Research Article

Entropy monitoring effect in hepatic cirrhotic patients undergoing major liver resection on sevoflurane consumption and hemodynamics. A randomized controlled study

Abstract

Background and Goal of study: Inappropriate titration of the anesthetic agents can lead to an under or excessive depth of anesthesia. Aim is to study effect of introducing Entropy monitoring during major liver resection among cirrhotic patients with chronic hepatitis C (Child A) undergoing major liver resection on general anesthetic requirements and hemodynamics.

Methods: 60 consecutive patients were randomly divided into two groups in a prospective hospital based comparative study registered in Menoufiya University, Egypt. Group I guided with Entropy, Group II also guided with standard practice but obscured from Anaethesist. Sevoflurane with O_2 /Air 50% at 2 l/min adjusted to achieve a State (SE) and Response (RE) Entropy (40-60 with a gradient of 5-10. Boluses of Fentanyl (1 - 2 µg/kg) were given if the difference between SE and RE was more than 10 for more than two minutes. Sevoflurane (ml) consumed were monitored by GE Datex-Ohemda S/5 Anesthetic Delivery Unit System.

Results: Age, weight and fentanyl consumption were comparable between both groups (P>0.05). Mean (SD) Sevoflourane consumption (ml) after 2hr, 4hr, and 6hr in GI (Entropy) versus II (Standard) were 16(2.19) vs 20.8(1.88), 10.7(1.94) vs 17.4(1.92), and 9(1.22) vs 14.1(2.19), P<0.01. Reduced end tidal sevoflourane (%) in G I (Entropy) vs GII after 2hr and 4hr (1.4 (0.12) vs 1.6 (0.07) and 1.4 (0.11) vs 1.6 (0.07). Total sevoflurane consumped was reduced by 31% in G I (Entropy) when compared with GII (Standard Practice). The Propofol induction dose with entropy was also lower (GI, 156.6+22.2 mg vs G II, 184.6+15 mg, P<0.05). An increase in anesthesia depth was observed in patients not monitored by Entropy in G II vs GI, repectively. SE after 2hr of anesthesia was 47 (4.44) vs 54 (6.58). RE after 2hr was 48(4.38) vs 53(6.96). Mean arterial pressure was reported to be higher in GI (Entropy) compared to GII during surgery. Extubation time and intensive care stay was shorter with Entropy (GI, 4.52±2 vs GII, 7.72±2 min, P <0.01) and (1.40±0.50 vs 1.64±0.48, days P=0.09) respectively. Blood loss (ml) in GI 567.22±70.72 vs GII 571.2±72.28, P>0.05. Anaesthesia time was comparable between both groups with the same surgical and an aesthetic team.

Conclusion: Entropy monitoring for hepatic patients reduced general anaesthetic agent consumption during induction and surgery and enhanced recovery with favourable haemodynamic consequences. Encouraging the use of Anaesthesia depth monitors can have an important economic impact when applied on a larger scale.

Keywords: anaesthesia depth, liver resection, cirrhotics

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Introduction

Liver cirrhosis is a progressive disease characterized by loss of functional hepatocytes with concomitant connective tissue and nodule formation in the liver. The morphological and physiological changes associated with the disease substantially affect drug pharmacokinetics.[1] Liver resection is the surgical removal of a part of the liver and it is a major lengthy operation with greater risk of hemodynamic instability during surgery.[2,3] In these patients, lower levels of anaesthetic are often used to prevent adverse effects on the cardiovascular system and these levels can be inadequate so; unintended intraoperative awareness may be unavoidable to achieve other critically important anaesthetic goals.[4] Anaesthesia is a balance between the amount of the anesthetic drugs administered and the state of arousal of the patient which can vary throughout surgery with different metabolic and hemodynamic circumstances. Inappropriate titration of the anesthetic agents can lead to an under or excessive depth of anesthesia (DOA) which might compromise patient outcome in particular those with co-existing medical disease.[5,6] The traditional signs for light anesthesia such as hypertension, tachycardia and lacrimation are unreliable indicators of the anesthetic depth.[7]

