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Effect of Target-Controlled Infusion of Propofol-Fentanyl versus Desflurane in Cirrhotic Patients Undergoing Major Hepatic Resection with Transoesophageal Doppler Monitoring A Randomized Control Study

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Abstract

Background and aim: The choice of anaesthetic agents is important for cirrhotics undergoing liver resection. Aim is to compare Target Controlled Infusion (TCI) Propofol-Fentanyl versus Desflurane (Des) on recovery, hemodynamics monitored with Transoesophageal Doppler (TED), the effect on hepatocellular, kidney functions and economics.

Patients and methods: Prospective randomized controlled study, 50 patients (Child A) divided equally. In (Des) group induction with fentanyl (1microgram/kg), propofol (2 mg/kg) and rocuronium (1 mg/kg) and maintenance with Desflurane. In (TCI) group the Propofol blood target concentration (Ct) for induction was set at 4 µg/min and Fentanyl infusion was set at 3 µg/kg for 30 seconds , 2 µg/kg/h for 30 min, 1.5 µg/kg/h from 31-150 min, and 1 µg/kg/h until 30 min before end. Both propofol and fentanyl maintained with Navigator pharmacokinetic software and Entropy guidance. TED, urinary micro albuminurea (microalb), blood Glutathione-S-transferase (GST) were monitored.

Results: Extubation time prolonged with TCI vs. Des (15.2 ± 2.6 vs. 9.7 ± 1.5 min respectively, (P<0.05). Post-resection systemic vascular resistance (SVR) decreased significantly in both groups, but was better preserved with Des vs. TCI (836 ± 8 vs. 779 ± 36 dyn.sec.cm-5, P<0.01), this was reflected in higher mean blood pressure and stroke volumes (91 ± 3 vs. 81 ± 5 mmHg and 86 ± 3 ml vs. 78 ± 5 ml, respectively, P<0.01). Post-resection changes in GST and microalb were comparable between Des and TCI (GST: 441.0 ± 20.8 vs. 437.5 ± 22.2, IU/ml, P>0.05), (Microalb. 17.7 ± 2.5 vs. 18.64 ± 1.19, (µgm/ml) respectively, P>0.05). Des more economic than TCI (33.5 ± 8.2 vs. 69.1 ± 8.1 US Dollars), (P< 0.05) respectively during same surgical time and with comparable hemoglobin concentrations.

Conclusion: Recovery was enhanced better with Desflurane. TED monitoring demonstrated a significant preservation of SVR and MABP post-resection with Des vs. TCI. Neither was superior to the other with respect to liver and kidney functions. Further studies on a larger scale are recommended.

Keywords: Propofol; Desflurane; Cirrhosis; Liver resection; Transoesophageal doppler

Introduction

Hepatocellular carcinoma (HCC) is not uncommon in patients with chronic liver disease resulting from infection with hepatitis C virus (HCV) [1,2]. In Egypt, between 1993 and 2002, there was an almost twofold increase in HCC amongst chronic liver patients [3]. Liver resection improves overall survival in patients with small, non-invasive and non-metastatic tumors [3,4], but this surgery may be followed by clinical or subclinical hepatocellular derangements, metabolic, hemodynamic, coagulation and electrolyte changes due the temporary liver dysfunction frequently encountered in the immediate postoperative period [5-8] the anaesthetic technique and management should take this in consideration. Few studies were designed to address this issue in cirrhotic patients with use of the minimal invasive transoesophageal Doppler to monitor these perioperative haemodynamic changes [5]. Primary goal is to compare Target-controlled infusion of propofol-fentanyl versus desflurane based anesthesia for cirrhotic patients undergoing liver resection as regards recovery, hemodynamic parameters, hepatic and renal affection with a secondary goal to assess the economic impact.

Patients and Methods

Prospective hospital based randomized controlled study, written informed consent and Institutional Research and Ethics Committee approval from National Liver Institute, Menoufiya University, Egypt (12/2013) were obtained. The study was registered at the Cochrane research data base of South Africa (PACTR 201402000759256), (www.pactr.org).

Fifty adult cirrhotic (Child A) patients were admitted for major liver resection. They were categorized randomly (using the closed envelope technique) into two equal groups, to receive either intravenous Propofol/Fentanyl target controlled infusion (TCI) or inhalational Desflurane (Des) for general anesthesia maintenance.

