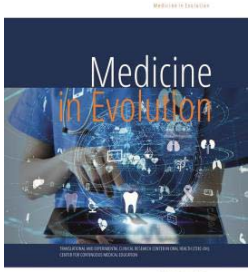
The influence of Entropy in general consumption of anesthetics regarding sex and age



Timar C.[1,2], Negrău M.[1,2], Pantiş C.[1,2], Juncar M.[2]

[1]*Emergency County Hospital Oradea (Romania), Department of Anaesthesia and Intensive Care (ATI1), Oradea, Romania*
[2]*University of Oradea, Department of Dental Medicine, Faculty of Medicine and Pharmacy, Oradea, Romania*

Correspondence to:
Name: Timar Călin
Address: Gh. Doja 65, Oradea, Romania
Phone: +40 745135488
E-mail address: calin_bh@yahoo.com

Abstract

The study that we conducted highlights the role of entropy monitoring in general anesthesia, with a focus on its potential benefits for both patients and hospitals. The study aimed to investigate how entropy monitoring during general anesthesia can reduce the need for sevoflurane, as well as hypnotic and opioid medications. The study was conducted over half a year in 2019 and involved 30 patients who required general anesthesia within institution. The 30 patients were divided into three groups: Group1: Patients with metabolic disorders; Group2: Patients without metabolic disorders; Group3: Control group.

The study found that entropy monitoring resulted in a nearly 20% reduction in the need for intrasurgical anesthetics in patients with metabolic disorders (Group 1) compared to the control group (Group 3). This reduction could lead to faster postoperative awakening and potentially fewer complications related to anesthesia.

The study also examined sevoflurane consumption patterns based on age and gender.

Keywords: entropy, metabolic disorders, sevoflurane, age, sex

INTRODUCTION

Commonly used anaesthetic drugs can be dosed according to total body weight or ideal body weight based on lipid solubility. The volume of distribution is changed in obese patients with regard to lipophilic drugs. This is especially true of benzodiazepines and barbiturates, among the commonly used anaesthetic drugs [1-6].

The choice of volatile agents is based on the physical characteristics of tissue solubility, expressed as blood-gas partition coefficients and fat-blood partition coefficients. Some evidence suggests that desflurane may be the anaesthetic of choice because of a more consistent and rapid recovery profile that is seen with sevoflurane and propofol [7-9,10]. However, a more recent study has suggested that the difference in immediate recovery between sevoflurane and desflurane is not clinically significant [11]. Even though nitrous oxide provides some analgesic effect and is eliminated rapidly, we prefer to avoid it because of the high oxygen demand in the obese [12].

Aim and objectives

The ability to monitor the levels of patient consciousness while undergoing general anaesthesia is clinically important because an inadequate level of anaesthesia can result in patient intra-operative awareness, an overdose of anaesthesia can result in a prolonged recovery and an increased risk of postoperative complications [13-18]. The use of depth of anaesthesia monitors is claimed to provide a more accurate assessment of the level of anaesthesia and aid the tailoring of the anaesthetic dose to the individual patient. Tailored dosing potentially reduces drug consumption and the number of adverse effects, with possibly faster emergence from anaesthesia with an earlier patient discharge from the recovery room [19].

Entropy is one of the most important steps in the complex management of patients is the modulation of anaesthesia for every patient needs. We also believe that by individualizing the anaesthesia by monitoring the entropy it is possible to obtain an appropriate management for hemodynamic complications during anaesthesia including tachycardia, bradycardia, hypotension and hypertension. [31]

MATERIAL AND METHODS

We conducted a study over half a year (2019) for 30 patients who need general anaesthesia from a total of 1626 patients available within the host institution, and meet the inclusion criteria for monitoring the entropy. Patients were subsequently divided into 3 groups of 10 patients: in group A patients with metabolic disorders obesity and/or diabetes mellitus, the group B patients without metabolic disorders and control group C patients without monitoring entropy. [31 32]

Inclusion Criteria: age limit: between 18 years to 80 years; gender: male and female; ASA physical status I, II, III. [31,32]