Processed electroencephalogram (EEG) as Entropy can monitor the depth of anesthesia and hypnosis level. Liver cirrhosis leads to a reduction in liver mass and hepatic blood flow with an effect on drug clearance and cardiovascular stability. Entropy monitoring allows for the quantification of cerebral neural activity. The increase and decrease in entropy scores are related to the level of consciousness under anesthesia. EEG entropy is a monitor based on EEG analysis used in measuring hypnosis levels. EEG-entropy has two measurements:

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State entropy (SE) receives information from the brain waves and response entropy (RE) incorporates information from the frontal electromyography. SE is computed using EEG data from the previous 15 s, between 0.8 and 32 Hz, and shows the value in the range of 0–91. RE is computed from 32 to 47 Hz with 1.92 s, and reflects fast muscular activity from the frontal muscle, and shows the value in the range of 0–100.[8–10]

An EEG signal measured with frontal electrodes includes a significant electromyographic (EMG) component originating from facial muscle activity.[11] While the lower frequencies (up to about 32 Hz) contain predominantly EEG signals, EEG power decreases exponentially at higher frequencies. In contrast, the EMG has a wide noise like spectrum and dominates at frequencies higher than 32 Hz. While EMG activity normally is treated like an artefact, the M-Entropy module claims to separate out both EEG and EMG activity and generates two distinct numbers, the state entropy and the response entropy.[11]

RE becomes equal to SE when the EMG power is equal to zero, as the RE–SE-difference might then serve as an indicator for EMG activation. SE should provide a measure of the current cortical state of the patient. RE by reflecting EMG activity is thought to be an indirect measure of adequacy of analgesia, since EMG activity may increase as a result of intensive nociceptive stimulation and during decreasing levels of anesthesia. Patients with liver disease carry a risk of peri-operative morbidity and mortality related to the extent of their liver dysfunction.[12,13] In patients with compromised liver function preservation of the remaining function is essential, otherwise, peri-operative complications are high.

Anesthesia and surgery can precipitate an overt hepatic dysfunction in patients suffering from liver disease and this varies from a patient to another according to the severity of the illness. The primary aim of this study is to investigate the intra-operative effect of entropy monitoring on the general anesthetic requirements during major liver resection among cirrhotic patients with chronic hepatitis C (Child A). The appropriate anesthetic depth is maintained with entropy monitoring in one group and with the traditional monitoring method without entropy. The effect of Entropy on consumption, economic cost and end tidal concentration will be observed and reported. The secondary aim will be whether adopting entropy to guide general anesthetic requirements will have an effect on the haemodynamic parameters during the surgery.

Patients and methods

After local ethics committee approval of the National Liver Institute, Menoufiya University, Egypt (Chairman Prof Hossam Abdel Latif on 15th December 2010, RCT,16/2010) and written informed consents. 60 consecutive hepatic patients Child-Pugh classification A (Child A) with cirrhosis undergoing major liver resection (more than 3 segments) for hepatic tumors were included in this prospective hospital based randomized controlled study. In Group I the general anesthetic depth during induction and maintanence was guided with the Entropy monitoring, while in Group II the depth was guided with standard practice of titrating an anesthetic depth using haemodynamics and clinical signs of an aesthetic depth, the Entropy monitor was kept away (Obscured, blinded) from the anesthetic team managing this group.

Clinical laboratory and ultrasound evidence were used to diagnose cirrhosis. They were divided into two equal groups by a simple random technique (closed envelopes).

Inclusion criteria include Age18-60 year, CHILD classification A and undergoing major liver surgery for more than 6 hours. Exclusion criteria include patients with known neurologic or psychiatric disorders, chronic use of anticonvulsant or other centrally active medications, patients with clinically significant cardiovascular, respiratory or renal diseases, patients with long-term drug or alcohol abuse, patients with body mass index > 40 (morbid obesity) and non-major hepatic surgical procedures. In the operating room, standard monitors were applied (Mean arterial blood pressure, ECG, Pulse oximeter, and Capnograph), and a left (Right handed patients) wrist or forearm vein was cannulated for infusion of intravenous fluids. Baseline heart rate and mean arterial blood pressure were obtained in the operating room before induction of anesthesia. After administration of 100% oxygen, anesthesia was induced with Propofol 2mg/kg IV, and Fentanyl 2μg/kg IV. Rocuronium 0.6mg/kg IV was administered to facilitate tracheal intubation. After tracheal intubation, the patient was mechanically ventilated with a tidal volume of 6-8ml/kg and peep adjusted to 5mmHg, with the ventilatory rate maintaining an end-tidal carbon dioxide concentration (partial pressure) of 30–35mmHg. Followed by Sevoflurane 2% (initial inspired concentration) in combination with air and oxygen (FiO2 50 %), the fresh gas flow rate was set to 2L/min for maintenance of general anesthesia.