Inclusion Criteria includes Written and informed consent, age 21

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years or older (Maximum age 73 years), scheduled for major elective liver resection and classified as Child A according to the Child-Pugh classification with no abnormal conventional coagulation test as International Normalization Ratio (INR) and Platelets count. Exclusion criteria includes; Esophageal disease, perioperative arrhythmia (frequent ectopic beats) or bleeding tendency, recent anesthesia (within 7 days before the resection surgery), history of allergic reactions to drugs, patients who bled profusely during their operation, who are hemodynamically unstable, or who need inotropic support or with preoperative renal dysfunction.

In Desflurane group (Des) Induction with fentanyl (1 mg/kg), propofol (2 mg/kg) and rocuronium (1 mg/kg). Endotracheal intubation and general anaesthesia maintained with a 1 l/min mixture of air, oxygen and Desflurane ($ETCO_2$ 32-36 mmHg). Anaesthesia depth maintained with Entropy (40-60). (Anaesthesia Work Station, General Electric, Helsinki, Finland).

In TCI group, Propofol venous blood target concentration (C_t) for induction of anesthesia was set at 4 μg/ml for the younger patients (less than fifty years) and 3 μg/ml for the elderly (more than fifty years). If anesthesia was not induced within 5 min, the C_t was increased sufficiently to complete the induction of anesthesia, when consciousness is lost, rocuronium 1mg/kg, was given and trachea was intubated. Fentanyl 3 μg/kg for 30 seconds prior to induction, followed by a continuous infusion of fentanyl 2 μg/kg/h for 30 min, 1.5 μg/kg/h from 31-150 min, and 1 μg/kg/h until 30 min before skin closure, both propofol and fentanyl were maintained with Navigator pharmacokinetic software (GE Healthcare Finland) and Entropy was kept (40-60). Syringe pumps were from Fresenius Orchestra Base Primea (Fresenius Kabi, France). If MAP or HR remained elevated after 5 min supplemental dose of fentanyl (0.5 μg/ kg) was given. Atropine 0.5 mg was given if heart rate drops below 45 beats/min.

Navigator Pharmocokinetic software (GE, Helsinki, Finland)

A software that collects data from the anesthesia machine, incorporated syringe pumps and monitoring system. This Pharmacokinetic/pharmacodynamic (PK/PD) model is used in conjugation with monitoring of hypnotic level of depth by spectral entropy, calculates appropriate drug doses and predicts the synergistic effects of the anaesthestic drugs with a feedback of brain electrical activity from the monitored and processed electroencephalogram (Entropy). Martorano et al. in a case study used the Navigator system to maintain adequate hypnosis and rapid recovery [9].

Transoesophageal Doppler (TED)

A cardiac output (CO) monitor (Deltex Medical, chichester, UK) with a continuous, beat to beat, minimally invasive CO monitor measuring blood flow velocity in the descending aorta by an oesophageal Doppler probe passed nasaly into the mid-oesophagus till aortic blood flow signals were identified [10-13].

TED Parameters includes Corrected Flow Time (FTc) which is the time needed for blood to flow in a forward direction within the aorta during systole corrected for heart rate (330-360 ms), Stroke volume (SV); Volume of blood ejected from left ventricle/beat (50-100 cc/beat), Cardiac output (COP) (4-8 l/min) and Systemic vascular resistance (SVR) (1900-2400 dynes.sec/cm) [5].

In both groups a left sided radial arterial catheter (A-line) was inserted for each patient to for blood sampling and for direct measurement of arterial blood pressure. The central venous catheter was inserted through the right internal jugular approach with ultrasound guidance to increase patients' safety (Sonosite, Nanomex, UK). The central venous catheter was connected to a pressure transducer, and the pressure trace displayed continuous on a monitor perioperatively. Replacement of intraoperative fluid loss (colloid) was guided by an algorithm depending on the Doppler estimations of stroke volume and FTc. This algorithm was similar to that used by Sinclair et al. [14] Post-resection 200-ml of 6% hydroxyethyl starch in saline (6% HES 130/0.4 Voluven; Fresenius-Kabi, Bad Homburg, Germany) was given when the FTc reached less than 0.35 s. The procedure was started immediately after probe placement and continued until maximum stroke volume and targeted FTc values had been reached.

