

Comparative Study on Propofol and Sevoflurane on Hepatic Blood Flow

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Abstract:

Introduction: There are various concepts behind the choice of anaesthetics in surgery due to the anaesthetic agents affect the various parameters One of the parameters which is long been discussed is hepatic blood flow and pressure. There is significant variation and effects on hepatic blood flow and pressure due to different choice of anaesthetic agents. Other parameters including hemodynamic parameters and intra-operative parameters. Frequent anaesthetic agents like sevoflurane and propofol are debatable in terms of their effect on these parameters. There are several studies and experiments on animals to find out some conclusion but there is hardly any strong evidence to present.

Aims and Objective: To find out the significance of hepatic blood flow and hepatic blood pressure between using sevoflurane and propofol.

Methods: This is a prospective study which considered patients of Appendectomy and classified them into two groups, namely, sevoflurane and propofol. The baseline characteristics were determined before the surgery and the intra-operative parameters were assessed during the surgery. The hepatic blood flow and pressure are also determined to find out any possible significance.

Results: The study found that the lactate formation in patients with sevoflurane is significantly higher than the patients inducted with propofol ($p < 0.05$). The study further found that the patients who were given sevoflurane needed significantly more vasopressor support than patients inducted with propofol ($p < 0.05$).

Conclusion: The study found that the hepatic blood flow and pressure were found insignificant between the patients inducted with propofol and sevoflurane. It was found that patients anaesthetized with sevoflurane had shown higher lactate formation and had to give more vasopressor support than the patients who were given propofol.

Keywords: sevoflurane, propofol, hepatic blood flow, hepatic blood pressure.

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Introduction

Numerous pathogenic processes, such as liver ischemia or reperfusion and liver fibrosis, can cause liver damage [1, 2]. In the case of liver ischemia or reperfusion injury, cellular damage is brought on by

hypoxia after the restoration of blood flow and oxygen supply following transplant surgery, tissue resections, hemorrhagic shock, and other procedures [3, 4]. Since liver resection and liver transplantation surgery continue to be primary causes of

graft dysfunction or non-function and have a high mortality rate, it is therefore an important factor to take into account when managing hepatobiliary surgery [5]. Typically, liver Ischaemia-Reperfusion injury occur as a result of hepatic surgery or severe shock. Additionally to having an impact on liver health, it greatly raises the risk to the respiratory and circulatory systems. Because of all these problems, liver ischemia or reperfusion is a crucial clinical issue that needs to be researched and fixed [6].

With 25% of the heart's output going to it, the liver is the largest visceral organ in the human body. It has a special circulatory system that links the capillaries of the liver with those from various gastrointestinal organs. The hepatic artery and portal vein provide the liver with two separate blood supplies [7]. A branch of the celiac trunk, the hepatic artery supplies 30% of the blood to the liver. 70% of the blood that goes to the liver is supplied by the portal vein, which is made up of the mesenteric and splenic veins. The hepatic artery supplies 50% of the oxygen needed, and the portal vein provides 50% [7]. The portal vein transports nutrient-rich, oxygen-poor blood to the liver while the hepatic artery transports oxygenated, nutrient-rich blood. The liver is then supplied with nutrients and oxygen by the blood as it flows through it [7]. In the first 30 minutes after induction of anesthesia, GA can reduce hepatic blood flow by 40%, particularly if baseline blood pressure is not maintained [8]. Under anesthesia, compensatory reduction in portal blood flow does not occur in individuals with hepatic disease, particularly in cases of cirrhosis [9].

It has been noted that the commonly used anesthetic propofol protects against ischemia/reperfusion harm to the heart, brain, and lower limbs [10, 11]. Similar to this, propofol is often utilized in liver transplantation since liver failure has no impact on its metabolism [12]. After liver

ischemia, it has been demonstrated that volatile anesthetic substances can keep the liver's blood flow and cell activity intact. An intravenous anesthetic is propofol (2,6-diisopropylphenol). Total intravenous anesthesia (TIVA) is a technique that is frequently utilized in many locations, and its pharmacokinetic profile makes it particularly suitable for it [11]. It is especially beneficial in the ambulatory situation due to its quick onset and reduced side effects, such as postoperative nausea and vomiting [10-12].

