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Original contribution

Sevoflurane preserves regional cerebral oxygen saturation better than propofol: Randomized controlled trial☆

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ABSTRACT

Study objective: To investigate possible effects of volatile induction and maintenance anesthesia with sevoflurane (VIMA) and total intravenous anesthesia with propofol (TIVA) on regional cerebral oxygen saturation ($rcSo_2$) during laparoscopic cholecystectomy.
Design: Randomized, prospective and single-blinded study.
Setting: Academic hospital.
Patients: ASA physical status of I and II surgical patients, scheduled for elective laparoscopic cholecystectomy from March 2013 to October 2014.
Measurements: Changes of regional cerebral oxygen saturation were measured by near-infrared spectroscopy on the left and right sides of forehead at different time points: before anesthesia induction (Tbas), immediately after induction (Tind), after applaying a pneumoperitoneum (TCo_2), 10 minutes after positioning the patient into reverse Trendelenburg's position ($TrtCo_2$), immediately after desufflation of gas (Tpost) and 30 (Trec30) and 60 (Trec60) minutes after emergence from anesthesia.
Main results: Study population included 124 patients, 62 in each group. There was no significant difference between these groups according to demographic characteristics, surgery and anesthesia times as well as in the basal $rcSo_2$ values. Statistically higher $rSco_2$ values were noted in the VIMA group when compared to the TIVA group in all time points Tind, TCo_2, $TrtCo_2$, Tpost, Trec30 and Trec60 and incidence of critical $rcSo_2$ decreases was statistically lower in VIMA group ($P < .05$). There were no serious perioperative complications.
Conclusions: VIMA technique provides significantly (4%-11%) higher $rcSO_2$ values during general anesthesia for laparoscopic cholecystectomy, when compared with TIVA and also provides significantly less number of critical $rcSO_2$ decreases.

1. Introduction

Surgical patients, especially those with significant comorbidities while undergoing some types of surgery such as laparoscopic abdominal surgery are at particular risk for perioperative cerebral hypoxia and ischemia consequently [1]. Few clinical studies in humans have proven that cerebral oxygenation desaturation during surgery is undoubtely associated with serious perioperative complications (neurological or cognitive) which can manifest immediately after emergence from general anesthesia [2,3]. Direct monitoring of brain oxygenation can be obtained by Near-infrared spectroscopy (NIRS) which allows continuous, non-invasive and bedside monitoring of cerebral oxygen saturation through the scalp and skull. NIRS monitoring is based on the different absorption characteristics of near-infrared spectrum of oxygenated and deoxygenated hemoglobin: oxygenated hemoglobin absorbs more infrared light (850-1000 nm) and less red light (600-750 nm) versus deoxygenated hemoglobin absorbs more red light and less

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infrared light. Unlike to pulse oxymetry NIRS does not require pulsatility and measures average oxygen saturation of hemoglobin in arterial (15%) and venous blood (85%) of brain, and is not affected by hypercarbia or hypoxia. This method uses two sensors (30 mm = shallow detector and 40 mm = deep detector) with aim to minimize extracerebral signal interference. By subtracting the shallow signal from the deep one, extracerebral signals are suppressed and the net result is a measurement of predominantly cerebral hemoglobin oxygen saturation [4]. Continuous non-invasive measuring of regional cerebral saturation ($rcSO_2$) by Near-infrared spectroscopy (NIRS) on forehead provides accurate information about episodes of cerebral desaturation during general anesthesia [4-8]. Decreasing of $rcSO_2$ is well known risk for the neurological adverse events (neurocognitive decline or even a stroke) during perioperative period in different types of surgery [9]. Keeping regional cerebral saturation above a safety threshold (a decline of $rcSO_2$ <20% compared to the basal $rcSO_2$ value) during general anesthesia is associated with fewer postoperative complications and shorter hospital stay [10]. Major limits of NIRS are difficulties to determine normal (baseline) values and wide patient-to-patient variability [4].

There is a paucity of data about the impact of general anesthetics on regional cerebral saturation as well as about critical changes of regional cerebral saturation during different types of general anesthesia for laparoscopic cholecystectomy. It is known that volatile anesthetics decrease cerebral metabolic rate and increase cerebral blood flow whereas intravenous anesthetics decrease cerebral metabolic rate and decrease cerebral blood flow. This difference of the amount of blood flow through the cerebral vasculature during volatile and intravenous anesthesia may be the reason for changes of ratio between oxygenated and deoxygenated hemoglobin concentrations measured by NIRS.

This study was conducted to investigate the possible effects of two common general anesthesia techniques such as volatile induction and maintenance anesthesia (VIMA) with sevoflurane and total intravenous anesthesia with propofol (TIVA) on regional cerebral oxygen saturation ($rcSO_2$) during laparoscopic cholecystectomy. Primary endpoint was to investigate possible benefits of one type of general anesthesia technique over another (VIMA vs. TIVA) in preserving of regional cerebral oxygen saturation ($rcSO_2$). Since it is well known that hemodynamic fluctuations have an influence on cerebral perfusion our secondary endpoint was to show the hemodynamic changes (mean arterial pressure, heart rate) during these two different anesthesia techniques.

2. Materials and methods

This study was approved by the University Hospital Osijek Ethics Committee (Approval number 25-1:12 682-2/2012, 19.11.2012.) and a written informed consent was obtained from all participants enrolled in this prospective randomized single blinded study. Patients who were scheduled for elective laparoscopic cholecystectomy were enrolled prospectively (from March 2013 to October 2014).