Ringer acetate in both groups was infused intraoperatively at approximately constant rate (6 mL/kg/hr) to cover fluid deficit and basal fluid requirements, later postoperatively in the intensive care unit to keep CVP between 6-10 mmHg and maintain urine output at 1 ml/kg/hour. (TED was removed with extubation)

Blood products

Packed red blood cells (300 ml) were transfused when Haematocrite percentage (Hct) was <25 %. Fresh frozen plasma (unit of 200 ml) was administrated when aPTT>70 s, fibrinogen was <2 g/dl, or International Normalized Ratio (INR) >2. Rotational thrombo elastometry is available but only used to guide blood transfusion during severe bleeding or coagulopathy. Hemodynamic parameters were monitored continuously and recorded before induction (t0), immediately after induction, before intubation (t1), 15 min after the intubation (t2), during dissection (liver mobilisation) (t3), during hepatic resection (t4), post resection near end of surgery (t5), 24 hours postoperatively (t6) (when applicable) and 48 hours postoperatively (t7) (when applicable). Laboratory investigations: liver function tests Glutathion-S-transferase (GST), (IU/ml); kidney functions tests will include serum urea and creatinine (mg/dl) and microalbumin in urine (μgm/ml), metabolic parameters and electrolytes. Laborartory samples collected preoperatively, immediate postoperatively (post-resection) and 48 hours postoperatively.

Serum GST is measured by Cayman's Glutathione -S-transferase Assay Kit item No 703302. Cayman Chemical Company, USA (Reference range 0.01-0.03 IU/ml in healthy individuals).

Microalbumin is measured by DRG Microalbumin enzyme linked immunosorbent assay ELISA (EIA-3881). (DRG International Inc., USA) (Reference range in urine 0-25 microgram/ml Albumin).

Total amount of inhalational agent in (ml) used intraoperatively was calculated automatically by using the Aisys GE Healthcare Finland (Datex-Ohmeda, Helsinki, Finland) anaesthesia machine and then recorded.

Amount of propofol used in TCI group was also recorded. The anesthetic costs were calculated according to the latest British National Formula announced prices.

Statistics methodology

Double-blinded randomized controlled comparative study. Classification of the Methods of Blinding: participants (level 1), health care providers (level 2), and the main outcome assessor (level 3). In the present study blindness was only carried out for participants (level 1) and the main outcome assessor (level 3).

Sample size and power of the study

The sample size of patients was determined by power analysis (α=0.05, β=0.80), which showed that 25 patients would be required in each group to reveal a significant difference in recovery extubation time (min) between the two groups after discontinuation of the inhaled agent. This was based on a previous study, [15] which showed a mean difference of 10 and 9.7 min and standard deviation of 4.6 min and 6.5 min in desflurane and TCI groups respectively.Calculation was performed using MedCalc software version 9.2.0.0. Calculation of sample size was done using (IBM SPSS Sample power) software and was also confirmed using Lenth Java Applets for Power and Sample Size [Computer software] [16]. Data were collected and entered to the computer using SPSS (Statistical Package for Social Science) program for statistical analysis. Kolmogorov-Smirnova test was carried out and revealed no significance in the distribution of variables, all variables included were normally distributed and parametric statistics was carried out.

Descriptive statistics data include the minimum and maximum, range, mean, standard deviation, median and inter-quartile range for each variable. Comparisons were carried out between the two studied groups using independent t test (t test). Box and Whiskers graph was done. Chi- square test and fisher exact test were used to measure association between qualitative variables. Correction of p value for multiple testing was set p to 0.01 to detect significance (Bonforroni correction of multiple comparisons). In the present study an alpha level was set to 1% with a significance level of 99%, and a beta error accepted up to 20% with a power of study of 80%.

Results

Fifty five patients undergoing major liver resection at the Liver Institute, Menoufiya University, Egypt (Hepato-pancreatico surgery specialized tertiary referral hospital) were enrolled during a period of 8 month.

Five patients were excluded intra-operatively due to extension of the tumor beyond the surgical treatment and the procedure was terminated. Fifty patients were only included, randomized and equally divided into two groups. Their perioperative data were recorded and stored in a computerized Excel sheet for later statistical analysis. Patient characteristics in Desflurane (n=25) versus TCI Propofol/Fentanyl (TCI) (n=25) were comparable regarding age (53.61+10.48 vs. 55.24+12.11 years, P=0.62), and weight (76.48+10.33 vs. 79.72+9.02 kg, P=0.24). Male/female ratio was 18/7 in Des group and 24/1 in TCI group, X2=6.64, P=0.01, data presented in Table 1.