A brand-new inhalation anesthetic called sevoflurane has recently been developed and is now widely utilized [13]. Similar to other inhalation anesthetics, sevoflurane is known to operate as a bronchodilator by directly relaxing the bronchial smooth muscle through a decrease in Ca^{2+} concentration and alteration of calcium homeostasis [14-16]. Propofol and sevoflurane have been compared in the past, with varying degrees of success [17]. Propofol may be less likely to cause direct anesthetic metabolite harm to the body than sevoflurane when used for total intravenous anesthesia in OLV, according to certain reports [18, 19]. Sevoflurane, however, might provide greater defense against reperfusion impairment during one-lung ventilation in thoracic surgery [20].

HBF has been demonstrated to be affected by anesthetics. Animal studies showed that both intravenous and volatile anesthetic drugs alter HBF. Studies on animals have shown that propofol raises total HBF. The increased portal HBF appeared to be the main cause of this rise. Similar effects of propofol on the hepatic circulation have only been seen in one human investigation [21, 22].

Sevoflurane's effects on HBF are still unknown. Mean arterial blood pressure (MAP) and cardiac output (CO) are all reduced by volatile anesthetics in a dose-dependent manner. Consequently, the hepatic circulation is impacted.

Sevoflurane had no effect on total HBF in studies done on dogs, but it was thought that it lowered portal HBF and caused an increase in arterial HBF as a result [21-24]. The given compare study give idea about usefulness of both anesthetic drug simultaneously hepatic blood flow.

Materials and Methods

Study Design

This is a prospective study which was conducted during the period of eleven months. The study considered adult patients of more than 18 years old who were scheduled for Appendectomy(open procedure)in our hospital. On a random basis, the patients were anaesthetized either with propofol or sevoflurane and were classified as propofol group or sevoflurane group based on the anaesthetic agent they received. The primary outcome of this current study was based on the effective comparison between the two groups on their respective effects on total hepatic blood flow (HBF). The patients were given American Society of Anesthesiologists (ASA) standard anaesthesia monitoring intra-operatively. An additional catheter was placed in left femoral artery for hemodynamic evaluation. Prior to anaesthesia induction, 4mg intravenous ondansetron was given for preventing post-operative nausea and vomiting. The patients were given goal directed hemodynamic therapy according to the protocol of our hospital. The hemodynamic target was followed, as cardiac index $> 2.2 \text{ L min}^{-1} \text{ m}^{-2}$. The mean arterial pressure (MAP) was targeted more than 60 mmHg and a Pulse Pressure Variation $< 12\%$. Hepatic Blood Flow and Pressure was determined by blood flow measurements using perivascular ultrasound transit time flow probes. Probe sizes varied according to the type of probe used and the vessel size (which is ranging from 2 mm to 12 mm). Pulsatility of the blood flow is determined by the vascular resistance of the downstream flow, calculated by subtracting minimum value

of volumetric peak flow from maximum value of volumetric peak flow and dividing the resultant by mean volumetric volume [22-24]. Also, the study used 25-gauge needle which was directly placed in the portal vein and had connection with pressure transducer for measuring pressure parameters. Simultaneously, parameters like regional hepatic flow, systemic hemodynamic and portocaval pressure were assessed during the time of apnea for minimizing the ventilation.

Inclusion and Exclusion Criteria

The patients with more than 18 years, who underwent Appendectomy in our hospital were only included. The included patients were those who were given general anaesthesia either with propofol or sevoflurane. The patients who were allergic to medication, renal abnormalities, cardiovascular abnormalities, BMI of more than 35, history of hemodynamic instability, coagulopathy and history of severe post-operative nausea and vomiting, were all excluded. Applying inclusion and exclusion criteria, the study finally considered 100 patients.

Ethical Approval

The author. The study was conducted according to the protocol of the Ethical Committee of the hospital. The patients were explained before the surgery and obtained required consents from the patients and the whole study process have been approved by the Ethical Committee.

Statistical Analysis

The study has conducted ANOVA test for effective statistical analysis using SPSS 25 and excel software for other calculation. The descriptive measurements were expressed as mean \pm standard deviation. The level of significance was considered to be $\alpha = 0.05$.

