RESEARCH ARTICLE

Comparing the Effect of Propofol and Sevoflurane on Hemodynamics and Coagulation Status During Liver Transplant Anesthesia and Hepatic and Renal Function of the Patients after Liver Transplant

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Background: At present, no documented anesthetic technique exists for use in liver transplant surgery. Presence of some controversies in anesthesia plan led us to compare effects of inhaled and intravenous anesthetics in liver transplant surgery.

Methods: All those brain dead patients who met the criteria of organ donation were included in the study. The donor's liver is matched with the recipient according to our liver transplant protocols and assigned consecutively to the recipients. In this study 78 patients who met the inclusion criteria, were divided into two groups.

All patients in group 1 were anesthetized with inhalation of sevoflurane and patients in group 2 were anesthetized with the IV injection of propofol. Percent of sevoflurane in inhaled gases and IV infusion dose of propofol was determined by a BIS guide to keep BIS between 40 and 45. Patients were monitored by NIBP, ECG, CO – Oximetry and BIS before and during induction of anesthesia. An arterial line from radial artery and Swan–Ganz–Catheter from right internal jugular vein were inserted for all patients.

Results: Mean of PCO2, PO2 and HCO3 were different between 2 groups (p=<0.05) and were higher in propofol group. Also, mean of Na and K were different in both groups and were higher in sevoflurane group, and no other significant differences found.

Conclusion: The results showed that the effect of propofol and sevoflurane on hemodynamics, coagulation status during liver transplant anesthesia, and hepatic and renal function of the patients after liver transplant is the same.

Keywords: Liver transplantation; Propofol; Sevoflurane; Hemodynamics; Coagulation status

Liver transplantation is a surgical process within which the patient's liver is removed and replaced with a healthy one. When the liver function fails and the patient is in the end stage of liver disease (ESLD), the liver transplantation will be required as an accepted method [1].

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Liver failure may be the result of a long-term disorder such as sclerosing cholangitis, chronic hepatitis with cirrhosis, primary biliary cirrhosis, biliary atresia, liver cancer, alcohol consumption, etc. or it may occur acutely just like the occurrence of infection or the complications of a specific drug [2]. The first liver transplantation in human was carried out in 1963 by a team led by Dr. Thomas Starzl in the US [3]. Liver damage is usually associated with a coagulation disorder. The results showed that liver disorder is associated with multiple changes in the hemostatic system and its reason is the changes in plasma level of procoagulants and anticoagulants which are synthesized by hepatocytes and sinusoidal cells [4]. Therefore, the evaluation of patient's coagulation status under liver transplant surgery is one of the main issues after receiving transplanted liver in patients. In carrying out a liver transplant surgery, general anesthesia is needed. Drugs that are used for general anesthesia often affect the performance of brain and have other effects such as muscle relaxant. General anesthesia is carried out by intravenous agents such as 'Propofol, Etomidate, Ketamine, Benzodiazepines, Barbiturates or inhalational anesthetics such as 'Sevoflurane, Desflurane and Isoflurane. Anesthesia will be achieved by the constant supply of gas or intravenous agent with an analgesic and muscle relaxant. The side effects

of drugs used in general anesthesia are different and depend on these three factors: type of drug, applied technique, and the patient. Patient's hemodynamic changes are one of the concerns of anesthesiologist during and after the surgical process [5]. Several reports have confirmed this issue that by injection of the drug and applying anesthesia, blood pressure drops and an increase in heart rate will appear and even these changes may lead to death [6-7]. Therefore, the hemodynamic changes of patients under anesthesia and after surgery are controlled by blood pressure monitoring during surgery and after that. During surgery, the anesthesiologist checks cardiac status of the patient by ECG. Experiences of some researchers have been published in the form of scientific texts and have showed that anesthesia by intravenous injection of drugs such as propofol has better hemodynamic results than the inhalation method [8]. Despite conducting several experiments about the effects of anesthetics on hemodynamic and liver and kidney function of patients under liver transplant surgery, there are still some unknown facts and even paradoxical findings that cause some problems in the formation of a reliable pattern in this area. This study was designed with the aim of examining the effects of propofol (injection) and sevoflurane (inhalation) as two important anesthetics used in liver transplantation on the hemodynamics and coagulation status during liver transplant anesthesia and hepatic and renal function of the patient after liver transplant surgery. The conditions of each of them were studied and compared together.