Intermittent bolus doses of rocuronium (0.05mg/kg IV) were administered according to the results of the train of four (TOF). Subsequently, anesthesia was maintained with sevoflurane and fentanyl. The processed EEG parameters were obscured in the standard practice group (Group II), and dosage adjustments of anesthetics were decided by the attending anesthetist based on standard clinical signs and aiming to provide a rapid recovery. Group I patients (CHILD A) guided with M-Entropy module of the S/5e Anaesthesia Monitor by GE Healthcare Finland (former, Datex-Ohmeda, Helsinki, Finland).[9] After the skin in the forehead was cleansed, an entropy sensor was positioned as recommended by the manufacturer in Group 1. Recording of the biosignal from the patient's forehead was started while the patient was awake. The impedance for the entropy sensor was checked and noted before induction. A 1-channel raw EEG is collected from the fronto-temporal region of the patient's head with a self-adhesive Entropy Sensor (GE Healthcare, Finland) consisting of three electrodes. The signal is amplified, digitized, and processed in the M-Entropy module. Sevoflurane end tidal concentration was adjusted to achieve a State and Response Entropy of 40–60 with a gradient of 5-10. Intermittent intravenous boluses of Fentanyl (1-2μg/kg) were given if the difference between SE and RE was more than 10 for more than two minutes.

The SE (range from 0 to 91) and the RE (range from 0 to 100). RE becomes equal to the SE when there is no electromyographic activity. Recommended range for adequate anesthesia for both parameters is from 40 to 60, when SE increases above 60 the anesthetic drug dosage was increased. In contrast, if SE is in the recommended range, but RE increases 5–10 units above it, this is interpreted as a sign of uncovered nociception, and more analgesic medication (Fentanyl) was required.

Group II patients (CHILD A) guided with standard traditional practice of titrating anesthetic depth. Standard practice includes the clinical techniques used to assess intraoperative consciousness as checking for movement, response to commands, eyelash reflex, pupillary responses or diameters, perspiration, and tearing. Conventional monitoring systems include standard monitoring (Hemodynamic parameters and Capnography) as well as end-tidal anesthetic analyzer. During the maintenance period (Group II), if the patient displayed autonomic signs consistent with inadequate anesthesia (e.g., increased heart rate, blood pressure, or lacrimation) supplemental dose of fentanyl was administered. However, the

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inspired sevoflurane percentage was increased by 1% if the patient manifested a sustained (5 minutes) increase in the mean arterial blood pressure (MAP) 20% of the pre-incision baseline value.

In response to clinical signs of excessive anesthetic effect (e.g., a decrease in MAP 20% of the pre-incision value), the inspired concentration of sevoflurane was decreased by 1%. Hypotension was treated with IV fluid replacement guided with Transoesophageal Doppler monitoring[14] or by a decrease in sevoflurane concentration, and finally, by ephedrine 3–6mg IV if it was judged necessary. The Sevoflurane concentration was decreased in case of bradycardia or IV atropine 0.5–1mg IV was administered. Rescue drugs such as ephedrine, atropine or adrenaline were recorded.

Sevoflurane (ml) consumed in both groups were monitored by GE Datex-Ohemda S/5 Anesthetic Delivery Unit System. The surgical team was the same for all the procedures; an ultrasonic dissector was used to divide the liver parenchyma. No Pringle maneuver was performed. The middle hepatic vein was preserved. Measures to reduce intraoperative bleeding included: maintaining a low positive central venous pressure during the process of resection, careful parenchymal transection with Cavitron Ultrasonic Surgical Aspirator (CUSA), bipolar elctrocautery and harmonic scalpel. Low-molecular-weight heparin (40mg of enoxaparin) was given subcutaneously once daily for all patients from the second postoperative day until hospital discharge but was repeatedly revised with coagulation studies. Any blood products given were reported.

