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RESEARCH ARTICLE

Perioperative effects of desflurane versus propofol on hemostasis guided by thromboelastometry in splenectomy with liver cirrhosis

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ABSTRACT

Background: Cirrhotic patients have impaired hemostasis with variable incidence of hypersplenism necessitating splenectomy. Rotation thromboelastometery (ROTEM) facilitates diagnosis and guides management. This study evaluates perioperative effects of desflurane versus propofol on hemostasis in cirrhotic patients undergoing splenectomy guided by ROTEM and laboratory hemostatic tests.

Methods: Thirty hepatic Child A patients, ASA II- III, of either sex, aged 25–55 years, undergoing splenectomy were randomly allocated into two equal groups: Group D; anesthetized with desflurane 1 MAC (6%) and Group P; with propofol Target Controlled Infusion 2–5 µg/ml. Six blood samples were collected; preoperatively, after splenic artery ligation, immediately, first, third postoperative day then one month later. The samples were handled to measure complete blood picture, liver and kidney functions, screening coagulation tests (INR, PT and PTT), specific hemostatic factors (P-Selectin/CD62P, fibrinogen and D-dimer) as well as ROTEM criteria; clotting time (CT), clot formation time (CFT) and maximum clot firmness (MCF) via EX-TEM, IN-TEM and FIB-TEM commercial kits.

Results: This study displayed postoperative hemoglobin reduction; however, platelet and WBCs as well as CT, CFT and MCF increased versus baseline. Screening and specific hemostatic factors as all other changes were within reference range and comparable between both groups.

Conclusions: The current study concluded comparable effects of desflurane and propofol anesthesia on coagulation parameters within acceptable range as monitored by ROTEM and laboratory coagulation tests in cirrhotic patients with hypersplenism. Thus both anesthetics are considered safe in such patients who have high incidence of coagulopathy.

KEYWORDS
Desflurane; Propofol; Coagulation; Splenectomy; Cirrhosis; Thromboelastometry

1 Introduction

Patients with cirrhosis have impaired hemostasis which is multifactorial including impaired synthesis, function and clearance of coagulation factors as well as quantitative and qualitative platelet disorders. Accordingly, these patients suffer from bleeding or even thrombotic problems [1] in addition to a higher risk of bacterial infection secondary to the associated leucopenia [2].

There is a varying incidence of hypersplenism in these patients ranging from 11 to 64% and surgical splenectomy is considered the gold standard management [3,4]. Postoperative high platelet counts can lead to various venous thromboembolic events [5] which can be reduced by different peri-operative hemostatic management involving the protective effects of some anesthetic agents [6].

Isoflurane, sevoflurane and desflurane anesthesia were reported to have relative clinical anticoagulant properties during minor surgical procedures [7]. Desflurane showed better postoperative hepatic function tests and INR results when compared with both isoflurane at equivalent doses [8] and total intravenous anesthesia (TIVA) with propofol-remifentanil [9]. In vivo, propofol had significant inhibitory effects on platelet aggregation which is clinically irrelevant [10].

Postoperative deep venous thrombosis, splenic or portal vein thrombosis following splenectomy can be screened by certain biomarkers as plasma s-platelet selectin denoting platelet activation, fibrinogen reflecting the clotting ability as well as D-dimer representing the final product of simultaneous blood coagulation activation and fibrinolysis [11–13].

Point of care (POC) coagulation monitoring devices as rotation thrombelastometry (ROTEM) can evaluate the

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viscoelastic characteristics of the whole blood sample [14]. It is a bedside monitor, allowing faster assessment and providing valuable data on coagulation profile. Moreover, the real time clot progress is visually exhibited. However, the measurement of coagulation process in the cuvette where no blood flows should be considered as a mean difference between in vitro and in vivo conditions. Therefore, the clinical situation should be reviewed during interpretation of the obtained results. This monitoring device helps in the diagnosis of probable bleeding causes, directs blood transfusion elements and anticipates hemorrhagic risk [15].

We hypothesized that ROTEM use can help in identifying the anesthetic agent with the least effect on hemostatic mechanism. The aim of this randomized prospective research is to compare the effect of TIVA using propofol versus desflurane anesthesia on perioperative coagulation process in cirrhotic patients scheduled for splenectomy using ROTEM and laboratory coagulation tests. Postoperative measurement of maximum clot firmness (FIBTEM-MCF) by ROTEM is considered as a primary outcome. Other ROTEM parameters, laboratory hematological tests as well as hepatic and renal functions were considered as secondary outcomes.

