Effects of propofol or sevoflurane anesthesia induction on hemodynamics in patients undergoing fiberoptic intubation for cervical spine surgery: A randomized, controlled, clinical trial

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Abstract

Background and Aims: In patients undergoing surgery for cervical myelopathy, induction of general anesthesia can induce systemic arterial hypotension that may worsen spinal cord hypoperfusion and precipitate spinal injury. In this randomized, controlled, clinical trial study, we compared the hemodynamic changes related to anesthesia induction with intravenous (IV) propofol- and sevoflurane-based inhalational induction in patients undergoing fiberoptic intubation for cervical spine surgery.

Material and Methods: A total of 72 patients were studied. Hemodynamic effects were assessed measuring mean arterial pressure (MAP), and the echocardiographic evaluation of the left ventricular function. A Student’s t-test with Bonferroni correction or Chi-squared test was used, when appropriate, to assess differences in hemodynamic (extent of MAP drop and incidence of episodes of severe arterial hypotension) and other variables (occurrence and duration of episodes of apnea).

Results: Patients assigned to total IV anesthetic approach had a lower MAP and more significant changes in cardiac function compared to those who received the inhalational approach (68.1 ± 9.3 mmHg vs. 75.5 ± 10.3 mmHg; 25% vs. 5.5%).

Conclusion: Anesthesia induction with both propofol or sevoflurane is safe and effective. However, total IV anesthesia induction is associated with more pronounced MAP drop which can worsen spinal cord hypoperfusion.

Keywords: Arterial blood pressure, cervical myelopathy, cervical spine surgery, fiberoptic intubation, hemodynamic, hypoperfusion, neuroanesthesia, propofol, sevoflurane, spinal cord

Introduction

In patients undergoing surgery for cervical spine myelopathy, anesthesia induction and endotracheal intubation can determine systemic arterial hypotension that may worsen spinal cord hypoperfusion and can lead to neurological damage.[1,2] Several intubating devices have been proposed for the management of airways in patients with neurological conditions to minimize spinal cord compression and distortion due to mechanical effects of intubation,[3,4] and many anesthesiological approaches have been proposed to minimize the hemodynamic instability after anesthesia induction.[3] Among these, fiberoptic intubation (FOI) with topical anesthesia and mild systemic sedation are the preferred intubating techniques[5] as they guarantee minimal neck motion and adequate conditions for endotracheal tube positioning as well as hemodynamic stability.[5,6]
Propofol is one of the most commonly used agents for total intravenous (IV) anesthesia induction in patients undergoing FOI; however, it has shown to have the potential risk to induce apnea, arterial hypotension, and collapse of upper airways.\(^{7-11}\) Anesthesia induction with inhalational agents is suitable in patients with high risk of difficult intubation and in patients requiring tracheal intubation without neuromuscular blocking drugs. Sevoflurane, as an induction agent, has shown to induce a lower rate of respiratory complications when compared with propofol.\(^{9,11}\) Several studies have compared hemodynamic and respiratory variables occurring during anesthesia induction with sevoflurane or propofol; however, there is yet a lack of data with regard to patients undergoing cervical spine surgery for cervical myelopathy.\(^{8,9}\)

The aim of this prospective randomized study is to test if there is a difference (\(>20\%\)) in arterial pressure drop and hemodynamic changes (assessed through transthoracic echocardiogram) after anesthesia induction with propofol or with sevoflurane in patients undergoing FOI intubation for cervical spine surgery; we further aim to test whether the use of these techniques is safe for this group of patients.

**Material and Methods**

Ethical approval for this study (Ethical Committee N 394/11) was provided by the Ethical Committee of Policlinico Umberto I, according to the principles of the Declaration of Helsinki, and written informed consent was obtained from each patient. Inclusion criteria were: Patients aged >18 years, with acute or chronic symptoms or signs of cervical myelopathy undergoing cervical spine surgery. Exclusion criteria were: patients with preoperative hemodynamic instability or heart failure, pregnancy, known allergies to any anesthetic agent, chronic use of opiate analgesics, family history of malignant hyperthermia, coagulopathy, medical history of asthma, chronic obstructive pulmonary disease, recent history of airway infection, or chronic cough.