Results

The study found the baseline characteristics of the patients in each

group. The mean age of propofol and sevoflurane group were found to be 49.95 ± 12.25 years old and 48.55 ± 11.90 years old. The baseline characteristics

were formed by findings basic parameters about the patients like age, gender, mean Body Mass Index (BMI), ASA classification, number of smokers, etc.

Table 1: Baseline characteristics of the patients

Baseline characteristics	Propofol group N=50	Sevoflurane group N=50
Age (years)	49.95 ± 12.25	48.55 ± 11.90
Gender		
Male	26	28
Female	24	22
BMI (kg/m ²)	24.85 ± 2.8	24.5 ± 2.5
ASA classification		
Grade I	14	17
Grade II	22	18
Grade III	14	15
Smokers	3	4

The hemodynamic parameters findings of this study show that there is no statistical significance between patients induced with propofol and patients induced with sevoflurane in the hemodynamic parameters, except lactate. The study

found that the lactate formation in patients with sevoflurane is significantly higher than the patients induced with propofol ($p < 0.05$). Table 2 shows the detailed findings of hemodynamic characteristics of the patients.

Table 2: The hemodynamic parameters of the patients in each group

Hemodynamic parameters	Propofol group N=50	Sevoflurane group N=50	p-value
Mean Arterial Pressure	76.26 ± 5.35	74.22 ± 8.65	$p > 0.05$
Heart Rate	79.45 ± 9.5	80.14 ± 10.5	$p > 0.05$
Central Venous Pressure	5.4 ± 1.8	5.2 ± 1.5	$p > 0.05$
Cardiac Index	3.1 ± 0.6	3.4 ± 0.42	$p > 0.05$
Systemic Vascular Resistance	1085 ± 206	1002.45 ± 325	$p > 0.05$
Pulse Pressure Variation	9.3 ± 1.8	9.6 ± 2.3	$p > 0.05$
Lactate	10.1 ± 2.8	19.2 ± 4.2	$p < 0.05$
P _a CO ₂	41.89 ± 6.3	42.55 ± 5.3	$p > 0.05$
pH	7.39 ± 0.06	7.32 ± 0.04	$p > 0.05$

The study has also found that intraoperative parameters including amount of blood loss, urinary output, vasopressor support, duration of surgery. The study found that the patients who were given sevoflurane needed significantly more vasopressor support than patients induced with propofol ($p < 0.05$).

Table 3: Intra-operative parameters as recorded in each group

Intra-operative parameters	Propofol group N=50	Sevoflurane group N=50	p-value
Loss of blood (ml)	28.55 ± 3.24	29.48 ± 3.12	$p > 0.05$
Urinary output (ml)	471.88 ± 139	801.36 ± 214	$p > 0.05$
Vasopressor support	4	18	$p < 0.05$
Duration of surgery (minutes)	481.25 ± 56	576.12 ± 42	$p > 0.05$

The study also found hepatic blood flow and hepatic blood pressure, which showed that there is no significant differences between propofol and sevoflurane group. Table 4 shows the detailed findings of Hepatic Blood Flow (HBF) and Hepatic Blood Pressure.

Table 4: Findings of Hepatic Blood Flow (HBF) and Hepatic Blood Pressure

Parameters	Propofol group N=50	Sevoflurane group N=50	p-value
Total HBF	891.74±223	879.65±317	p>0.05
Arterial HBF	253.85±113.45	249.6±187	p>0.05
Portal HBF	12.7±3.6	11.3±5.6	p>0.05
Portal Venous Pressure (mmHg)	6.3±3.1	10.84±4.6	p>0.05
Caval Venous Pressure	5.6±3.69	7.4±4.75	p>0.05

Discussion

According to earlier research, sevoflurane rather than propofol may lessen the consequences of ischemia-reperfusion injury following liver resection [25]. However, a comparable study examining the effects of sevoflurane and propofol on the survival of hepatic grafts found no differences in the effects of the two anesthetic drugs [26]. For the life of the allograft and the patient, maintaining an appropriate HBF is essential.

HBF is impacted by sevoflurane and propofol, respectively [21]. Regarding propofol's impact on HBF, contrasting outcomes have been reported. According to earlier research, propofol raises total HBF. The proposed mechanism for this rise in HBF varies amongst the studies, though. A rise in both artery and portal HBF increased total HBF, according to a rat research. Both portal venous and hepatic artery resistance were decreased by propofol in an identical way [21].