2 Patients and methods

After obtaining Ethical Committee approval and written informed consents, thirty hepatic patients scheduled for splenectomy under general anesthesia were enrolled in this study. It was registered at public trial register (www.clinicaltrials.gov) with identification code: NCT02079064 on 27/2/2014.

Patients were of either sex, aged 25–55 years, ASA class II- III (Child A) suffering from pancytopenia or only thrombocytopenia. Pancytopenia is defined as anemia (hemoglobin < 13.5 g/dL in male; <12 g/dL in female); leucopenia (total leukocytic count < 4000/mm^3) and thrombocytopenia (platelet count < 150,000/mm^3). Patients were excluded from this study if they were Child B or C hepatic patients, Hb < 10 g/dl, platelet count < 45,000/mm^3, White blood cell counts (WBCs) <2000/mm^3, prothrombin time (PT) more than 16 s and INR greater than 1.7, extremes of age, obese patients having body mass index (BMI) more than 35 kg/m^2 and those using oral anticoagulants or other antithrombotic drugs.

This study was performed to be a pilot one since no previous research was found to compare the effects of both anesthetics on coagulation by ROTEM and fifteen patients for each group was considered as a sample size.

2.1 Anesthesia technique

All patients were premedicated with i.v. midazolam 0.02–0.04 mg/kg. In the operating room, continuous ECG, non-invasive arterial blood pressure, pulse oximetry, PET_{CO2}, end-tidal anesthetic agent, neuromuscular monitoring and core temperature (Infinity Kappa, Dräger, Lübeck, Germany) were monitored throughout the operation. Bispectral index (BIS) for monitoring the anesthetic depth was applied. Patient's temperature was controlled by a warm air blanket (Bair Hugger) as well as warming of all IV fluids given at a rate of 5–7 ml/kg/h acetated Ringer's solution. A computer generated list randomly allocated the patients to one of two equal groups of 15 patients each according to maintenance of anesthesia:

Group D received inhaled desflurane at 1 MAC (6%) while Group P received Target Controlled Infusion (TCI) of propofol at an effector site concentration (C_E) of 2–5 µg/ml. Anesthesia was adjusted to keep BIS numerical level between 40 and 50 by adjusting the concentration of volatile anesthetics or the C_E of propofol.

In both groups, induction of anesthesia was performed by using intravenous fentanyl 1.5–2 µg/kg followed by propofol 2–2.5 mg/kg. Atracurium 0.5 mg/kg was administered for neuromuscular blockade. Ventilation was controlled to keep ET_{CO2} at 30–-35 mmHg with fresh gas flow of 30–40% O_2/air. Twenty percent rise of heart rate and blood pressure above the baseline despite adequate anesthetic depth monitored by BIS was managed by 0.5 µg/kg fentanyl while their decrease by more than 20% was treated by IV bolus of atropine 0.5 mg or ephedrine 5 mg respectively.

No synthetic colloid transfusion was allowed. Packed RBCs was transfused if hemoglobin decreased below 8 g/dl. Platelets or fresh frozen plasma was administered if indicated by ROTEM and the remaining measurements following such infusions were excluded from the study. At the end of surgery, neuromuscular blockade was antagonized with 0.05 mg/kg neostigmine and 0.02 mg/kg atropine Postoperative pain was controlled by IV acetaminophen 15 mg/kg/ 6 h and IV mepridine 0.5 mg/kg/8 h.

2.2 Blood sampling

Six blood samples were collected; before operation, post-ligation of splenic artery, immediate postoperative, after one and three days then one month later. Each time, five ml of venous blood was collected and the following parameters were assessed:

- Complete blood picture (hemoglobin, WBCs and platelet counts) performed using EDTA blood samples on automated cell counter Medonic, (Boule Diagnostics, Sweden).