Methods

This randomized clinical trial study was started after obtaining approval from the ethics committee of Tehran University of Medical Sciences (IR.TUMS.VCR.REC.1395.1854). We enrolled 39 patients in each group of liver transplant candidates. In-group 1 we used Sevoflurance and in-group 2 we used Propofol for maintenance of anesthesia. Premedication and induction of anesthesia was the same for both groups. We used midazolam 25 microgram/kg and fentanyl 1 microgram /kg for premedication and thiopental 5 mg/kg and Atracurium 0.5 mg/kg for induction of anesthesia and relaxation. We used continuous infusion of 0.5mg/kg/h Atracurium and 1 microgram /kg/h fentanyl for all patients at both groups.

All patients were monitored by NIBP-ECG, CO–Oxymetry and BIS before and during induction of anesthesia. After induction of anesthesia an arterial line from radial artery and Swan –Ganz Catheter from right internal jugular vein were inserted for all patients.

Cardiac Output (CO), Systemic Vascular Resistance (SVR), Pulmonary Vascular Resistance (PVR), Central Venous Pressure (CVP), Pulmonary Artery Occlusion Pressure (PAOP), Pleth Variability Index (PVI) and Invasive Blood Pressure (IBP) were measured for all patients.

The rate of intravenous infusion of propofol or inhaled concentration of sevoflurane was set in order to keep BIS between 40 and 45 during maintenance of anesthesia. We used 5% albumin as maintenance fluid and our goal for amount of fluid administration during anesthesia was PVI of less than 15%. If PVI was more than 15%, 100-200 ml of 5% Albumin was infused to the patient to lower PVI to less than 15%. Maintenance of 3-5 cc/kg/h of 5% albumin was used for all patients.

We treated acid base and electrolyte abnormalities during anesthesia. We kept blood glucose between 120-180 mg/dl by infusing glucose or insulin. Patients hemodynamic abnormalities were treated with vasodilator, vasoconstrictor inotrope or fluid administration according to normal range of systemic vascular resistance, cardiac output, mean arterial pressure and PVI.

Patients' coagulation status was monitored by rotational thromboelastometry (ROTEM pentapharm Germany) in three phases of anesthesia.

Coagulation disorders were treated by infusing Fibrinogen, Prothrombin Complex Concentrate, Tranasmine and DDAVP. All coagulation disorders were corrected by aforementioned interventions and bleeding stopped so there was no need for platelet transfusion in any of our patients. Our threshold for transfusing RBC was Hb<8 g/dl for non coagulopathic and hemodynamically stable patients, but for coagulpathic and hemodynamically unstable patients we applied Hb of 10 g/dl as transfusion threshold.

After induction of anesthesia, patients in both groups were ventilated with controlled mandatory ventilation (CMV) with tidal volume of 6cc/kg and respiratory rate of 10-12 /min to keep ET CO2 between 35-40 mmHg. For preventing atelectasis because of surgical exposure and proximity of surgical site to lung we applied 5 cm H2O of positive end expiratory pressure (PEEP) for all patients. At the end of surgery all patients were transferred to ICU intubated with the same ventilator parameters. In ICU patients, analgesia was provided by infusion of 50 microgram /h fentanyl and patients extubated after 5-6 hours.

Patients' hemodynamic status between two groups was compared according to their MAP- CO –SVR- SV-HR – PVR – PVI and usage of norepinephrine –epinephrine or IV fluids. Patients' coagulation status was compared according to EXTEM – INTEM- FiBTEM and APTEM and usage of fibrinogen, DDAVP, PCC and transamine between two groups.

In ICU patients, renal and hepatic status was compared between two groups by renal function tests (BUN, CR, K, Mg, ABG)and need for dialysis – and liver function tests (ALT, AST, BiL, LDH, ALK.PH) and need for retransplant and thrombectomy surgery.

Results

In this randomized clinical trial study, 78 patients were included into two groups, 39 for each group. Number of females was 14 (35.9%) patients, and number of males was 25 (64.1%) patients in Propofol group. Number of females was 11 (28.2%), and number of males was 28 (71.8) in Sevoflurane group. And according to p value they had no difference related to the sex of the patients (p= 0.467).

In this study, our patients were divided into five groups according to the age: (less than 30), (30 - 40), (40 - 50), (50 - 60) and (more than 60) years of age in both groups. We had 8 patients (20.5%) in Propofol group and 2 patients (5.1%) in Sevoflurane group, in the first group (less than 30 years of age). Also we had 5 patients (12.8%) in Propofol group and 6 patients (15.4%) in Sevoflurane group in the second group (30-40 years of age). There were 8 patients (20.5%) in Propofol group and 6 patients (15.4%) patients in Sevoflurane group in the third group (40-50 years of age). The higher number was in the fourth group (50-60) which had 13 patients (33.3%) in Propofol group and 17 patients

(43.6%) in svoflurane group. The last group of patients was older than 60 years of age and the number of patients was 8 (12.8%) in Propofol group and 8 (20.5%) in Sevoflurane group. And according to p value there was no difference between both groups (p= 0.267).