The extubation time was prolonged in TCI group in comparison to the Des group (15.2 ± 2.6 vs. 9.7 ± 1.5 min, (P<0.01). TED monitoring revealed a significant reduction in systemic vascular resistance (SVR) post-resection in both groups with least reduction in Des vs. TCI (836 ± 8 vs. 779 ± 36 dyn.sec.cm^{-5}, P<0.01), (Figure 1), this was associated with a better mean arterial blood pressure and stroke volumes for Des versus TCI (91 ± 3 vs. 81 ± 5 mmHg and 86 ± 3 ml vs. 78 ± 5 ml, respectively, P<0.01) (Figures 2 and 3). Heart rates increased in both groups post-resection with an associated increase in stroke volume with Desflurane only.

Blood loss in Des group was 578.2 ± 79.72 ml and in TCI group was 583.2 ± 77.28 ml with no significant difference between both groups, P>0.05. Blood transfusion requirements between both groups were comparable, 2 packed red blood cells units (PRBCs) were transfused for 3 patients in the Desflurane group and 4 in TCI group. No fresh frozen plasma was required during the course of the surgery for both groups.

Variables	Groups	Mean ± SD	t- test	*P*- value
Intraop Crystalloid (ml)	TCI DES	2772 ± 703.87 2990 ± 391.84	1.353	0.184 NS
Intraop UOP (ml/hr)	TCI DES	121.92 ± 11.6 124.72 ± 11.8	0.843	0.403NS
Extubation time (minutes)	TCI DES	15.20 ± 2.629 9.76 ± 1.507	8.972	0.000*
ICU stay (days)	TCI DES	1.60 ± 0.50 1.44 ± 0.51	1.124	0.267NS
Hospital stay (days)	TCI DES	6.12 ± 1.129 6.08 ± 1.077	0.128	0.899NS
Anaesth time (min)	TCI DES	222.60 ± 10.42 220 ± 26.496	0.457	0.651NS
Anaesth. cost (US Dollars)	TCI DES	62.65 ± 8.233 33.70 ± 3.836	15.95	0.000*

All data presented as mean ± standard deviation. TCI: Target Controlled Infusion; Des: Desflurane; Inrtraop: Intraoperative; UOP: Urine Out Put; ICU: Intensive Care Unit; *significance compared with the other group (P<0.01)

Table 1: Perioperative surgical and anaesthetic data.

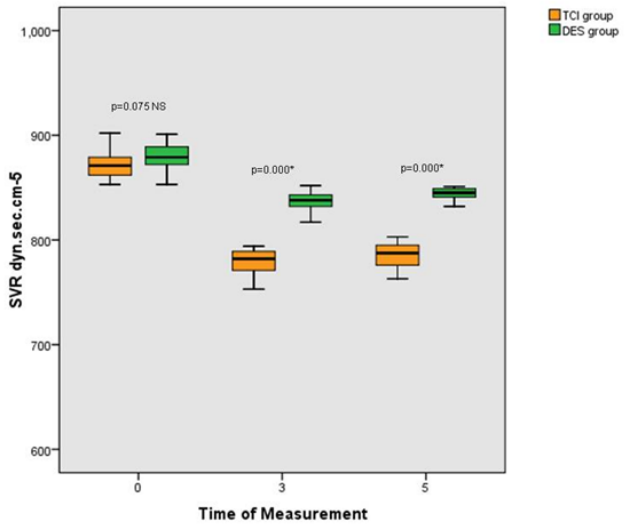

Figure 1: Box and Whisker plot of SVR expressed as minimum, maximum, median (line within the box) and 25th and 75th percentiles (error bars).TCI: Target Control Propofol/Fentanyl Infusion; DES: Desflurane. T0:15 min after intubation; T3: during dissection and T5: near end of the surgery. Comparisons with independent t test (t test). Significant changes over time within each group with Repeated measures ANOVA. P<0.01.

Both groups demonstrated comparable and stable central venous pressure (CVP) and corrected flow time (FTc) during the procedure (Figures 4 and 5). No significant difference in intraoperative crystalloids (Ringer's Acetate) consumption between Des and TCI groups (2990+391.8 vs. 2772+703.8 ml, P=0.184, respectively). This was reflected in the mean intraoperative hourly urinary output which demonstrated no statistically significant difference between the Des and the TCI groups (124.7+11.8 vs. 121.9+11.6 ml/hr, P=0.40, respectively). The volume of the colloids administered (HES) in Des group in mean ± SD (1194 ± 130.95 ml) versus TCI group (1176 ± 130.79), this difference was not found to be statistically significant, P=0.62.