- Liver and kidney functions pre- and postoperative performed on serum samples using auto analyzer (Hitachi 736, Hitachim, Japan).
- Screening hemostatic tests were carried out on semi-automated coagulation analyzer BFT II (Siemens, Germany). Prothrombin Time (PT) and International Normalized Ratio (INR) performed using Thromborel® S Reagent (Cat. No. OUHP29), Partial Thromboplastin Time (PTT) performed using Pathromtin® SL Reagent (Cat. No. OQGS29). Control plasma Normal & Pathological (Cat. No. ORKE41) & (Cat. No. OUPZ17) respectively (Siemens, Germany).
- Specific hemostatic tests were carried out on plasma samples using fully automated Coagulation System STA® Compact Max hemostasis analyzer (Diagnostica Stago, Seine, France):

  STA®-Liatest® D–Di (Cat. No. 00515) is a rapid, automated, quantitative immuno-turbidimetric assay. Microlatex particles coated with two different mouse monoclonal anti-human D-dimer antibodies. The reporting units are in µg/ml Fibrinogen equivalent units (FEU). STA®-Liatest® Control N + P (Cat. No. 00526US) normal and abnormal control plasmas for immuno-turbidimetric assays performed on STA® Compact Max analyzers.

  STA®-Fibrinogen 5 (Cat. No. 00674) for quantitative determination of Fibrinogen by (Clauss Method). Freeze-dried human thrombin (□80 NIH units/ml) with heparin inhibitor and calcium. STA®-Coag Control N + ABN (Cat. No. 00676) is multi-constituent normal and abnormal plasma controls for routine assays performed on the STA® Compact Max analyzers.

  Human P-Selectin/CD62P Immunoassay (Cat. No. BBE6, Lot No. 117317) R&D Systems, Inc. Minneapolis, MN, USA. For quantitative determination of human Platlet-Selectin (P-Selectin) in EDTA plasma samples using ELISA technique. The procedures given by the manufacturer were followed.

At each sample time (0.3 ml blood) was taken for measuring the following ROTEM variables [16]:

- The time until initial fibrin generation (clotting time; CT).
- The fibrin development kinetics and clot progress (clot formation time; CFT and α- angle).
- The eventual potency and solidity of the clot (maximum clot firmness; MCF).

Blood samples were activated extrinsically; EX-TEM (by tissue factor) and intrinsically; IN-TEM (by contact activator) via commercially available tests. Furthermore, fibrinogen levels were evaluated by quantifying clot potency (MCF) by addition of platelet suppressor (e.g., FIB-TEM). This adapted MCF exhibits the functional fibrinogen as the fibrin clot was formed with platelet nonexistence.

2.3 Statistical methods

The statistical package SPSS (Statistical Package for the Social Sciences) version 23 was used. Quantitative data were expressed by mean ± standard deviation whereas categorical data were represented by count and percentage. Comparisons between groups were made in normally distributed quantitative ingredients via unpaired *t*-test while non-parametric Mann-Whitney test was applied with non-normally distributed quantitative ingredients. For comparison of serial measurements within each group repeated measures ANOVA was used in normally distributed quantitative variables although non-parametric Friedman test was applied with non-normally distributed. Chi square ($\chi 2$) test was done for comparing categorical records; instead, Exact test was performed when the predictable incidence is <5. P-value < 0.05 was defined to be statistically significant [17].

3 Results

Demographic data as regards age, gender, weight, height, BMI, as well as etiology of cirrhosis, surgical duration, ASA classification and preoperative MBP and HR were all statistically comparable between both groups (Table 1). No significant difference was detected regarding liver and kidney functions postoperatively versus preoperative level as well as among both groups at different timings. All readings were within laboratory reference range.

There was postoperative reduction in Hb concentration compared to preoperative value which reverted to near baseline after one month. Platelet count and WBCs showed significant postoperative increase in both groups when compared to preoperative values with no significant difference between both groups (Table 2).

PT, PPT and INR showed post-ligation and postoperative increase relative to baseline exhibiting a later decline after that (Table 3).

P-Selectin/CD62P, Fibrinogen and D-Dimer showed postoperative increase versus baseline but comparable between groups within the reference range (Table 4).

Concerning *EX-TEM*, CT revealed postoperative significant increase in group D only, when compared to preoperative level. In both groups CFT and MCF showed postoperative increase at various timings relative to preoperative levels while alpha angle revealed no statistical significant changes. All previous

Table 1. Demographic data, etiology of cirrhosis, preoperative hemodynamics, ASA classification and duration of surgery.