The results showed that the causes of liver failure for Propofol group of 39 patients were, 1 (2.6%) Alcoholic Cirrhosis, 6 (15.4%) HCV, 3 (7.7%) NASH, 1 (2.6%) PBC, 2 (5.2%) Wilson disease, 4 (10.3%) AIH, 1 (2.6%) ASH+PSC, 3 (7.7%) Budd-Chiari syndrome, 8 (20.5%) Cryptogenic, 1 (2.6%) Drug induced acute hepatitis, 1 (2.6%) Fulminant Hepatitis, 4 (10.3%) HBV, 1 (2.6%) HBV+HCC, 1 (2.6%) HCC+AIH, 1 (2.6%) PSC, 1 (2.6%) AIH+PSC. And the results showed that the causes of liver failure for Sevoflurane group of 39 patients were, 2 (5.1%) Alcoholic Cirrhosis, 3 (7.7%) HCV, 3 (7.7%), NASH, 2 (5.1%) AIH, 1 (2.6%) AIH+Plavix, 2 (5.1%) Budd-Chiari syndrome, 10 (25.6%) Cryptogenic, 1 (2.6%) Fulminant Hepatitis, 4 (10.3%) HBV, 2 (5.1%) HBV+HCC, 1 (2.6%) Hemochromatosis, 1 (2.6%) Hydatid Cyst, 7 (17.9%) PSC. According to the p value, the results showed that there is no significant difference between 2 groups (p=0.504).

Need for Vasopressor was seen in 19 cases (48.7%) in propofol and 18 (46.2%) in sevoflurane, and according to p value, the results showed that there was no significant difference seen about the need for vasopressor in both groups (p=0.821), and the same results were also obtained as far as the hemodynamic variables between 2 groups according to p-value (Table 1).

Table 1- Hemodynamic variables in both the groups.

Group		MAP	PAP	PCWP	PVR	HR	CVP	BIS	SV	SVR	CO	PI	PVI
	P Value	0.553	0.526	0.685	0.156	0.590	0.499	0.619	0.337	0.513	0.415	0.98	0.119
Propofol	Mean	76.05	18.05	13.26	58.31	89.31	9.77	39.36	90.21	773.95	7.79	1.36	11.13
	Std. Dev	7.640	4.984	4.278	33.299	17.928	3.883	4.727	29.999	230.609	2.215	1.112	2.462
Sevoflurane	Mean	74.74	17.38	12.90	48.18	87.26	9.26	38.92	96.85	739.85	8.26	1.82	12.10
	Std. Dev	11.378	4.215	3.463	28.924	15.478	2.673	2.709	30.638	227.876	2.731	1.315	2.972
Total	Mean	75.40	17.72	13.08	53.24	88.28	9.51	39.14	93.53	756.90	8.03	1.59	11.62
	Std. Dev	9.650	4.598	3.871	31.401	16.671	3.321	3.833	30.308	228.399	2.481	1.232	2.755

Std. Dev: Standard Deviation, MAP: Mean arterial pressure, PAP: Pulmonary artery pressure, PCWR: Pulmonary wedge pressure, PVR: Pulmonary vascular resistance, HR: Heart rate, CVP: Central venous pressure, BIS: Bispectral index, SV: Stroke volume, SVR: Systemic vascular resistance, CO: cardiac output, PI: Perfusion index, PVI: pleth variability index

Table 2- The mean of PCO2, PO2, HCO3, Na and K in both the groups.

group		PCO2	PO2	HCO3	Na	K
P Value		0.020	0.036	0.010	0.002	0.013
Propofol	Mean	37.38	235.69	19.72	135.49	3.77
	Std. Dev	3.167	49.388	2.294	4.994	0.583
Sevoflurane	Mean	35.44	208.08	18.26	138.90	4.15
	Std. Dev	4.018	64.044	2.593	4.430	0.745
Total	Mean	36.41	221.88	18.99	137.19	3.96
	Std. Dev	3.726	58.490	2.541	4.994	0.692

Std. Dev: Standard Deviation

Table 3- Hb (measured by ABG), Hb (measured by CO-Oximetry) and Glucose in both the groups.

