DISCUSSION

Haemodynamics

The present study results demonstrated favorable haemodynamic stability with Des group versus TCI group; this could be attributed to the better preservation of the systemic vascular resistance when desflurane was 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,[142] which necessitates the use of an anaesthetic technique that maintains their vascular tone or minimizes the effect that a general anaesthestic imposes on their vascular tone. This was in favor of Desflurane, as Propofol/Fentanyl infusion resulted in a sustained decrease in SVR due to its peripheral vasodilating effect, this was associated with a decrease in MABP and SV in an already peripherally vasodilated cirrhotic patients.

In a study by El 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 in their results demonstrating significant haemodynamic changes that associate the procedure of liver resection itself, particularly in the immediate post-resection, this was similar to our findings. The use of transoesophageal Doppler (TED) was also able to demonstrate significant haemodynamic changes that could be summarized in a post-resection increase of SV and cardiac output together with an associated decrease in SVR despite stable and normal readings of both central venous pressure (CVP) and the corrected flow time (FTc), a Doppler parameter reflecting volume status.

Similar changes in cardiac output (COP) were previously described also by Niemunn et al.[6] in patients with healthy livers undergoing the same procedure (major hepatic resection) for living donor liver transplantation. In Neimunn et al.[6] 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 our study which could be available in operating suites and intensive care units and which is easy to use and less invasive.

These significant haemodynamic changes after hepatotomy in the present study observed in both groups could be explained by the possible reduction in portal blood flow[143] or to the release of various splanchnic mediators such as endotoxin, during liver surgery[144] and changes in the levels of nitric oxide, a potent vasodilator, which could be elevated in response to endotoxin and cytokine release.[145]

Boermeester et al.[146] found that these haemodynamic changes improved after the administration of endotoxin‑neutralizing protein.

These significant finding implicates that the anaesthetic agent used should not worsen the already lower SVR known to exist in hepatic patients and which will also decrease further as a consequent of the liver resection, Desflurane as shown in our results exerted a minimal effect on SVR.

Hepatic and renal functions:

The present study revealed also that the two anaesthetic techniques can be tolerated well by the kidneys, there is was no serious changes in urea, creatinine and urinary micro albumin levels observed , all where within a normally accepted ranges during surgery and in the immediate postoperative course**.** Desflurane in particular is expected to have the least effect towards the renal function as Desflurane is known among all the class of volatile anaesthetics agents for it's very little degradation and minimal excretion of organic or inorganic fluoride. In patients with renal dysfunction Desflurane can maintain the renal blood flow and renal functions even after prolonged exposure.(146;147)

Liver is known to be involved in the extensive biotransformation and metabolism of propofol. The kidneys are known to help in the elimination of the propofol metabolites which appears to have no pharmacological activity, hence continuous infusion of propofol during surgery can be affected by any hepatic and/or renal dysfunctions.(148)

On the other side the effects of TCI with propofol-fentanyl on perioperative hepatic and renal functions appears from our results to be relative safe for both liver and kidney functions provided that haemodynamic stability pertains. Propofol should not have a negative impact on hepatic and renal functions as long as hepatic and renal blood flows are intact and the patient is not subjected to episodes of hypotension peri-operatively as demonstrated in the results section.

The use of continuous cardiovascular monitoring and the guided fluid management with the corrected flow time parameter of the transoesophageal Doppler helped to establish a status of haemodynamic stability together with the new advances in the surgical dissection of the liver, which lead to a reduction in blood transfusion requirements as demonstrated from the results of in this current study.

Central venous monitoring during the liver resection procedure might not be reliable. The pressure of the retractors on the diaphragm and mobilization of the liver can compress the portal vein and vena cava reducing venous return and lowering CVP. Compression of the liver can release a significant quantity of blood. A review of 30 living donors who underwent a right or left hepatectomy for a transplant found no correlation between maintaining a low CVP and blood loss. The average CVP in their study was 7.7 ± 2.8 cm H2O which is similar to the present study. According to the authors of the above mentioned study, maintaining a low CVP is desirable (but not essential) to reduce hepatic venous bleeding and improve haemostatic control during resection. Meticulous surgical haemostasis appears to be more important.(149) The results of the present study agrees with the fact that surgical technique used in resection plays an important role in reducing blood loss and that despite CVP in the present study was between 6-7 mmHg, the blood loss was kept to the minimal with no blood transfusion required. Careful surgical technique of anterior parenchymal transection with Cavitron Ultrasonic Surgical Aspirator (CUSA), bipolar electrocautery, harmonic scalpel and Habib sealer). are important contributers in reducing blood loss, in addition to the improvement in the learning curve of surgeons working in high flow liver centers

Symrniotis et al.(150) studied in 2005 the various techniques of vascular control and maintenance of a low central vein pressure (CVP) used in order to prevent intraoperative blood loss and postoperative complications and came to the conclusion that the Pringle

maneuver if used should be accompanied with a CVP 5 mm Hg or less and that the selective vascular clamping should be used whenever CVP remains high despite adequate anaesthetic management. Both techniques were not adopted by the surgeons in the present study but instead the advanced developments in surgical techniques of liver dissection and resection were used in all patients included in the study. 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 in which keeping an adequate filling pressure is important for other vital organ perfusion.(5;58;149)

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 during and after resection by the anaesthetic team as the use of a transoesophageal doppler adopted in the present study.