According to anesthesia technique which was applied, patients were allocated into two groups, sevoflurane anesthesia induction and maintenance (VIMA) group and total intravenous anesthesia group with propofol (TIVA) group. Randomization was done by pulling out the envelope in which it was written the group division.

The main inclusion criteria were American Society of Anesthesiologists (ASA) physical status I and II and age above 18 years. Exclusion criteria were: history of cerebrovascular disease or presence of neurological signs, uncontrolled hypertension or diabetes, significant respiratory and cardiovascular disorders, or surgical conversion to laparotomy. All patients were examined, brief clinical neurological and routine laboratory tests (full bood count, urea, creatinine, glucose, sodium, potassium, prothrombine time) were done before surgery.

Thirty minutes before induction of anesthesia, patients were premedicated with midazolam, 2.5 mg intravenously, and usual demographic and clinical data were noted. Standard non-invasive monitoring (electrocardiogram, non-invasive blood pressure, peripheral oxygen saturation and bispectral index sensor, BIS) was set up before induction of anesthesia. Also, two Near-infrared spectroscopy (NIRS) sensors (INVOS 5100; Somanetics Corp, Troy, MI) for regional cerebral saturation monitoring ($rcSO_2$) were placed at above the eyebrow on the both sides of the forehead, left ($rcSO_2$ L) and right ($rcSO_2$ R). There was no external compression on INVOS electrodes during recording. The patient's basal values of $rcSO_2$, peripheral blood oxygen saturation (SpO_2), heart rate (HR), mean arterial pressure (MAP), were recorded just before anesthesia induction. Basal value of $rcSO_2$ in awake but sedated pre-medicated patient just before anesthesia (Tbas) was taken as initial point for assessment of $rcSO_2$ changes in different time points of the procedure. Sudden fall in $rcSO_2$ value higher than 20% of initial basal value was marked as critical. In the case that basal value was lower than 50%, decrease of $rcSO_2$ more than 15% was defined as critical. In the case of the critical $rcSO_2$ decrease the following algorithm was used. First, the neck position was checked and adjusted and possible external compression on carotid arteries or jugular veins was excluded. If the recovery of $rcSO_2$ value did not occur, second step was to increase the inspired concentration of oxygen (FiO_2) to 1.0. If there was no recovery of $rcSO_2$ after increasing of FiO_2, the propofol infusion rate (50% or more) or inspired concentration of sevoflurane (up to 2 MAC value) was increased to decrease the metabolic requirements of the brain (aim target of BIS values at these moments were 20-30).

In the TIVA group, anesthesia was induced by 1.5 mg/kg of propofol intravenously and the tracheal intubation was facilitated by 0.6 mg/kg rocronium bromide. Anesthesia was maintained by continuous propofol infusion of 75-250 μg/kg/min and 0.5 μg/kg of sufentanyl was applied for analgesia. In the VIMA group, vital capacity breathe technique with 8% sevoflurane in oxygen/air mixture (50%:50%) and fresh gas flow of 6 L/minute was used for anesthesia induction. Tracheal intubation was facilitated by 0.6 mg/kg rocronium bromide, and 0.5 μg/kg of sufentanyl was applied for analgesia. Afterwards, the sevoflurane concentration was decreased depending on BIS value. Supplemental doses of sufentanyl and rocuronium were applied in both groups if was needed. Patients were mechanically ventilated (controlled mechanical ventilation mode) with air and oxygen mixture 50%:50% with fresh gas flow of 1 l/min, 12 times per minute, tidal volume of 6 ml/kg and positive end-expiratory pressure (PEEP) of 5 cmH_2O. Thereafter, tidal volumes and respiratory rates were adjusted to reach adequate peripheral oxygenation and optimal end-tidal carbon dioxide ($ETCO_2$) values. Ephedrine and atropine intravenously (IV) were applied if the patient developed hypotension and/or bradycardia. Urapidil (10-50 mg) IV was given if there was marked hypertensive reaction lasting more than 3 minutes. Target values of MAP, HR, BIS, SpO_2 and $ETCO_2$ during anesthesia are shown in Table 1.

After induction of anesthesia, a pneumoperitoneum was created with carbon dioxide (CO_2) to reach maximally 15 mmHg of intraabdominal pressure and each patient was positioned in reverse Trendelenburg's position (30°) three minutes after. There were no changes in the degree of the tilt or head rotation during procedure what was standardized by research protocol. Regional cerebral oxygen saturation $rcSO_2$, MAP, HR, SpO_2 and $ETCO_2$ were noted two minutes

Table 1
Target values of MAP, HR, BIS, SpO_2 and $ETCO_2$ during anesthesia.

Parameter	VIMA group	TIVA group
[a]MAP/mmHg	±20% of baseline value	±20% of baseline value
[b]HR/min	50-90	50-90
[c]BIS/%	40-45	40-45
[d]$ETCO_2$/mmHg	32-35	32-35
[e]SpO_2 [e]/%	≥95	≥95

[a] MAP = mean arterial pressure,
[b] HR = heart rate,
[c] BIS = bispectral index,
[d] $ETCO_2$ = end tidal concentration of carbon dioxide,
[e] SpO_2 = peripheral oxygen saturation.