Exclusion Criteria: cardiac pacemaker; atrial fibrillation at the time of presentation in the operation theatre; any subject with an epidural catheter, placed pre-operatively; allergy to Propofol or another anaesthetic drugs; pregnancy; the presence of neuromuscular disease; the presence of neurologic disease. [31,32]

We employed in the three groups of patients undergoing general anesthesia a number of variables such as: age, sex, anesthetic duration (in minutes), change of heart rate baseline at 10 min, change of systolic blood pressure baseline at 10 minutes, the use of sevoflurane (mL),

fentanyl (mg) rocuronium (mg) and propofol (mg) and a flow of fresh gases amounting to 2 L/min (50% oxygen and 50% air). [31,32]

At the end of anaesthesia, we calculate the total consumption of intrasurgical anaesthetics for each patient and for patient groups.

Evaluating the impact of general anaesthesia guided with Entropy on the hemodynamic instability represented and characterized by high blood pressure episodes (hypertension), or low blood pressure (hypotension) and by high cardiac rate (tachycardia), or low cardiac rate (bradycardia). [31,32]

Data were centralized using Microsoft Excel, and statistical validation was performed using the MedCalc v18.11.3 program.

RESULTS

The minimum age of patients included in the study with diabetes and obesity in the first study group was 18 years, and the maximum age was 78 with a mean of 50.3 years, and the characteristics of the variables followed are presented in table 1.

Table 1. Clinical and intraoperative characteristics under general anaesthesia of patients with metabolic disorders and entropy monitoring (Group 1)

Sex/Age (years)	HR before intubation	TAS before intubation	Entropy RE/SE before IOT	OR time (min)	Sevofluran (mL)	Rocuroniu (mg)	Fentanyl (mg)	Propofol (mg)
F/39	94	131	94/89	85	18	60	0.40	150
M/78	92	163	99/89	225	104	110	0.40	150
M/18	91	141	99/91	50	17	50	0.60	150
M/49	83	150	97/89	240	56	200	0.65	300
F/58	71	122	97/87	50	16	50	0.20	160
F/31	81	131	98/90	50	18	50	0.20	170
M/66	63	130	96/85	45	13	40	0.35	100
M/56	60	116	95/88	60	13	50	0.30	180
F/46	130	180	95/88	60	16	50	0.30	150
F/62	87	171	96/85	240	73	100	0.65	150
Average years 50,3	Total			1105	344	760	4.05	1660

State Entropy (SE), Response Entropy (RE), HR (heart rate), TAS (systolic blood pressure), OR (operation time), IOT (orotraheal intubation)

Patients without comorbidities, from the second group studied, had a minimum age of 18 years and a maximum of 80 years with an average of 53.2 years, and the characteristics of the monitored variables can be seen in table 2.

Table 2. Clinical and intraoperative characteristics of patients under general anaesthesia without metabolic disorders and entropy monitoring (Group 2)

Sex/Age	HR before intubation	TAS before intubation	Entropy RE/SE before IOT	OR time (min)	Sevofluran (mL)	Rocuroniu (mg)	Fentanyl (mg)	Propofol (mg)
F/34	130	127	100/91	60	18	40	0.30	120
M/31	75	134	97/91	70	20	50	0.35	150
M/64	47	128	96/88	105	17	110	0.40	120
F/70	70	189	100/89	150	20	80	0.60	60
M/48	65	133	99/90	120	19	70	0.30	170
F/18	107	124	100/89	45	12	40	0.30	80

Sex/Age	HR before intubation	TAS before intubation	Entropy RE/SE before IOT	OR time (min)	Sevofluran (mL)	Rocuroniu (mg)	Fentanyl (mg)	Propofol (mg)
M/68	73	148	97/88	60	14	40	0.25	150
M/45	75	129	99/89	45	16	35	0.25	150
M/74	75	140	97/91	60	22	50	0.30	180
F/80	95	150	99/98	230	78	50	0.45	150
Average Years 53,2	Total			945	236	565	3.5	1330

The patients in the control group are noticeable in table 3, the minimum age being 18 years and the maximum age 79 years, with an average of 51,4 years (table 3).