Disruption in hepatocellular integrity was reported after general anaesthesia with all modern inhalation anaesthetics.(98) In these studies, GST a more specific marker was used to determine the degree of hepatocellular injury, GST is more sensitive than the other conventional hepatic enzymes. Advantages of using GST in the detection of hepatocellular injury includes its low molecular weight (51 kDa), high cytosolic concentration (4%–5% of all hepatocellular protein) and short half-life in blood (<90 min). Since GST is rapidly released into circulation after hepatocellular injury, it can be used as a rapid marker for any changes in hepatocellular integrity.(151) The changes in GST concentrations observed in the present study in both groups reflects a minor derangement of hepatocellular integrity due to combined effect of the surgical stress and injury to the liver cells during excision of the tumor and part of the surrounding liver tissue and also to the exposure to the general anaesthesia agents.

Arslan et al.(136) reported that, under Desflurane anaesthesia, GST peaked during the first postoperative day then start to decrease later on, they also reported no significant increase in GST and conventional liver enzymes as Aspartate aminotransferase (AST) and Alanine amino-transferase (ALT) with the use of Desflurane in non-hepatic surgeries.

AST and ALT are enzymes present in hepatocytes can leak into the blood during the resection process and the surgical interference with the liver cells integrity. Suttner et al.(152) study and Ko et al.(153) were able to demonstrate minimal effects when patients in both studies were exposed to Desflurane. In Suttner et al.(152) study the patients were elderly patients undergoing non-hepatic surgery and in the second study by Ko et al.(153) 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 (154) study is one of these studies among cirrhotic patients, they stated in their discussion of their results that hepatic inflow occlusion during the liver surgery may result in a transient ischemia period followed by reperfusion, and may initiate liver injury and lead to postoperative liver dysfunction. Especially in cirrhotic patients, the tolerance time of ischemia is much shorter and the outcome would be worse. Hence they conclude that the anti-ischaemic reperfusion injury

characteristics, of the volatile anaesthetics might be a more appropriate choice in cirrhotic patients undergoing liver surgery when vascular occlusion is adopted by the surgeons.

In the present study and in contrast to Tao et al.[154] 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. This could further explain why we experienced minimal effects on the liver enzymes post-resection. It is not only the anaesthetic choice that plays an important role in reducing the liver dysfunction but the surgical technique adopted by the surgeons also plays an important role together with haemodynamic 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 as it is multifactorial.

Recovery

Administration of intravenous anaesthetic drugs in cirrhotic patients several hours can accumulate and could lead to unpredictable recovery. In TCI Propofol/ Fentanyl group, this was overcome by using syringe pumps integrated with the model of Navigator system from GE (pharmacokinetic/pharmacodynamic (PK/PD) model) coupled with monitoring of hypnosis depth by spectral entropy. This lead to the titration of the intravenous drugs administration based on previous calculations of the predicted synergistic effects of the two drugs and on the feedback of the processed electroencephalogram activity in the form of Entropy value which was kept between 40-60. Despite all methods used above to improve recovery and avoid any unnecessary administration of anaesthetic agents that can have an effect on recovery. The extubation time was 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,[155] reported faster recovery with Desflurane anaesthesia when compared with other total intravenous anaesthesia,but this was not coinciding with the study reported by Ko et al,[153] in which they reported prolonged anaesthetic time with Des group compared with TCI group may be because fentanyl used in the present study was replaced with remifentanil in their study which is known to have a remarkable shorter duration of action.

Economic costs

In the present study, we 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.[155] also reported 30% higher costs with total intravenous anaesthesia when compared to Desflurane group.

Limitations of the study could be summarized in the limited number of the patient population involved, this may be attributed to the restricted inclusion of only 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 excluded 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 consider as an important weak point in the TED monitoring system which needs frequent attention from the attending anaesthetist.

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

Finally in TCI group, another limitation to the study was that fentanyl was infused at a fixed rate and was not monitored by the TCI technology with the ability to alter the infusion rate .

In conclusion and based on the results of the present study, Desflurane could be a more appropriate choice than TCI Propofol-Fentanyl in cirrhotic patients undergoing major hepatic resections from haemodynamic prospective, recovery and costs, but neither is superior to the other with respect to their effects on liver and kidneys.