No significant statistical correlation was detected between CVP and FTc values at different measuring time points. T1:10 min after induction of anesthesia, (r=−0.17, P=0.49). T2: During resection of the

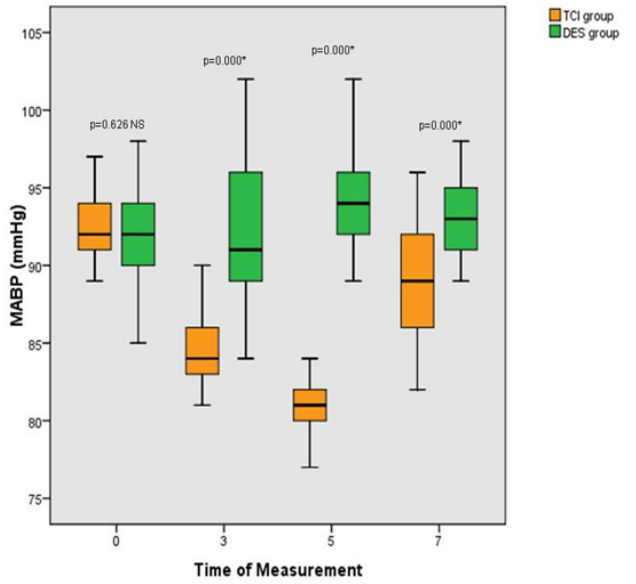

Figure 2: Box and Whisker plot of MABP in TCI group and Des group in patients undergoing hepatic resection. Result is expressed as minimum, maximum, median (line within the box) and 25th and 75th percentiles (error bars) are shown at selected time points. TCI: Target Control Prpopofol/Fentanyl Infusion; DES: Desflurane;T0: before induction; T3: during dissection; T5: near end of surgery; T7: 48hours postoperatively. *P*<0.01considered significant.

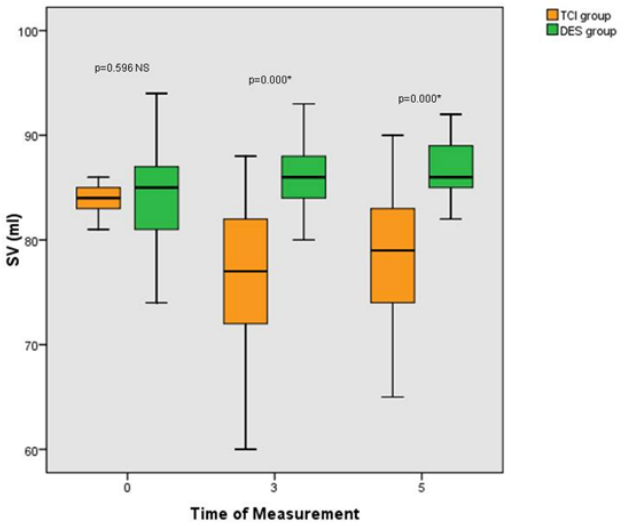

Figure 3: Box and Whisker plot of Stroke volume (SV) in TCI group and Des group in patients undergoing hepatic resection. Result is expressed as minimum, maximum, median (line within the box) and 25th and 75th percentiles (error bars) are shown at selected time points.TCI: Target Control Prpopofol/ Fentanyl Infusion; DES, Desflurane. T0: 15 min after intubation; T3: during dissection and T5: near the end of surgery. *P*<0.01 considered significant.

tumor with no Pringle maneuver, (r=0.244, P=0.31). T3: Immediately after right hepatectomy, (r=−0.075, P=0.76) T4: At the end of surgery, (r=0.356, P=0.14). T5: 24 h after surgery, (r=0.090, P=0.71). ALT and AST peaked in both groups post resection, Des. 378 ± 8 and 407 ± 3 U/L, TCI 467 ± 38 and 413 ± 39 U/L respectively, this increase was less in Des group P<0.05. No significant difference between Des and TCI regarding both GST and urinary microalbumin (Microalb) post resection (GST: 441.0 ± 20.8 vs. 437.5 ± 22.2, IU/ml, P>0.05 and urinary microalbminuria. 17.7 ± 2.5 vs. 18.64 ± 1.19 µgm/ml, respectively, P>0.05) (Table 2).