All patients were randomly assigned (using a computer-derived randomization list) to 1 of 2 treatment groups to receive anesthesia with propofol or sevoflurane as induction hypnotic. Patients were identified and assigned to the treatment group through a code, and the data were stored on a secure computer network, and only members of the research group had access to the data in accordance with good research practice. On arrival in the operating room, patients were monitored with a two-lead electrocardiogram for heart rate, pulse oximetry for arterial oxygen saturation (\(\text{SpO}_2\)), end-tidal \(\text{CO}_2\) (Biox, Ohmeda, France), invasive systolic blood pressure (SBP), diastolic blood pressure, and mean arterial blood pressure (MAP).

Intraoperative normothermia was actively maintained through a forced air warming system (Bair Hugger, 3M Company, United Kingdom). Immediately before anesthesia induction, all patients received isotonic saline solution through IV cannula-infusion rate 5 mL/kg of the ideal body weight (IBW), topical 2% lidocaine (1–5 mL, 20–100 mg), oropharynx anesthesia (which has shown to be safe and to ensure good conditions for FOI\(^{12,12}\)), and a single IV bolus of fentanyl (2 mcg/kg of IBW). All patients were preoxygenated for 3 min using a reservoir bag and 80% \(\text{O}_2\) with the fresh gas flow of 6.0 L/min\(^{13,14}\). In patients assigned to receive total IV anesthesia induction, propofol was administered by a target-controlled infusion system (Diprifusor, Fresenius, Grenoble, France with Schnider Pharmacokinetic Model) using a slow induction rate (injection rate 5 mL/min) with a target plasmatic concentration of 3.5–5 \(\mu\)g/ml titrated to abolish patient’s reaction (loss of consciousness confirmed by testing for loss of the eyelash reflex).\(^{9,15,16}\) In patients assigned to inhalational anesthesia induction, an 8% fraction of the inspired concentration of sevoflurane was delivered using a semi-closed circuit with a fresh gas flow of 6.0 L/min. The time needed to achieve a successful FOI, accomplished by the same operator throughout the study, was recorded. FOI technique included the insertion of a 6.5–8 mm internal diameter reinforced lubricated tube into the oropharynx; an adult fibroscope was passed through the tube and after visualizing the glottis straight ahead, lidocaine 2% was sprayed twice into the vocal cords (“spray as you go” technique). The fibroscope was then passed through the vocal cords visualizing the tracheal rings, and the tube was railroaded into the trachea. Correct tube placement was confirmed by bronchoscopy and capnography.\(^{17}\)

Left ventricular ejection fraction, end-systolic quotient (ESQ), and fractional shortening (FS) on transthoracic echocardiograms were prospectively recorded and interpreted offline by two independent observers blind to the clinical conditions\(^{18}\) to determine cardiac effects of the two tested regimens. A transthoracic echocardiogram was accomplished with a microconvex 2.25 MHz transducer (Hewlett Packard Sonos 2500); standard views were taken from the left parasternal (short- and long-axis views) and the heart apex (two-chamber and four-chamber views).

Percentage values of left ventricular FS were calculated according to the formula:

\[
FS = \frac{LVEDD−LVESD}{LVEDD} \times 100.
\]

LV ESQ was measured according to the formula:

\[
LV \text{ ESQ} = \frac{\text{SBP}}{LV \text{ESD}}.\]

\(\text{FS}\) is fractional shortening, \(\text{ESQ}\) is end-systolic quotient, \(\text{LV EDD}\) is left ventricular end-diastolic diameter, and \(\text{LV ESDD}\) is left ventricular end-systolic diameter.
Where, LV: Left ventricular, LVEDD: Left ventricular end-diastolic diameter, LVESD: Left ventricular end-systolic diameter, ESQ: End-systolic quotient, SBP: Systolic blood pressure.

Primary end-points included changes in MAP and echocardiographic data regarding cardiac function, recorded at four time points:
1. T1 (baseline): Before anesthesia induction
2. T2 (sedation steady state): After anesthesia induction when an adequate sedation level was achieved
3. T3 (intubation): Immediately after placement of the endotracheal tube
4. T4 (post-intubation): Five minutes after tracheal intubation.

Episodes of severe arterial hypotension, defined as MAP drop >20% from baseline values, were recorded.

Secondary end-points included the number of episodes of apnea during anesthesia induction and qualitative criteria associated with FOI.

The occurrence of apnea was defined as the cessation of spontaneous ventilation associated with an absence of expired carbon dioxide (by a sidestream carbon dioxide analyzer) lasting >10 s.[16,17] In patients who developed apnea, adequate pulmonary ventilation was ensured through a facial mask (hand-bag ventilation).