Similar findings were found in a dog research. However, in this investigation, propofol only slightly increased total HBF, which was predominantly due to an increase in arterial HBF [27]. Propofol increased total HBF in a rabbit study, mostly due to an increase in portal HBF [29]. On the other hand, one sheep study revealed a decrease in total HBF. There was only one human study conducted. In this study, a cross-over design was used to compare the effects of desflurane and

propofol in 20 individuals. When compared to patients receiving desflurane treatment, total HBF was considerably higher in patients receiving propofol [22]. Uncertainty surrounds the mechanism underlying the observed effects of propofol on HBF. It was thought that the hepatic oxygen requirement rises as a result of propofol metabolism. Then, a compensatory enhanced oxygen delivery would occur, predominantly by increasing portal HBF [28, 29], to maintain hepatic oxygen balance.

Sevoflurane's impact on HBF is still unknown. According to research done on animals, sevoflurane little affects total HBF. Sevoflurane caused a hepatic vasodilation in dogs, resulting in a decrease in portal HBF at 1.2 and 2.0 MAC, but only at 2.0 MAC was there a significant increase in arterial HBF. This result was supported by other animal experiments. Sevoflurane maintained total HBF and, despite a decrease in portal HBF, an increase in arterial HBF led to enough HBF to keep the liver supplying oxygen [21]. Human study findings are contradictory. While Kanaya et al. discovered no effect on HBF with sevoflurane, Hongo et al. demonstrated a reduction in total HBF in sevoflurane [30, 31].

Different methods were employed in earlier investigations to assess artery, portal, and total HBF in both animal and human subjects. Both direct and indirect

measurements of HBF are possible [31]. Although less invasive, indirect measurements are also less precise. Radio-labeled microspheres, sodium bromsulphthalein, and the indocyanine green (ICG) clearance test [21, 22, 30, 31] are a few examples of indirect measures. Inhibiting ICG's hepatic clearance by interaction with propofol may cause the genuine HBF to be underestimated [32, 33]. Transesophageal echocardiography was recently used to estimate total HBF indirectly by estimating blood flow at the hepatic vein [34]. Although it is a quick and accurate method, direct HBF measurement is also more invasive. In earlier research, the hepatic artery and portal vein were immediately encircled by Doppler or electromagnetic flow probes [27].

We evaluated the impact of a propofol- and sevoflurane-based anesthetic on HBF during GDHT in this work by Limmen et al. [21]. According to our findings, individuals receiving anesthesia with sevoflurane or propofol had identical portal, arterial, and total HBF values. We are not aware of any prior human studies evaluating and contrasting HBF with direct flow readings during anesthesia based on propofol and sevoflurane. The evaluation of the allograft's blood flow by TTFM during liver transplantation is crucial for determining the allograft's chance of survival [35, 36]. TTFM is often regarded as the gold standard for monitoring blood flow when flow measurements are required. As our work showed, it is possible to measure HBF using TTFM in a clinical steady state. TTFM is more useful in survival of allograft chance. [37]

Both a sevoflurane- and a propofol-based anesthesia regimen resulted in comparable hepatic blood flow. Pre-established hemodynamic targets were maintained in both groups following the application of GDHT; however patients who had sevoflurane anesthesia required much more vasopressor support. According to

the study's findings, HBF during propofol- and sevoflurane-based anesthesia was comparable when a GDHT was used, aiming for stable hemodynamic characteristics. Sevoflurane anesthetized individuals required much more vasopressor support and had greater blood lactate levels than those receiving propofol-based anesthesia in order to sustain these similar hemodynamic targets.

Conclusion

The study found that the hepatic blood flow and pressure were found insignificant between the patients inducted with propofol and sevoflurane. It was found that patients anaesthetized with sevoflurane had shown higher lactate formation than the patients who were given propofol. Again, patients who received sevoflurane had to be provided with more vasopressor support than those who received propofol. Therefore, although there is no significant hepatic blood flow and pressure between the patients receiving these anaesthesia, the patients inducted with propofol is significantly safer due to less lactate formation and vasopressor support than those with sevoflurane. The study authors suggested to carry out more studies on larger population and in more patients undergoing other surgeries for more validation of these findings. However, this current study has made remarkable conclusion which will be clinically useful in selection of anaesthetic agents.

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