were substantially larger. These results show that, when compared to sevoflurane anesthesia, propofol anesthesia had less of an impact on liver function after surgery in individuals who already have elevated liver enzymes. Therefore, propofol appears to be safer in terms of effects on postoperative liver function for this patient population undergoing general anesthesia and surgery.

This is consistent with the findings of **Oh et al. [2],** who found that in patients undergoing non-hepatic operations and with preoperatively increased liver transaminase levels, the changes in ALT and AST levels following surgery were much lower after TIVA than after INHA. The action of propofol itself may be the reason for the TIVA group's higher postoperative decrease in ALT levels than the INHA group. It has been demonstrated that propofol's anti-inflammatory, immune-modulatory, and antioxidant qualities have organ-protective effects. Furthermore, while volatile anesthetics lower mean arterial pressure and hepatic blood flow, propofol raises total hepatic blood flow in both the hepatic arterial and portal venous circulation. Anesthetics can impact liver function by reducing cardiac output and total hepatic blood flow, even though the pathophysiology of liver injury after exposure to halogenated anesthetics is primarily attributed to their metabolism to hepatotoxic trifluoroacylated hepatic protein adducts by cytochrome P450 2E1 in genetically predisposed individuals.

This is in harmony with **Oladimeji et al. [6]** who examined changes in liver enzymes following anesthesia with inhalation group versus intravenous propofol. They found that serum AST levels increased progressively in the inhalation group from baseline through 24 hours postoperatively, exceeding the upper limit of normal in the immediate postoperative and 24-hour measurements. The differences in AST over time were not statistically significant within the inhalation group, but at 24 hours the AST levels were significantly higher compared to the propofol group. This indicates hepatocellular injury associated with inhalation anesthesia. In contrast, their study showed that changes in serum ALT levels were insignificant in both the inhalation and propofol groups, suggesting absence of extensive liver cell damage. Compared to our study where both AST and ALT were significantly more elevated postoperatively in the sevoflurane versus propofol groups, **Oladimeji et al. [6]** demonstrated more modest liver enzyme differences. Specifically, only AST at 24 hours differed significantly between inhaled versus intravenous anesthesia, and they interpreted their results as showing no hepatocellular harm. Together, these findings add to evidence that inhaled anesthetics like isoflurane and sevoflurane may confer some risk of transient liver dysfunction, while propofol appears relatively protective in patients at risk for hepatic changes.

In contrast, **Yang et al.'s study [21]** investigated the effects of target-controlled infusion of propofol in liver cirrhosis patients. In this patient group, they observed substantial increases in liver enzymes after propofol anesthesia. In particular, they noticed that the serum ALT had increased eighteen times, and the AST had increased to 6.5 times the upper limit of normal. Compared to the more modest liver enzyme changes seen in our study, these results from **Yang et al. [21]** indicate much more substantial hepatocellular injury can occur with propofol in patients with severe preexisting hepatic dysfunction from cirrhosis. Therefore, while propofol appeared relatively protective compared to sevoflurane in our cohort, **Yang et al. [21]** findings demonstrated this intravenous anesthetic can also impair liver function to a major degree in the setting of compromised liver function from end-stage disease. Since they included hepatic surgery, which was not included in our analysis, this discrepancy could be the result of differing inclusion criteria.

After hepatic surgery, ischemia, hepatic mass loss, hepatic oxygen deprivation, and stress response are the causes of postoperative liver dysfunction. **[22].**

The discrepancy between our findings and those of **Yang et al. [21]** can be explained by the different ways that anesthetic drugs and surgical techniques may cause post-operative liver damage. While hepatic arterial circulation may be maintained, augmented, or diminished, the

majority of anesthetics result in a drop in portal blood flow, which is correlated with a decrease in cardiac output. Total hepatic blood flow is decreased if the increase in hepatic arterial flow is insufficient to offset the decrease in portal blood flow. This could lead to a decrease in the elimination of both endogenous and exogenous metabolites that have a high blood extraction ratio, such as propofol, which increases the risk of buildup. **[23].**

According to **Kim et al. [24],** postoperative AST increased considerably in Group S as opposed to Group P, while the higher levels remained within the normal range. There were no variations in ALT between the two groups, and neither group showed alterations in postoperative ALT relative to baseline. No instances of AST and ALT rising above 100 IU/L were observed. They therefore postulated that there was no difference in hepatic function between the two groups and that postoperative hepatic impairment was clinically minor.

When **Sahin et al. [25]** examined the effects of TIVA and inhalational anesthetics on patients undergoing lumbar discectomy, they discovered no differences between the two groups and no alterations in postoperative liver function.

Nonetheless, sevoflurane anesthesia has been associated with liver failure in both adults and children with normal liver function [26]. Patients who received propofol over an extended period have also been reported to have fatty liver in addition to acute liver failure [27].

Yoon et al.'s study [28] on patients who had laparoscopic cholecystectomy revealed higher-than-normal postoperative AST and ALT levels.

Vasopressor use differed statistically significantly between the two groups in our investigation. In Group S, 5% of patients required vasopressors, while 95% did not. In contrast, Group P had a higher proportion of patients requiring vasopressors, with 20% receiving them and 80% not requiring vasopressor support.

In our investigation, group P experienced a significantly higher incidence of hypotension than group S.

This is consistent with Oh et al. [2] findings that the TIVA group experienced a higher frequency of intraoperative hypotensive episodes and vasopressor use.

This is contrary to the findings of Oladimeji et al. [6], who found a significant difference between the incidence of hypotension during the procedures in the isoflurane group (56.67%) and the propofol group (30%).

In our investigation, group S experienced a 15% incidence of nausea and vomiting, but group P did not experience any nausea or vomiting; this difference was statistically significant, $p<0.05$.

According to postoperative nausea and vomiting, this is consistent with the study by **Alhasanin et al. [16].** Between the two groups, there was a statistically significant difference. During the post-operative period, nausea and vomiting were experienced by six patients (30%) from the INHA group and by just two patients (10%) from the TIVA group.

CONCLUSIONS

In patients with preexisting elevated liver enzymes, our study findings indicate that the use of sevoflurane anesthesia is associated with a more pronounced disturbance in postoperative liver function with increased nausea and vomiting compared to propofol anesthesia. This is evidenced by significantly elevated levels of ALT and AST measured at 12 hour (H1), 24 hours (H2), and peak values within 3 days after surgery in the sevoflurane group. Additionally, the sevoflurane group exhibited shorter durations of anesthesia and surgery compared to the propofol group. However, it is noteworthy that the propofol group had a higher incidence of hypotension requiring vasopressors. Despite this, our results suggest that propofol may be a safer anesthetic option than sevoflurane for the maintenance of normal postoperative liver function in this vulnerable patient population.

Recommendations:

- When a patient requires surgery under general anesthesia and has borderline high liver enzymes, propofol TIVA should be used instead of sevoflurane. The risk of hypotension related to propofol should be closely monitored.
- More research is necessary to determine the best organ protective anesthetic practices for those with underlying liver failure.
- If inhalational anesthetic is necessary or preferred, the development of improved sevoflurane agents or strategies to lessen its hepatic impact and nausea and vomiting incidence could improve safety.

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