Table 3. Clinical and intraoperative characteristics under general anaesthesia of patients without entropy monitoring (Group 3)

Sex/Age	HR before intubation	TAS before intubation	Entropy RE/SE before IOT	OR time (min)	Sevofluran (mL)	Rocuroniu (mg)	Fentanyl (mg)	Propofol (mg)
F/60	78	119	No monitor	180	33	110	0.40	150
M/67	88	158	No monitor	105	44	60	0.35	150
F/18	109	167	No monitor	200	40	50	0.40	120
M/62	85	190	No monitor	98	16	70	0.30	150
M/64	85	130	No monitor	110	30	60	0.35	200
F/36	73	130	No monitor	230	45	200	0.50	250
F/45	109	167	No monitor	200	40	180	0.40	150
M/35	95	142	No monitor	230	84	120	0.50	200
M/48	88	158	No monitor	100	44	60	0.35	150
F/79	78	119	No monitor	180	33	110	0.40	180
Average Years 51,4	Total			1633	409	1020	3.95	1700

The monitorized characteristics were significantly different between the three groups of patients P <0.0001 (MedCalc v18.11.3).

At the end of anaesthesia, we calculate the total consumption of intrasurgical anaesthetics for each patient and for patient groups according to the figure 1. The average age distribution is shown in Table 4

Sevoflurane Consumption by Age:

Age-Related Trends: The data continues to show that there are variations in sevoflurane consumption based on age. Patients in their 30s, 60s, and 80s tend to have higher sevoflurane consumption compared to other age groups. Patients in their 30s have notably higher sevoflurane consumption.

Reduced Consumption in Some Age Groups: It's notable that some patients, such as those in their 60s and 80s, also have relatively high sevoflurane consumption, while others, such as those in their 40s and 50s, have lower consumption.

Sevoflurane Consumption by Gender:

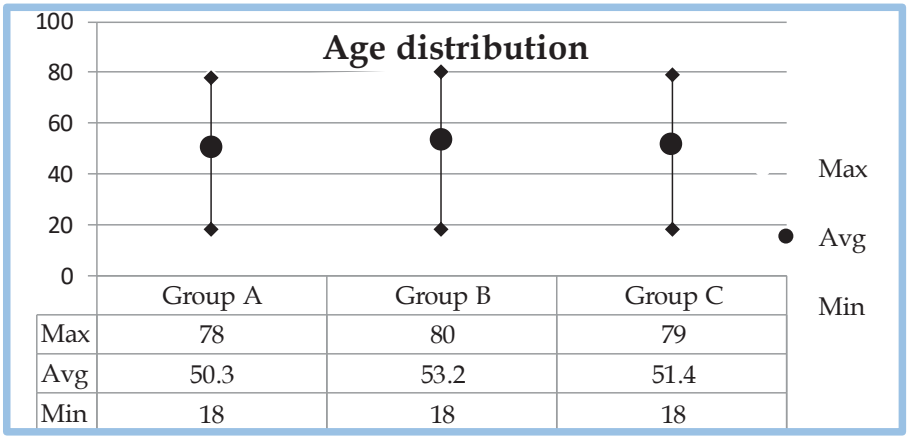
Gender Differences: Gender differences in sevoflurane consumption remain apparent in the updated data. On average, male patients still tend to require more sevoflurane than female patients.

Consistency with Previous Data: These findings align with the previous data, indicating that the gender difference in sevoflurane consumption is consistent.

Importance of Monitoring (No Monitor Group):

It's interesting to note that there is a group of patients labeled "No monitor" for Entropy monitoring. These patients appear to have relatively high sevoflurane consumption compared to those in previous data with Entropy monitoring. This observation suggests that the use of Entropy monitoring may influence sevoflurane consumption, as patients without monitoring tend to consume more sevoflurane. [31,32]