	Group D (n=15)	Group P (n=15)	P-value
Age (yrs.)	48.87 ± 3.54	48.73 ± 5.13	0.935
Gender			
Female	4 (26.7%)	5 (33.3%)	1.000
Male	11 (73.3%)	10 (66.7%)	
Weight (kg)	79.87 ± 4.85	79.20 ± 4.62	0.703
Height (cm)	159.87 ± 5.45	163.33 ± 5.07	0.082
BMI (kg/m2)	31.05 ± 1.89	29.71 ± 1.98	0.069
ASA-physical status			
II	12 (80.0%)	13 (86.7%)	1.000
III	3 (20.0%)	2 (13.3%)	
Etiology of cirrhosis			
HCV	11 (73.3%)	12 (80.0%)	1.000
Bilharzial	4 (26.7%)	3 (20.0%)	
Surgical time (min)	161.00 ± 22.06	158.67 ± 27.22	0.798
MBP (mmHg)	74.33 ± 4.72	73.80 ± 3.86	0.737
HR (bpm)	83.13 ± 5.07	82.93 ± 5.18	0.916

Data are expressed as mean ± SD or number (%). D; patients anesthetized with desflurane, P; patients anesthetized with propofol, BMI; body mass index, ASA; American Society of Anesthesiology Classes, HCV; Hepatitis C Virus, MBP: mean blood pressure. HR: heart rate. Bpm: beat per minute. $P > 0.05$ = not significant.

Table 2. Levels of Hb, WBCs and platelets.

	Preoperative	After ligation	Postoperative	First POD	Third POD	One month
Hb (g/dl)						
Group D	11.49 ± 0.47	10.36 ± 1.32*	10.58 ± 1.00*	10.43 ± 1.63*	10.28 ± 1.79*	11.39 ± 1.14
Group P	11.38 ± 1.83	10.53 ± 0.91*	10.5 ± 1.12	10.41 ± 1.86	10.31 ± 1.62*	11.48 ± 1.14
WBCs (cell/mcl)	4.11 ± 1.95	6.84 ± 2.32*	8.78 ± 1.74*	9.63 ± 1.16*	8.17 ± 1.54*	6.62 ± 1.15*
Group D						
Group P	4.33 ± 1.92	6.69 ± 2.58*	8.65 ± 1.50*	9.65 ± 0.75*	8.39 ± 1.61*	6.75 ± 1.34*
PLT (cell/mcl)	69.2 ± 23.21	87.87 ± 37.36	109.20 ± 67.1*	140.07 ± 74.76*	173.93 ± 65.25*	194.53 ± 22.88*
Group D						
Group P	68.07 ± 21.09	87.73 ± 31.02*	89.40 ± 25.23*	110.40 ± 29.66*	172.33 ± 55.11*	195.73 ± 48.66*

Data are expressed as mean ± standard deviation. D; patients anesthetized with desflurane, P; patients anesthetized with propofol. PLT: platelets. WBCs: white blood cells, Hb: hemoglobin, POD: postoperative day.
* $P < 0.05$ relative to preoperative (baseline) within the same group.

parameters were comparable between both groups. Regarding *IN-TEM*, both groups recorded significant postoperative increase in CT at different timings compared to preoperative readings. MCF and CFT changed significantly postoperatively versus preoperative levels. Alpha angle displayed significant increase postoperatively in group D only. No significant difference was detected between both groups. *FIB-TEM* maximum clot firmness showed significant changes postoperatively in comparison to preoperative values with comparable results between both groups (Table 5). No significant correlation was found between fibrinogen level and MCF of FIB-TEM.

4 Discussion

The current study evaluated perioperative effects of desflurane versus TIVA with propofol on coagulation in cirrhotic patients scheduled for splenectomy directed by ROTEM as well as laboratory coagulation tests. Assessment was carried preoperatively, post-ligation of splenic artery, immediate postoperative, after one day, three days and one month later.

Hemoglobin level showed postoperative decrease in both groups which nearly reverted to preoperative value after one month. This reduction was comparable between both groups which may be due to intraoperative hemodilution yet still within clinically

Table 3. Results of INR, PT and PTT.