The intraoperative administration of fentanyl (guided with processed EEG, Entropy) in Desflurane group was 370 ± 100 micrograms, which was significantly less than fentanyl consumed within the TCI Propofol/Fentanyl group (Figure 5).

The ICU/hospital stay were comparable between both groups

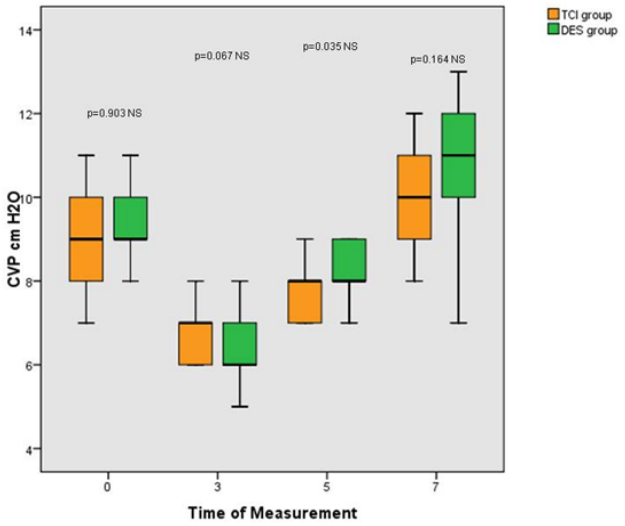

Figure 4: Box and Whisker plot of CVP in TCI group and Des group in patients undergoing hepatic resection. Results expressed as minimum, maximum, median (line within the box) and 25th and 75th percentiles (error bars) are shown at selected time points.TCI: Target Control Prpopofol/ Fentanyl Infusion; DES, Desflurane. T0: before induction; T3: during dissection; T5: near the end of surgery; T7: 48hours postoperatively. *P*<0.01 considered significant.

Variables	Time	Mean ± SD	
		TCI	Des
AST (U/L)	T1	37.68 ± 6.073	36.32 ± 2.64
	T2	413.52 ± 39.68	407.32 ± 35.68
	T3	148.32 ± 17.21	147.64 ± 12.43
ALT (U/L)	T1	43.88 ± 9.820	43.36 ± 5.50
	T2	467.24 ± 38.07	378.68 ± 80.33*
	T3	205.32 ± 39.31	154.24 ± 14.62*
INR	T1	1.13 ± 0.022	1.12 ± 0.033
	T2	1.19 ± 0.025	1.18 ± 0.017
	T3	1.25 ± 0.020	1.26 ± 0.050
GST (IU/ml)	T1	0.029 ± 0.0013	0.029 ± 0.001
	T2	0.044 ± 0.002	0.043 ± 0.002
	T3	0.031 ± 0.001	0.031 ± 0.001
Urea (mg/dL)	T1	34.68 ± 2.478	34.24 ± 1.562
	T2	32.20 ± 2.000	31.00 ± 2.020
	T3	31.96 ± 2.730	31.36 ± 1.976
Creatinine (mg/dL)	T1	1.36 ± 0.11	1.30 ± 0.093
	T2	1.30 ± 0.16	1.28 ± 0.200
	T3	1.38 ± 0.10	1.30 ± 0.144
Microalbumin (µgm/ml)	T1	19.16 ± 1.74	18.40 ± 2.62
	T2	18.08 ± 1.60	17.32 ± 2.15
	T3	18.64 ± 1.18	17.76 ± 2.57

Table 2: Laboratory investigations. T1; preoperative; T2; post-resection, T3; 48 hour postoperatively; TCI; Target Controlled Infusion; Des: Desflurane; AST: Aspartate aminotransferase; ALT: Alanine amininotransferase; INR: International Normalized Ratio; GST: Glutathion S transferase; *significance with other group; (*P*<0.01).