Qualitative criteria for FOI included the evaluation of four variables: jaw relaxation, resistance to FOI, vocal cord position, and neck movements during endotracheal tube positioning or cuff inflation (cough or movement). Each variable was rated as “excellent,” “good,” or “poor” according to the qualitative scoring system proposed by the consensus conference on the Good Clinical Research Practice in pharmacodynamic studies of neuromuscular blocking agents (GCP-nba) for FOI [Table 1].[19]

Sample size calculation was estimated on the basis of our previous experience; we determined that 30 patients for each group (propofol or sevoflurane) would be required to detect a 20% difference between the mean MAP of the two study groups at the end of anesthesia induction (T2: “sedation steady state”), using α and β values of 0.05 and 0.2, respectively. Considering a possible drop-out of 20% of patients, we planned to include 72 patients (36 for each study group). Data were entered into a database and checked by double entry and visual inspection. A Student’s t-test with Bonferroni correction or Chi-squared test was used, when appropriate, to assess differences in hemodynamic variables (extent of MAP drop and incidence of episodes of severe arterial hypotension) and other variables (occurrence and duration of episodes of apnea). Student’s t-test or Mann–Whitney U-test was used, when appropriate, to compare continuous normal and not normal distributed data. For categorical data, the Chi-squared statistic or the Fisher exact test was used. Results were expressed as mean ± standard deviation or where appropriate, as percentage. P < 0.05 was considered statistically significant.

**Results**

In an 18-month period, a consecutive series of 72 patients with acute or chronic symptoms or signs of cervical myelopathy undergoing cervical spine surgery were enrolled in this prospective, randomized study. Patients were aged 18–75 years and classified as the American Society of Anaesthesiology physical status (ASA-PS) I–III. All the patients enrolled completed the study. Demographic and clinical characteristics were similar between the two study groups [Table 2].

The mean baseline MAP values were similar in the two study groups. In both groups, anesthesia induction resulted in a significant reduction of MAP [Table 3]. However, at time point T2 (sedation steady state), a significantly higher number of patients receiving propofol developed severe arterial hypotension (MAP drop >20% from baseline values) compared to patients receiving sevoflurane (11/36 vs. 3/36; P = 0.042, by Chi-squared test) [Table 3]. At T3, the mean MAP values were significantly lower compared to the baseline, in particular, in the group receiving propofol. No differences were detected at T4 for both groups compared to the baseline.

Echocardiographic data showed that LV EF, LV EDD, and LV ESD values were in normal range in all patients at baseline and remained within physiological ranges throughout the study in both groups [Table 4]. In patients treated with propofol, LV FS and LV ESQ were significantly lower at T2 compared to baseline values, while in patients treated with sevoflurane, there were no significant changes of echocardiographic-derived variables. Interobserver variability in echocardiographic measures was <10%.

The incidence of apnea was higher in patients assigned to propofol treatment, while apnea duration was similar between the two study groups and it was not associated with episodes of oxygen desaturation (9/36 vs. 2/36; P = 0.049, by Chi-square test; 25 ± 4 vs. 22 ± 6 s; P = 0.08, by Student’s t-test). Intubating conditions during FOI, according to GCP-nba...
In this study, we originally describe the hemodynamic effects of anesthesia induction with propofol or sevoflurane in patients undergoing surgery for cervical spine myelopathy. We found that anesthesia induction with propofol determines a more pronounced drop in mean MAP and echocardiographic changes compared to inhalational anesthesia induction with sevoflurane.

The pathophysiological mechanisms involved in the development of cervical myelopathy are still unclear; however, there are several factors which can contribute to the progression of this pathology, that can be categorized as either static (such as disc degeneration, spondylisis, congenital stenosis) or dynamic mechanical factor (changes in neck flexion/extension canal), as recently reviewed by Dolan et al. Recent studies proposed that even several cellular mechanisms including ischemia, glutamatergic toxicity, neuroinflammation, and apoptosis could be involved in the progression of cervical myelopathy, suggesting that oligodendroglia of the spinal cord may be hypersensitive to hypotension and hypoperfusion, with consequent ischemic injury.

Therefore, in patients undergoing cerebral myelopathy surgery, close attention must be paid to avoid mechanical spinal cord compression and to maintain an adequate spinal cord perfusion to prevent further neurological damage. Several studies have discussed the risks related to laryngoscopy and cervical spine movements in these patients and several approaches have been proposed.