	Preoperative	After ligation	Postoperative	First POD	Third POD	One month
INR						
Group D	1.15 ± 0.05	1.17 ± 0.09	1.19 ± 0.04*	1.17 ± 0.09	1.14 ± 0.15	1.08 ± 0.11*
Group P	1.16 ± 0.06	1.21 ± 0.03*	1.2 ± 0.10*	1.18 ± 0.05	1.15 ± 0.05	1.13 ± 0.05
PT (Sec)						
Group D	13.07 ± 1.48	13.21 ± 1.21	14.11 ± 0.58*	13.29 ± 1.01	12.51 ± 0.97	12.01 ± 0.76*
Group P	13.38 ± 1.25	13.43 ± 1.16	14.07 ± 0.71*	13.32 ± 1.06	12.88 ± 0.73*	10.62 ± 3.85*
PTT (Sec)						
Group D	32.63 ± 1.61	33.04 ± 3.28	33.43 ± 4.44	34.39 ± 4.13	32.56 ± 4.06	29.93 ± 2.34*
Group P	13.38 ± 1.25	13.43 ± 1.16	14.07 ± 0.71*	13.32 ± 1.06	12.88 ± 0.73*	10.62 ± 3.85*

Data are expressed as mean ± standard deviation. D; patients anesthetized with desflurane, P; patients anesthetized with propofol. POD: postoperative day, INR: international normalized ratio, PT: prothrombin time, PTT: partial thromboplastin time.
* P value < 0.05 compared to preoperative level in each group.

Table 4. Results of P-selectin/CD62P, Fibrinogen and D-Dimer.

	Preoperative	After ligation	Postoperative	First POD	Third POD	One month
P-Selectin/CD62P (ng/ml)						
Group D	18.29 ± 3.77	17.72 ± 2.65	19.25 ± 3.51	21.98 ± 5.16*	25.28 ± 5.41*	22.84 ± 2.82*
Group P	18.81 ± 3.21	18.25 ± 1.97	17.90 ± 2.01	19.95 ± 1.61	23.87 ± 3.27*	23.46 ± 3.06*
Fibrinogen (g/l)						2.48 ± 0.65*
Group D	2.01 ± 0.33	2.20 ± 0.30	2.11 ± 0.30	2.13 ± 0.44	2.45 ± 0.53*	2.48 ± 0.65*
Group P	2.10 ± 0.34	2.06 ± 0.23	2.02 ± 0.40	2.01 ± 0.40	2.55 ± 0.57*	2.43 ± 0.56
D-Dimer (µg/ml)						
Group D	0.56 ± 0.23	0.85 ± 0.22*	0.76 ± 0.21*	0.71 ± 0.23	0.63 ± 0.21	0.56 ± 0.16
Group P	0.61 ± 0.20	0.84 ± 0.25*	0.82 ± 0.23*	0.78 ± 0.26	0.79 ± 0.26	0.60 ± 0.16

Data are expressed as mean ± standard deviation. D; patients anesthetized with desflurane, P; patients anesthetized with propofol. POD: postoperative day.
* P value < 0.05 compared to preoperative level in each group.

acceptable range. Brueckner et al. [18] reported similar postoperative hemoglobin decrease in patients undergoing total hip arthroplasty anesthetized by either isoflurane or spinal anesthesia. Yuceaktas et al. [19] demonstrated comparable effects of desflurane and sevoflurane anesthesia on Hb and Hct levels among patients undergoing laparoscopic cholecystectomy. Conversely, Elrashidy et al. [20] noted non-significant change in RBCs and Hb values from the baseline or within groups in patients receiving either sevoflurane or isoflurane during ophthalmic surgery. This may be attributed to negligible blood loss and minimal fluid replacement during such minor procedure.

The current study showed an initial WBC counts increase in response to surgical stimulus followed by their reduction not reaching the baseline after one month. This goes in accordance with Ardestani et al. [21] who reported postoperative increase in WBCs during open versus laparoscopic splenectomy. However, Rutherford et al. [22] noted that maximal WBC counts were comparable in patients after splenectomy with either bacteremia or negative blood culture result indicating that postoperative leucocytosis is not a valid evidence of infection [23].

Platelet count was comparable within groups showing progressive increase after ligation of splenic artery relative to the preoperative value due to removal of the sequestering organ. Postoperative increase in platelet counts and aggregation may also be attributed to variable aggregation-promoting agonists' release [24].

Table 5. Results of EX-TEM, IN-TEM and FIB-TEM; CT, CFT, MCF and α- angle.