Table 4. Average age distribution



	Group A	Group B	Group C
Max	78	80	79
Avg	50.3	53.2	51.4
Min	18	18	18

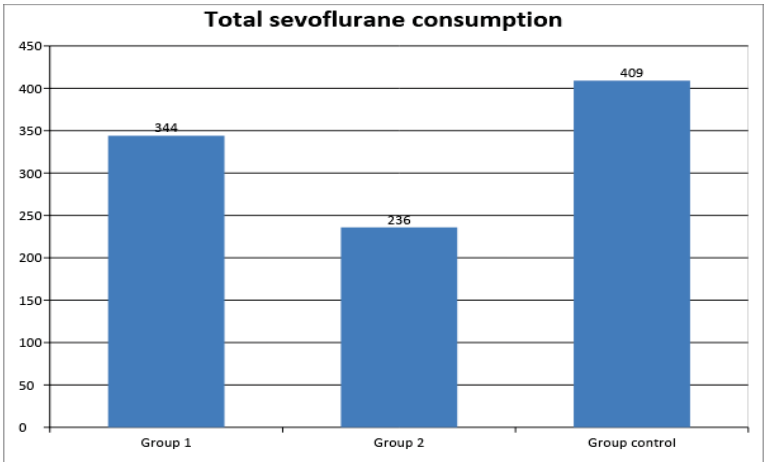


Figure 1. Total sevoflurane consumption (mL) in the three patient groups monitored

DISCUSSIONS

Entropy is a device which helps in analyzing electroencephalogram (EEG) and contains state entropy (SE) and response entropy (RE). SE is computed from the electroencephalogram in the 0.8- to 32-Hz range and should encompass mainly the hypnotic elements of the electroencephalogram, whereas response entropy is computed from 0.8 to 47 Hz, which includes a significant amount of the facial EMG. Thus when EMG activity is low, state entropy and response entropy should be the same, but with arousal and an increase in facial EMG, response entropy should increase. The initial clinical studies with this device showed that it produced results comparable to those of the BIS when tested with intravenous and inhaled hypnotic anaesthetics [20].

The GE Entropy Module uses the same unilateral self-adhesive fronto-temporal sensor as the BIS but specifically made for the GE product (i.e., they are not interchangeable). The module works only with GE monitoring systems with the appropriate software loaded. The

SE, RE, and a single channel of the raw electroencephalogram are displayed on the same screen as the other monitored variables. The displayed state entropy range is 0 (isoelectric EEG) to 91 (fully awake), and the response entropy range is 0 to 100. The anaesthetic range is 40 to 60, and the manufacturer recommends that state entropy outside this range may require a change in hypnotic dosing, whereas if the state entropy is in this range but the response entropy is more than 10 above the state entropy, more analgesic may be required [21, 22].

The GE Entropy™ Module is indicated for adult and pediatric patients older than 2 years within a hospital for monitoring the state of the brain by data acquisition of electroencephalograph (EEG) and frontal electromyograph (FEMG) signals. The spectral entropies, response entropy (RE) and state entropy (SE), are processed EEG and FEMG variables. In adult patients, response entropy and state entropy may be used as an aid in monitoring the effects of certain anaesthetic agents, which may help the user to titrate anaesthetic drugs according to the individual needs of adult patients. Furthermore, in adults the use of entropy parameters may be associated with a reduction of anaesthetic use and faster emergence from anaesthesia. The entropy measurement is to be used as an adjunct to other physiological parameters. Entropy is a measure of irregularity in any signal [23-28].

The results obtained in our study are clinically meaningful, with RE-SE difference of less than 10. Sevoflurane requirements are reduced with 16% and rocuronium with 25.5% at the patients with metabolic disorders and entropy monitor than the control groups without entropy, while maintaining hemodynamic stability. Complete blockade in the morbidly obese is necessary not just for surgeons, convenience but also to facilitate mechanical ventilation. The drug chosen is not as important as the state of paralysis [29, 30, 31,32].

This study shows the role of entropy in general anaesthesia for the patient and the hospital in order to reduce the need for volatile gases (sevoflurane) but also of hypnotic and opioids, bringing major benefits to the patient, and the economy of the hospital significantly reducing the costs of anaesthesia and reducing the number days spent in hospital, also avoiding postoperative complications related to anaesthesia.

With this study we demonstrate that the role of entropy in general anaesthesia for the patient safety is mandatory. The ability to monitor the levels of patient consciousness reduces the risk of an inadequate level of anaesthesia and intra-operative awareness which can cause significant suffering followed by post-traumatic stress disorder in some patients. Conversely, an overdose of anaesthesia can result in a prolonged recovery and an increased risk of postoperative complications and costs including permanent cognitive dysfunction for some patients. [31,32].