At the end of surgery, in both groups, anesthesia was guided to achieve rapid recovery, it was allowed to accept state entropy values >60 in the period 15 min before the end of surgery when the inhaled anesthetics were discontinued, and residual neuromuscular blockade was reversed with neostigmine 0.05 mg/kg IV and atropine 0.01mg/kg IV. Measurements include Entropy; State Entropy (SE), and Response Entropy (RE) values were recorded at 2 min intervals during the induction and every 2 hours during the maintenance period of the general anesthetic.

Propofol and Fentanyl induction dosage and consumption every two hours. Mean blood pressure, central venous pressure and the urine output will be recorded every 2 hours. The blood products required and any rescue drugs as ephedrine, atropine or adrenaline were recorded. After 24 hours follow-up, patients were asked if they can recall any events related to the operation. Operative time and Intensive care stay period is also reported.

Statistical analysis

All data were tested with Kolmogorov- Smirnov Z test and most of them were found normally distributed and so presented with mean ± SD in tables. Both parametric and non-parametric testes were used for associations or correlations as appropriate. Expected frequency of liver resection cases in the year is 50 cases. Percent of liver resection in cirrhotic cases is 20.0%. Confidence interval was estimated to be 95.0% and power of the study is 80.0%. Relative risk for liver resection in cirrhotic cases is 0.2 and sample size equals 20. Data was statistically analyzed using SPSS (statistical package for social science) program version 13 for windows and for all the analysis a (p<0.05) was considered statistically significant. Repeated measures ANOVA test and Friedman test were performed to differentiate changes in different follow up results. Spearman correlation coefficient.

Results

Sixty nine patients were included in the study, two were excluded due to a faulty Entropy electrode, while seven were not allowed to proceed for right hepatotomy resection due to surgical extension of the tumor and were not included in the study, two of these three were treated with intraoperative radiofrequency and the other five with a limited hepatic segmentectomy. The study demonstrated insignificance difference between both groups concerning sex, age and body mass index (BMI). 80% males and 20% females were in each group. Table 1 presents the mean value (SD) of age 50.9 (11.23) years in GI, versus 50 (10.71) in G II and the mean (SD) body mass index (BMI) G I 27.6 (2.6) versus 26.9 (3.6) kg/m^2 in G II respectively. Duration of surgery was 5.1(0.3) in G I versus 4.9(0.4) hours in GII, P >0.05.

Table 1 Patients' characteristics of the three studied groups. Group I, cirrhotic patients guided with entropy; Group II, cirrhotic patients guided by standard practice; Group III, non-cirrhotic patients guided by entropy

Variable	Group	Mean(SD)	P
Age (years)	I	50.9(11.23)	> 0.05
	II	50(10.71)	
BMI (kg/m^2)	I	26.5(3.8)	> 0.05
	II	27.6(2.67)	
Duration of surgery	I	7.1±0.3	<0.05
	II	7.5±0.4	

A. Parameters measured during induction

a. Propofol consumption during induction: On comparing doses of intravenous Propofol consumption for the 2 studied groups during induction, there was a significant increase in Group II 184.6 (15.06) mg compared to Group I Entropy monitored patients 156.6 (22.25), (P<0.05) (Table 2). Tables 3–5 demonstrates in details the following hemodynamic results findings during induction and maintenance.

b. Hemodynamic parameters: No significant differences between GI and GII in mean arterial pressure at the pre-induction time P>0.05. After two minutes from induction, there was significant decrease in MAP in both groups G II 88 (2.85) mmHg and G I 94 (3.61), but with no significant difference between them (P>0.05

Table 2 Propofol induction dose for the studied groups. Group I, cirrhotic patients guided with entropy; Group II, cirrhotic patients guided by standard practice

Variable	Group	Mean (SD)	P- Value
Propofol (mg)	I	156.6(22.25)	< 0.01
	II	184.6(15.06)	

After four minutes from induction, there was significant decrease in MAP for Group II patients 85 (2.59) mmHg in comparison with Group I Entropy monitored patients 89 (3.89), (P<0.05). After six minutes from induction, Group II patients MAP 80 (2.69)mmHg was still significantly less when compared to Groups I entropy monitored patients 86 (3.85) mmHg. According to heart rate, there was no significant change at preinduction time and during the follow up times of measurement at 2, 4 and 6 minutes after induction for the two studied groups P >0.05.

c. Entropy during induction:

i. State entropy (SE): The baseline of the state entropy; showed no significant change at pre-induction time and after two minutes of induction for the two studied groups. After four minutes of induction, there was significant decrease in patients not monitored by Entropy Group II, 47 (4.44) more than Group I monitored with Entropy, 54 (6.58). 6 minutes after induction, there was still a significant decrease in Group II 36 (3.37) versus Group I 42 (3.31) (Table 6).