	Preoperative	After ligation	Postoperative	First POD	Third POD	One month
P-Selectin/CD62P (ng/ml)						
EX-TEM						
CT (Sec)						
Group D	50.33 ± 8.15	50.33 ± 6.00	53.60 ± 8.04*	50.00 ± 2.48	50.07 ± 7.12	49.20 ± 5.98
Group P	53.53 ± 5.08	53.47 ± 4.07	54.07 ± 5.68	53.07 ± 7.08	51.93 ± 6.88	51.60 ± 4.53
CFT (Sec)						
Group D	115.73 ± 7.63	120.67 ± 7.66	127.53 ± 10.13*	121.73 ± 5.86*	121.73 ± 5.86*	114.4 ± 5.73
Group P	116.47 ± 5.36	122.73 ± 7.45*	129.47 ± 12.94*	124.13 ± 5.33*	120.8 ± 5.73*	117.33 ± 4.06
MCF (mm)						
Group D	54.60 ± 3.74	57.47 ± 4.10	52.53 ± 5.79	59.60 ± 5.40	63.60 ± 6.49*	67.13 ± 5.9*
Group P	54.53 ± 4.76	54.53 ± 4.76	51.27 ± 3.90	58.93 ± 5.50*	63.2 ± 5.31*	66.47 ± 3.29*
α angle (o)						
Group D	69.80 c 5.41	69.33 ± 5.37	67.27 ± 4.56	70.07 ± 5.16	70.47 ± 3.18	71.60 ± 1.72
Group P	69.67 ± 3.5	69.13 ± 4.42	67.07 ± 4.5	69.53 ± 2.95	70.40 ± 4.29	71.0 ± 4.61
IN-TEM						
CT (Sec)						
Group D	161.93 ± 5.35	174.53 ± 16.19*	188.8 ± 11.8*	177 ± 93 ± 9.88*	169.33 ± 9.13*	164.4 ± 8.42*
Group P	161.33 ± 8.89	177.93 ± 9.88*	189.53 ± 10.67*	178.6 ± 12.13	171.47 ± 10.28*	168.07 ± 9.54*
CFT (Sec)						
Group D	87.73 ± 8.79	89.47 ± 4.97	89.8 ± 4.75	79.93 ± 10.61	77.33 ± 2.23*	69.8 ± 7.36*
Group P	86.13 ± 4	90.13 ± 4.42*	90.8 ± 5.31*	85.13 ± 5.99	78.13 ± 4.0*	71.13 ± 6.29*
MCF (mm)						
Group D	58.53 ± 4.44	57.47 ± 4.1	55.13 ± 3.52*	63.67 ± 6.99*	67.2 ± 5.07*	67.8 ± 3.05*
Group P	58.27 ± 4.11	55.47 ± 6.15	55.2 ± 3.73	60.0 ± 8.4	63.33 ± 51*	65.27 ± 4.06*
α angle (o)						
Group D	75.4 ± 2.5	75.33 ± 3.18	75.0 ± 1.81	75.53 ± 3.07	77.27 ± 2.76*	78.6 ± 1.5*
Group P	75.13 ± 3.44	74.47 ± 3.02	74.4 ± 1.68	75.2 ± 3.28	77.2 ± 2.01	77.07 ± 2.89
FIB- TEM)	MCF (mm)					
Group D	15.73 ± 2.81	15.67 ± 3.35	12.8 ± 3.88*	l6.4 ± 4.19	19.2 ± 5.03*	20.13 ± 2.92*
Group P	15.6 ± 2.95	15.6 ± 3.64	14.0 ± 1.56	16.33 ± 3.99	19.0 ± 2.1*	19.93 ± 2.96*

Data are expressed as mean ± standard deviation. D; patients anesthetized with desflurane, P; patients anesthetized with propofol. POD: postoperative day, CT: clotting time, CFT: clot formation time. MCF: maximum clot firmness.
* P value < 0.05 compared to preoperative level.

In the present study, PT, PTT and INR showed postligation increase continuing up to the first postoperative day then declining afterwards. Toprak et al. [8] found better liver function tests and international normalized ratio in living donors scheduled for right hepatectomy and anesthetized by one MAC desflurane versus isoflurane. Concerning the effects of different inhalational anesthetics on coagulation, PT, INR and PTT were increased at different postoperative times when compared to the baseline level in non-hepatic patients undergoing cholecystectomy [25]. In contrast to these results, Brueckner et al. [18] found a significant decrease in PT two hours after skin incision under general anesthesia with isoflurane during orthopaedic surgery. They also reported slight increase of PTT not reaching a significance level. Yuceaktas et al. [19] demonstrated comparable effects of desflurane and sevoflurane on PT as well as aPTT in patients undergoing laparoscopic cholecystectomy. These discrepancies in results may be attributed to different types of surgery as well as anesthetic agents.