Group		Hb (ABG)	Hb (co oximeter)	Glucose
	P Value	0.234	0.132	0.614
Propofol	Mean	9.79	11.69	137.33
	Std. Dev	1.321	1.321	41.706
Sevoflurane	Mean	10.18	11.18	141.72
	Std. Dev	1.502	1.636	34.485
Total	Mean	9.99	11.44	139.53
	Std. Dev	1.419	1.500	38.081

Std. Dev: Standard Deviation

Table 4- Total Amount of Solution, Total Amount of Fibrinogen, Total Amount of Tranexamic acid, Total Amount of P.C and Total Amount of Urine in both the groups.

Group		Total Amount of Solution	Total Amount of Fibrinogen	Total Amount of Tranexamic acid	Total Amount of P.C	Total Amount of Urine
P Value		0.728	0.784	0.224	0.498	0.429
Propofol	Mean	6.0000	3.8500	0.9444	4.3871	731.28
	Std. Dev	1.31789	1.81442	0.16667	9.61484	448.848
Sevoflurane	Mean	6.1026	3.6429	1.1667	3.0769	842.56
	Std. Dev	1.27310	2.56026	0.50000	1.99846	751.016
Total	Mean	6.0513	3.7647	1.0556	3.7895	786.92
	Std. Dev	1.28828	2.11859	0.37920	7.19309	617.179

Std. Dev: Standard Deviation, P.C: Packed cells

There was just one (2.6%) patient in Propofol group had post-operative port vein thrombosis (PVT), and none of the patients in Sevoflurane group had post-operative port vein thrombosis (PVT). According to p value there was no significant difference in both groups (p value= 0.314).

Need for kidney dialysis after surgery was seen in one patient (2.6%) in Propofol group, and was seen in 2 patients (5.1%) in Sevoflurane group. And according to p value, the results showed that there is no significant difference in both groups (p= 0.556).

None of the patients in both groups had post-operative hepatic artery thrombosis (HAT).

None of the patients in both groups was given platelet (Plt) and fresh frozen plasma (FFP), and just one patient in sevoflurane group was given 500 IU of PCC.

The only significant differences that were seen in the results between both groups were in the arterial blood gas variables which included PCO2, PO2, HCO3, Na and K. (Table 2). But according to p value, both groups had no significant difference related to Hb (measured by ABG and by CO-Oximetry) (Table 3).

No significant differences were seen in the other variables between 2 groups according to p-value (Table 4).

Discussion

We compared the effect of propofol and sevoflurane on hemodynamics and coagulation status during liver transplant anesthesia and hepatic and renal function of the patients after liver transplant. Our results showed that there are no significant differences in postoperative liver and renal function as measured in clinical outcomes in the 2 groups.

Numerous strategies have been designed to reduce ischemia/reperfusion injury after liver resection. Two protective strategies to prevent ischemic-reperfusion injury have been clinically accepted: ischemic preconditioning [9-10] and intermittent clamping [11] of the portal triad. Both procedures require a surgical intervention and prolong the overall time of the surgical procedure. In this study, we wanted to know whether the Sevoflurane and Propofol affect postoperative hepatic function in patients undergoing liver transplant surgery.

Many previous studies compared the effects of these two anesthetics on renal and hepatic function. Sahin et al. [12] compared the effects of inhalational anesthetics and TIVA on patients with lumbar discectomy, and found that there were no changes in postoperative liver function, and found no differences between the two groups. Their findings agree with the results of the present study. In retrospective comparative study between sevoflurane and propofol in maintaining anesthesia during liver transplant and their effects on kidney and liver function, Alonso Menarguez et al. [13] mentioned that the effect of Sevoflurane and Propofol is same and both of them are safe for liver and renal function in liver transplant anesthesia. And our results agreed with their results. One of the previous studies done by Song JC et al. [14] compared the liver function after hepatectomy with inflow occlusion between Sevoflurane and Propofol anesthesia, the results showed that both of these anesthetics are in same patterns of liver function tests after hepatectomy with inflow occlusion and their data suggested that they are equivalent in their clinical study, our results according to their results are same. The results of our study also agreed with studies performed by Yoon et al. [15] and Oh et al. [16] on laparoscopic cholecystectomy patients, in that they found no differences in liver function after surgery with either inhalational anesthesia or anesthesia with propofol. Similarly, study was done by Kim et al. [17] on patients undergoing thyroidectomy, their results agreed with our results where they found that the changes of hepatic and renal function after inhalation anesthesia with sevoflurane and TIVA with propofol and remifentanil for thyroidectomy were clinically insignificant, and there was no difference between the two methods.

Conclusion

The results showed that there is no significant difference between the effect of Propofol and Sevoflurane on hemodynamics and coagulation status and also on renal and hepatic function for the patients undergoing liver transplant anesthesia. Both anesthetics can be used safely in this type of surgery and that there is no advantage of one drug over the other.

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