The effects on the hemodynamic system as well as the risk of neurological complications are yet to be deduced. To ensure an adequate spinal cord perfusion, MAP values should be maintained in line or above patient’s baseline values. Recent studies proposed that even several cellular mechanisms including ischemia, glutamatergic toxicity, neuroinflammation, and apoptosis could be involved in the progression of cervical myelopathy, suggesting that oligodendroglia of the spinal cord may be hypersensitive to hypotension and hypoperfusion, with consequent ischemic injury.

The strength of our work is the ability to underline the clinical relevance of an adequate hemodynamic management in this group of patients, where most of the attention is generally addressed and limited just to the choice of the technique used for tracheal intubation. In this context, we advocate the use of transthoracic echocardiography as a noninvasive tool for hemodynamic monitoring and management.

We propose a practical approach to the clinical management of anesthesia induction comparing two types of drugs which are commonly used, demonstrating for the first time in this group of patients that sevoflurane is less hypotensive than propofol. The challenge in patients undergoing cervical myelopathy surgery is that it is very important to maintain hemodynamic stability, but at the same time to ensure an adequate depth of anesthesia during intubation to avoid secondary spinal cord injury by mechanical damage.
Our results confirm and extend previous evidence recorded in a different subset of patients, where propofol anesthesia induction caused more pronounced hemodynamic changes compared to sevoflurane anesthesia induction presumably because of its side effects on myocardial contractility and direct vasodilation.[19-22] Despite these statistically significant differences, both techniques are suitable for clinical use as recorded differences were rarely associated with MAP values below the safety threshold[21] at any time point. The reduction of LV FS and LV ESQ values at T2 in patients who received propofol suggests a reduction of afterload and preload rather than changes in cardiac contractility.[23] However, to minimize hemodynamic changes related to total IV anesthesia induction with propofol, we have selected a slow induction rate protocol that requires longer time but induces minimal effects on arterial pressure.[24]

Furthermore, we observed that the incidence of apnea was higher in propofol-treated patients as previously described,[17] however, the duration of apnea was similar in the two study groups and lasted <30 s in all the cases.

**Limitations**

There are several limitations in this study. First, bispectral index (BIS) monitoring has not been used to assess anesthesia depth. Although it might have been informative, BIS-derived measures do not have conclusive evidence,[25] and we considered that the clinical criteria used in this study could adequately describe the level of anesthesia achieved before intubation. Second, the use of sevoflurane-based inhalational induction could not induce deep anesthesia state. This is unlikely in our patient population because the time required for the intubation was limited. However, should the patient present a difficult and protracted intubation, it needs to be reminded that the anesthesia depth might be lighter when sevoflurane is used compared with propofol. Finally, a more accurate estimation of the effects of anesthesia induction on cardiac hemodynamics would require a more aggressive monitoring (such pulmonary artery catheterization or other invasive monitoring techniques including the measurement of cardiac output, central venous pressure to the degree of venous drainage impairment and to assess venous pressure). However, due to a lack of evidence supporting the use of invasive hemodynamic monitoring in patients undergoing these procedures, these techniques were not performed. Finally, it would be very useful in these patients the calculation of spinal cord perfusion pressure (SPP), to assess the correct value of MAP to achieve. However, at present, the only reliable way to measure spinal cord perfusion is through the insertion of a pressure probe placed subdurally in the spine and calculating spinal cord perfusion as SPP = MAP - spinal cord pressure.[26] Again, this invasive procedure was not applicable in this case.

**Conclusion**

In patients undergoing surgery for cervical spine myelopathy, attention should be addressed to minimize arterial hypotension related to anesthesia induction to ensure adequate spinal cord perfusion, by preemptive volume replacement and with the use of an adequate anesthesiological slow induction rate protocol. Both total IV anesthesia induction with propofol and inhalational anesthesia induction with sevoflurane are safe and suitable techniques for anesthesia induction and FOI without nbas. However, total IV anesthesia induction with propofol, even used at slow induction rate, can cause a significant drop in MAP even when the value is within the safety threshold for spinal cord perfusion. Further studies are needed to understand the effects of different techniques of anesthesia induction in patients with cervical spine myelopathy, to minimize the risk of neurological and systemic complications in this group of patients.

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Conflicts of interest
There are no conflicts of interest.

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