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ii. Response entropy (RE): Response entropy at the pre-induction time and two minutes from induction showed no significant changes. Four minutes after induction, there was significant decrease in Group II 48 (4.38) when compared with Group I 53 (6.96). Six minutes after induction, there was significant decrease in Group II 36 (3.32) more than Group I 42 (3.22) (Table 7).

B. Parameters measured during maintenance

a. Sevoflurane consumption: After two hours from induction in the studied groups. Group II consumed 20.8 (1.88) ml more than Group I patients monitored by Entropy 16 (2.19) ml. Sevoflurane consumption after four hours from induction still showed the least value in Group I 10.7 (1.94) ml, when compared to Group II 17.4 (1.92) ml. Six hours from induction Group I continued to consume less Sevoflurane than Group II Entropy guided patients, 9 (1.22) ml versus 14.1 (2.19) ml respectively (Table 8).

b. End tidal sevoflourane: End tidal sevoflourane; Group I Entropy guided had the least value 1.4 (0.12) after two hours from induction then Group II 1.6 (0.07). Four hours from induction Group I 1.4 (0.11) also showed the least value when compared to Group II 1.6 (0.07) and also after six hours from induction Group I 1.3 (0.17) showed the least value when compared to Group II 1.6 (0.05) (Table 9).

c. Fentanyl during maintenance: There was no significant change between the two studied groups in fentanyl consumption after two, four and six hours from induction P>0.05 (Table 10).

d. Central venous pressure and urine output during maintenance: Central venous pressure and urine output; showed no significant change between the two studied groups after two, four and six hours from induction P >0.05. 2 Packed Red blood cells units were required for 4 patients in Group II versus 2 patients in Group I. Fresh frozen plasma (4 units) were required in Group I for 3 patients versus 3 patients in Group II.

Table 3 Parameters measured during induction and maintenance of general anesthesia, Sevoflurane consumption, and End tidal Sevoflurane Percentage and Fentanyl consumption

Variable	T1	T2	T3	T4	T5	P-value
MAP (mmHg)						
GI	96.4±3.3	94.3±3.6	89.7±3.8	86.7±3.8	87.3±3.2	<0.05
GII	94.5±3.4	92.9±3.2	89.2±3.5	86.7±3.8	89.2±3.5	
HR (beat/min)						
GI	87±12.3	89±12.3	82±9.7	77±9.0	87±11.3	<0.05
GII	92±8.8	85±8.9	80±11.4	76±10.8	89±8.7	
State entropy (SE)						
GI	90±0.6	61±4.2	54±6.5	42±3.3	63±4.2	<0.05
GII	90±0.9	63±4.7	52±5.3	41±3.6	60±3.6	
Response entropy (RE)						
GI	100±0.0	64±4.1	53±6.9	42±3.2	62±5.6	<0.05
GII	99±0.6	65±4.9	53±5.6	41±3.6	61±4.2	

Changes of mean arterial pressure (MAP), heart rate (HR), state entropy (SE) and response entropy (RE) in GI (Group I, cirrhotic patients) and GII (Group II, healthy liver). Values are expressed as mean ± SD, P-value < 0.05 was considered statistically significant. Before the induction (T1), 5 min, 10 min and 15 min after induction (T2, T3 and T4) respectively, and at end of surgery (T5).