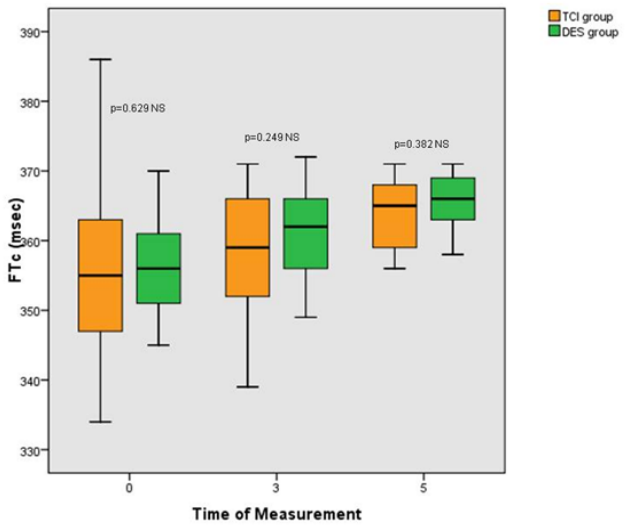

Figure 5: Box and Whisker plot of Transoesophageal Doppler corrected flow time (FTc) in TCI group and Des group in patients undergoing hepatic resection. Results are expressed as minimum, maximum, median (line within the box) and 25th and 75th percentiles (error bars) are shown at selected time points. TCI, Target control Prpopofol/Fentanyl Infusion; DES: Desflurane. T0:15 min after intubation; T3: during dissection and T5: near end of surgery.

(Des 1.5 ± 0.5 vs TCI 1.6 ± 0.5 and 6.4 ± 1.5 vs 6.8 ± 1.6 days, $P>0.05$, respectively). Des was more economic intraoperatively than TCI 33.5 ± 8.2 vs 69.1 ± 8.1 US Dollars ($P<0.05$) respectively during same surgical time and with the same surgical team (Table 1).

Discussion

Recovery after administration of continuous intravenous anaesthetic and sedative drugs in cirrhotic patients for several hours can lead to accumulation of these drugs and an unpredictable recovery. In TCI Propofol/Fentanyl group, this was overcome by using syringe pumps integrated with this model of Navigator system (pharmacokinetic/pharmacodynamic (PK/PD) model) coupled with monitoring of hypnosis depth by spectral entropy. Despite all methods used, the extubation time was still more prolonged in TCI group than in Des group, this may be due to the relatively larger doses of fentanyl used in this group and secondly to the peculiar nature of Desflurane which enjoy a low blood/gas solubility coefficient and low metabolic rate which can reach to 0.02% of administered Desflurane. Lendvay et al., reported faster recovery with Desflurane anesthesia when compared with other total intravenous anesthesia [17] similar to our study, may be because fentanyl in our study not remifentanyl which is known to have a remarkable shorter duration of action was used.

Hemodynamic results were in favour with Desflurane compared to TCI Propofol/Fentanyl; this could be attributed to the better preservation of the systemic vascular resistance with desflurane when used to maintain the general anaesthetic status in contrast to propofol. Cirrhotic patients are known to be peripherally vasodilated as a result of their liver disease [18] which necessitates the use of an anaesthetic technique with the least effect on their vascular tone. Propofol/Fentanyl infusion resulted in a sustained decrease in SVR due to its peripheral vasodilating effect and this was associated with a decrease in MABP

In a previous study by Sharkawy et al. [5] designed to monitor the haemodynamic changes among cirrhotic patients undergoing liver resection with Transoesophageal Doppler (TED), the authors were able to present data demonstrating significant haemodynamic changes that associate liver resection procedure, particularly in the immediate post-resection. Reporting an increase in SV and cardiac output as monitored by TED, together with an associated decrease in calculated SVR despite stable and normal readings of both central venous pressure (CVP) and corrected flow time (FTc).

The present study demonstrated similar changes in SVR but with stroke volume increase only demonstrated with Desflurane. Similar changes were previously described also by Niemunn et al. in patients with healthy livers undergoing the same procedure (major hepatic resection) for living donor liver transplantation with inhalation anaesthetic agent [19]. In Neimunn et al. study they had to inject Indocyanine green and measure plasma levels with a pulse dye densitometry, not usually available in the operating theaters and which is still considered as a research tool. In contrast to the TED used in this current study which is easy to use and less invasive and could be available in operating suites.

These haemodynamic changes after hepatotomy could be due to the possible reduction in portal blood flow [20] or to the release of various splanchnic mediators such as endotoxin, during liver surgery [21] and changes in the levels of nitric oxide, a potent vasodilator, which could be elevated in response to endotoxin and cytokine release [22]. Boermeester et al. found that these haemodynamic changes improved after the administration of endotoxin-neutralizing protein [23].

This current study also revealed that the two anaesthetic methods used were tolerated well by the kidneys as there were no serious changes in urea, creatinine and urinary microalbumin levels observed. Desflurane in particular is expected to have the least effect towards the renal functions due to its very little degradation and minimal excretion of organic or inorganic fluoride [24-27].