Clinical Significance: The study found that the differences between RE (response entropy) and SE (state entropy) were less than 10, indicating that the results obtained are clinically meaningful. Sevoflurane Consumption by Age:

Age-Related Trends: Looking at sevoflurane consumption, there appears to be a trend where younger patients (age <40) have higher average sevoflurane consumption, especially in the male group. This could be indicative of different anesthesia requirements based on age.

Reduced Consumption in Older Patients: In general, as patients get older (age 50-59, 60-69, and 70-79), the average sevoflurane consumption decreases. This suggests that older patients may require less sevoflurane during anesthesia, although the sample size for some of these age groups may be limited.

Sevoflurane Consumption by Gender:

Gender Differences: In the data presented, there seems to be a notable gender difference in sevoflurane consumption. On average, male patients appear to require significantly more sevoflurane than female patients, regardless of age.

Possible Gender-Specific Factors: These differences in sevoflurane consumption could be due to various factors, including physiological differences between genders, differences in

body composition, or variations in the types of surgeries performed on male and female patients.

Reduced Anesthetic Requirements: Patients with metabolic disorders who were monitored with entropy required 16% less sevoflurane and 25.5% less rocuronium compared to the control groups without entropy monitoring. Importantly, this reduction in anesthetic requirements did not compromise hemodynamic stability.

Individualized Anesthesia: The study suggests that, based on patient weight and individual responses, larger amounts of benzodiazepines, fentanyl, or sufentanil can be used. Conversely, smaller amounts of propofol are needed when considering real body weight. Vecuronium or rocuronium dosing should be based on ideal body weight initially and adjusted based on the neuromuscular blockade status.

Role of Paralysis: Complete neuromuscular blockade is emphasized in morbidly obese patients to facilitate mechanical ventilation during surgery. The choice of neuromuscular blocking agent is noted to be less important than achieving the desired state of paralysis.

Reduced Costs and Complications: The study highlights the potential benefits of entropy monitoring in terms of reducing the need for volatile gases and anesthetics. This, in turn, can lead to significant cost savings for the hospital and reduce the number of days patients spend in the hospital. It may also help prevent postoperative complications related to anesthesia.

CONCLUSIONS

Reduction in Anesthetic Use: The study concludes that entropy monitoring can lead to a nearly 20% reduction in the use of intrasurgical anesthetics in patients with metabolic disorders (diabetes and/or obesity) compared to the control group.

Faster Postoperative Awakening: Patients monitored with entropy experienced a faster postoperative awakening, which resulted in fewer hospitalization days for these patients.

Cost Savings: The use of entropy monitoring was associated with reduced postoperative costs and complications, particularly in patients with comorbidities.

Safety and Individualization: The study underscores the importance of entropy monitoring for patient safety. It reduces the risk of inadequate anesthesia levels and intra-operative awareness, which can lead to significant patient suffering and post-traumatic stress disorder. Conversely, it helps prevent anesthesia overdose, which can result in prolonged recovery and cognitive dysfunction. Need for Further Studies: The study suggests that there is a need for wider and more comprehensive studies on entropy monitoring in anesthesia, given its potential benefits to the field of medicin In conclusion, the updated data reinforces previous observations regarding sevoflurane consumption based on age and gender. Additionally, the presence of a "No monitor" group suggests the potential influence of monitoring on anesthetic consumption. Further analysis and consideration of clinical relevance and confounding factors are essential for a comprehensive understanding of the findings. Larger sample sizes and additional research may help validate these preliminary conclusions and explore contributing factors in more detail.

In conclusion, while these preliminary observations suggest some trends in sevoflurane consumption based on age and gender, a more in-depth analysis and consideration of clinical implications are necessary. Additionally, it's essential to interpret these findings in the context of the specific patient population and clinical practice guidelines. Further research and statistical testing may be needed to validate these initial conclusions and explore potential contributing factors.

In summary, the study indicates that entropy monitoring during general anesthesia can lead to significant benefits for both patients and hospitals, including reduced anesthetic requirements, faster recovery, cost savings, and improved safety. These findings highlight the potential of entropy monitoring as a valuable tool in the field of anesthesiology.

Declaration of conflicting interest: The authors declare that there is no conflict of interest.

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