Discussion

Preoperative recognition of compensated or Entropy was used in the current study to monitor the titration of general anesthesia administration during hepatic resection surgery in cirrhotic patients. Many previous studies on healthy liver patients reported the influence of the depth of anesthesia monitoring on the consumption of hypnotic drugs, but only few studies monitored the effect among the cirrhotic patients. Patients with liver disease pose major challenges in operating room and intensive care units because stress of anesthesia and surgery can precipitate overt hepatic dysfunction. In this current study, the results clearly demonstrated that the propofol dosage used in induction guided by entropy showed a significant reduction in the level of consumption in the entropy guided group of cirrhotic livers undergoing a major abdominal surgery respectively (group I) when compared with a similar group of cirrhotic patients, but guided by standard clinical practice (group II). Vakkuri et al also demonstrated similar results when they used the spectral entropy monitoring. They found a reduction in the anaesthetic concentrations in association with faster emergence.[15]

Wang PC et al.[16] also proved that the use of spectral entropy for monitoring the depth of anesthesia or level of hypnosis in surgery or painful procedures can reduce the consumption of drugs and shorten the recovery time of total intravenous anesthesia such as propofol in cirrhotic patients. Aimé et al.[17] investigated BIS and spectral entropy monitoring during sevoflurane– sufentanil anesthesia in comparison with standard practice for 140 adult patients, they demonstrated that BIS and spectral entropy guidance for the titration of sevoflurane results in a reduction of 29% in sevoflurane consumption which is close to our current study the savings in sevoflurane (31%). The price of 250ml of sevoflurane in Egypt is currently 1000 L.E. while the entropy electrode price is 50 L.E. The cost-benefit balance can easily be calculated knowing the price of electrodes and sevoflurane, and the duration of the procedures.

The savings were far less significant by Yli-Hankala et al.[18] study, their study concluded that the use of Bispectal Index (BIS) monitoring refunded the cost of the electrode in anesthetics lasting longer than 282 min; their use of a fresh gas flow of 3 L/min could explain this discrepancy. Pavlin et al.[19] used a BIS monitor to titrate the dose of sevoflurane and found that end tidal concentration (ET) was reduced by 13%. Instituting BIS monitoring throughout an entire operating room was associated with a reduction in mean end-tidal gas concentration of a potent inhaled anesthetic (sevoflurane), suggesting that a similar reduction in anesthetics use occurred if we assume equivalent total gas flows in the two groups. There was a significant inverse correlation between mean end-tidal sevoflurane concentrations and mean BIS values. Choi SR et al.[20] had also performed a study to evaluate the effect of entropy monitoring on end-tidal sevoflurane

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concentration and recovery characteristics in pediatric patients undergoing Sevoflurane anesthesia. They found that the blood pressure (BP) values were higher, end-tidal sevoflurane concentration during maintenance was lower and recovery was faster in the Entropy group compared with the Standard group. In their study, the difference in an anesthetic concentration between Entropy and control patients was significant. Without Entropy monitoring, there was a tendency for anesthesiologist to maintain general anesthesia at a higher end-tidal sevoflurane concentration. However, with Entropy monitoring, there was a reverse trend to maintain their patients at smaller end-tidal sevoflurane concentrations. Similar to our current study results which showed that the entropy guided groups (I) had lower end-tidal sevoflurane concentration than the standard clinical practice group (II).

Takamatsu et al.[21] also investigated the accuracy of response entropy, state entropy and BIS as indicators of nociception during sevoflurane anesthesia to determine whether the difference between response entropy and state entropy can indicate inadequate analgesia. They concluded that neither response entropy and state entropy nor BIS was sufficiently accurate to determine the strength of noxious stimulation. Lacking of exact guidelines for the adjustments of fentanyl boluses in the entropy group according to RE in relation to hemodynamic changes was a shortcoming in their study protocol. In our study hemodynamic responses guided the fentanyl dosage in the standard practice group (II), while in entropy groups (I) the use of the response–state entropy difference of more than 5-10 was used to titrate analgesics during anesthesia. The fentanyl dosage did not differ significantly in either groups. Whether SE-RE difference reveals a different kind of information about intraoperative nociception than mere hemodynamic changes, still warrants further studies.