On the other side the effects of TCI with propofol-fentanyl on perioperative hepatic and renal functions appear from our results to be relative safe for both liver and kidney functions provided that haemodynamic stability pertains and their hepatic and renal blood flows are intact. Liver is known to be involved in the extensive biotransformation and metabolism of propofol and kidneys are known to help in the elimination of the propofol metabolites [28].

Disruption in hepatocellular integrity was reported after general anaesthesia with all modern inhalation anaesthetics. In these studies, GST was used to determine the degree of hepatocellular injury; GST is more sensitive than the other conventional hepatic enzymes as it is rapidly released into circulation after hepatocellular injury [29-31]. The changes in GST concentrations observed in our study in both groups reflects a minor derangement of hepatocellular integrity due to combined effect of anaesthesia and surgical stress, together with injury to the liver cells during excision of the tumor.

AST and ALT present in hepatocytes can leak into the blood during the resection process. Suttner et al. study [32] and Justin Sang Ko et al. [32,33] were able to demonstrate minimal effects when patients in both studies were exposed to Desflurane. In Suttner et al. study the patients were elderly patients undergoing non-hepatic surgery and in the second study by Ko et al. the patients enrolled in his study where healthy donors undergo liver resection for living liver transplantation donation. Few studies monitored the effect of Desflurane in cirrhotic patients undergoing liver resection. Tao et al. study [34] is one of these studies among cirrhotic patients, they stated that hepatic inflow occlusion during the liver surgery may result in a transient ischemia

period followed by reperfusion, and may initiate liver injury. Especially in cirrhotic patients, the tolerance time of ischemia is much shorter and the outcome would be worse. In our study and in contrast to Tao et al. [34] study we were able to perform all the liver resections with no occlusion of the hepatic and portal blood flow (Pringle Maneuver) which could explain in part why there was no difference between inhalational anaesthetics represented in Desflurane and other techniques as total intravenous anaesthesia when both techniques were able to maintain hepatic blood flow to the liver cells by maintaining a haemodynamic status of stability throughout the procedure. It is not only the anaesthetic choice that plays an important role in reducing the liver dysfunction but the surgical technique adpoted by the surgeons also plays an important role together with haemodynmic stability. Our results support the importance of a combined and mutual understanding between the Anaesthesia management and the adopted surgical technique to achieve the appropriate level of protection to both the liver and kidneys. Avoiding the Pringle maneuver during the surgical procedure (i.e no ischemic reperfusion injury) and the preservation of the middle hepatic vein in all the patients contributed to minimal perioperative blood transfusion due to the reduced liver maneuvers required during dissection. This lead to no haemodynamic supportive therapy being used and allowed for the use of less invasive techniques for monitoring as the Transoesophageal doppler adopted in the current study. Selective vascular occlusion of hepatic inflow was not adopted by the surgeons in our study, but instead the anterior parenchymal resection was used and this technique did not require significant reduction in the CVP. An average of 6 to 7 mmHg was adequate particularly in cirrhotic patients with no reported haemodynamic instability [5,35,36].

Economically, the current study reported around 40% higher costs in TCI Propofol/Fentanyl group compared to Desflurane group and this could be due to the low flow circuit used for Desflurane administration and the high dose of propofol/fentanyl used. Lendvay et al. [17] also reported 30% higher costs with total intravenous anaesthesia when compared to Desflurane group.

Limitations of the study could be summarized in the number of the patients involved, this may be attributed to the restricted inclusion of only major liver resection procedures performed for cirrhotic patients.

Another limitation observed when the liver was mobilized during resection of hepatic tumors was the frequent requirement to reposition the Doppler probe. The patient exclude from the study due to inoperability of the tumor could be an example, The patient required frequent maneuvers and mobilization of the liver, this repeatedly affect the TED probe position and hence readings. This can be considered as an important weak point in the TED monitoring system which needs frequent attention from the attending anesthetist.

Another TED limitation was the inability to continue monitoring with the TED post-extubation unless it is inserted nasally which could be uncomfortable with a nasogastric tube in place as well. TED traces on the monitor were also affected by the periods of Diathermy interference.

In conclusion and based on the results of this current study, Desflurane was able to preserve better the hemodynamic parameters as systemic vascular resistance and mean arterial blood pressure than TCI Propofol-Fentanyl in cirrhotic patients undergoing major hepatic resections and to enhance recovery with reduced costs, but neither was superior to the other in respect to their effects on liver and kidneys.

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