Clinically relevant antithrombotic effects of 1 MAC isoflurane, sevoflurane and desflurane was observed 15 min after intubation, by using platelet function analyzer (PFA-100) during minor surgery. Also, no significant difference was reported in INR, PT, aPTT as well as Hct, Hb and platelet count, at various timings [7].

Concerning desflurane effects on hemostasis, it did not affect bleeding time nor platelet function at 0.5 MAC concentration [26]. However Berlet et al. [27] described desflurane differential effects on different characteristics of platelet activation; these conflicting results may be attributed to variation in measurement methodology and test tubes either in vivo or in vitro studies.

The present study revealed postoperative increase of P-Selectin/CD62P, Fibrinogen and D-Dimer versus baseline but comparable between groups within the reference range. Areda et al. [28] showed decreased plasma d-dimer value following orthopedic surgery in patients anesthetized by spinal blockade versus general anesthesia which may be due to less inhibitory surgical stress. During laparoscopic cholecystectomy and constant pneumoperitoneum, the levels of fibrinogen, DD, PT, APTT, and INR were higher during regional anesthesia receiving combined spinal epidural compared to patients anesthetized by general anesthesia using sevoflurane and compared to preoperative values. This may be attributed to the effects of pneumoperitoneum and anesthesia techniques on portal vein flow [29].

In the present study, both groups showed intra- and postoperative increase in CT, CFT by EX-TEM and IN-TEM tests which decreased after one month relative to baseline. Regarding MCF by EX-TEM, IN-TEM and FIB-TEM tests, changes recorded intraoperatively and immediately postoperative were within the normal reference range reaching the base line value up to one month after surgery. Alpha angle changes were minor in each group. All ROTEM readings were comparable between both groups indicating minimal effects of both anesthetics on coagulation in these patients. Koo et al. [30] found comparable results between the propofol and sevoflurane with negligible effect on hemostasis despite the difference in patients' status being non-hepatic as well as minimally-invasive optical surgeries in their study. Yuceaktas et al. [19] demonstrated that desflurane produced a delay in thromboelastographic values extending up to 24 h postoperatively following laparoscopic cholecystectomy.

In addition, Lewis et al. [31] reported that TIVA using propofol at target controlled infusion 2–5 μg/ml did not affect coagulation as measured by thrombelastography nor intraoperative blood loss increase when compared with isoflurane inhalational anesthesia. Although in vivo propofol had significant reversible intra and postoperative inhibitory effects on platelet aggregation, yet, absence of bleeding time variation revealed no hemostatic clinical impairment [9].

Dumitrescu et al. [32] demonstrated that the measurements of both routine coagulation monitoring tests and ROTEM® parameters are useful to offer a more comprehensive image of the coagulation status in patients undergoing major hepatic surgery.

In this study no significant correlation was found between fibrinogen level and MCF of FIB-TEM. Solomon et al. [33] also verified discrepancies between the fibrinogen level and FIB-TEM data measured by the thrombelastography and thromboelastometry. This may be attributed to the effect of different blood factors as hematocrit and factor XIII not only on fibrinogen level [34,35]. These abnormal hematocrit or factor XIII levels, frequently present in perioperative hemorrhage and trauma-produced coagulopathy, thus it seems better to recognize the influence of fibrinogen administration on whole-blood clotting than to know the plasma fibrinogen level [33].

The limitations of the present study were the small sample size and inability of normal visco-elastic tests profile to exclude platelet dysfunction. A modification as Platelet Mapping based on impedance aggregometry can be useful to judge the extent of platelet suppression and is increasingly included within transfusion algorithms. This modification can be utilized to align patients on antiplatelet treatment for bleeding hazard and platelet transfusions requirement [36].

5 Conclusion

The current study concluded that anesthesia by desflurane or propofol has comparable effect on

coagulation parameters within acceptable range monitored by ROTEM and laboratory coagulation tests in cirrhotic patients with hypersplenism. Thus both anesthetics are considered safe in such patients who have high incidence of coagulopathy.

6 Recommendations

Future studies are considered necessary to assess prolonged propofol infusion effects on coagulation as in ICU patients with hemostatic disorders. Also, larger scale study is recommended for verification and better understanding of the involved hemostatic mechanisms.

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