Another study by Paul F et al.,[22] suggested that, the depth of anesthesia monitor should display a good correlation between the measured value and the patient's physiologic responses during the perioperative period, independent of the anesthetic agent being administered. In individual patients, increase in the RE-SE difference was seen already some minutes before the approaching emergence could be anticipated from SE. This observation was studied by A. Vakkuri et al.[15] study and was attributed to the findings of early recovery of other brainstem-controlled phenomena, such as the respiratory sinus arrhythmia[23] suggesting that the anesthetic drug effect may cease at the brainstem level earlier than in the cortex. Both indices based mainly on EEG content, i.e. SE and BIS, showed a delay compared with RE in returning to baseline at return of consciousness. This can be considered the result of a residual drug effect on EEG, although brain function has recovered sufficiently to react correctly to a simple request. The sedative effect does not cease the moment that the patient opens his eyes. One of the limitations of this current study was not discussing the recovery time because our main concern was to study the intraoperative consumption of general anesthetics, among cirrhotic patients subjected to a major surgery, so retrieval of measurements were at fixed times intraoperative; two, four and six hours after the induction.

V Bonhomme et al.[24] found an excellent global correlation between BIS and SE. BIS was higher than SE in the range of 10 units in awake patients and during induction of hypnosis. Agreement between BIS and SE was good in awake patients and in anaesthesied patients. In those conditions, clinicians may expect observing SE values similar to those that would have been observed with BIS, with a negative difference of approximately 10 units when the patient is awake. While in other conditions of recording, differences of more than 20 units could

frequently be observed. These discrepancies are partially explained by scale differences. They can also be related to site of recording, and possibly to the effect of EMG activity on BIS calculation. Wang CH et al.,[16] performed a study to assess factors influencing the end-tidal concentrations of isoflurane within a bispectral index (BIS) range of 45-55 among healthy live liver donors, chronic hepatitis B patients undergoing hepatectomy hepatocellular carcinoma, and end-stage liver disease patients undergoing liver transplantation. The study showed that end-stage liver disease patients required the least end-tidal isoflurane concentration. Patients with hepatocellular carcinoma with cirrhosis required intermediate end-tidal isoflurane concentrations; healthy live liver donors required the highest end-tidal isoflurane concentrations to provide sufficient an aesthetic depth. They concluded that liver function was the only significant factor influencing the likelihood of lowering the end-tidal isoflurane concentration by 4 hours after anesthesia induction because end-tidal isoflurane concentration requirements are different for patients with various liver status, they recommended that , this anaesthesia depth monitoring strategy may protect the patients from intraoperative recall or anesthesia over-depth as a consequence of insufficient or overdose of anesthesia, respectively, their results in cirrhotic patients with chronic hepatitis are in agreement with our current study results concerning the expected reduction in the inhalation agent consumption in cirrhotics undergoing surgery.

Schumann R et al.,[25] also studied the titration of volatile anesthetics and monitoring using the bispectral index, to decrease the anesthetic requirements and facilitate recovery from anesthesia unrelated to liver transplantation. They conducted a retrospective analysis in recipients with and without such monitoring. The BIS group received less inhalational anesthetic compared to the control group. Their opinion was that, unless this monitoring result was integrated into an intraoperative algorithm and an early extubation protocol for fast tracking enhanced recovery, this utilization does not appear to provide a clinical benefit but instead drives cost. We agree with this opinion and suggest that an enhanced recovery protocol utilizing anesthesia depth monitoring facilities now available in many theaters should be developed in future studies and applied clinically with cost effective economic basis.

Most of the above mentioned studies results coincides with this current study The end-tidal concentration requirements of inhalational anesthetics were lower for patients with impaired liver status. The use of entropy to monitor levels of end tidal inhalational anesthetics is preferable to avoid unnecessary high concentrations of general anesthetics for this group of cirrhotic patients and also to reduce cost during prolonged surgical procedures. The introduction of Anesthesia depth monitoring into the Liver Institute anesthetic practice can help improve monitoring of this group of hepatitis C patients in Egypt, which are increasingly requiring surgical procedures with the improvement in quality of medical care by the new introduced antiviral drugs which treat the virus but leaves the cirrhosis as it is.

Conclusion

In conclusion Entropy monitoring for hepatic patients reduced general anesthetic agent consumption during induction and surgery and enhanced recovery with favourable haemodynamic consequences. Encouraging the use of Anaesthesia depth monitors can have an important economic impact when applied on a larger scale.

Acknowledgments

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Conflicts of interest

The authors declare there is no conflict of interests.

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