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## CASE REPORTS

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# INHALATIONAL INDUCTION WITH “VASOPARALYTIC” SEVOFLURANE: ARE WE “HYPEROXYGENATING” WHILE ANESTHETIZING DEVELOPING BRAINS? A CASE SERIES DISCUSSION\*

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### Abstract

*Background:* The concerns for hyperoxia-related brain tissue injury are well known to the medical community. The cerebro-vasodilatory properties of sevoflurane may create relative cerebral tissue “hyperoxia” during inhalational induction as compared to a propofol-based intravenous induction of anesthesia.

*Study Objectives:* The objective for this case series discussion was to identify any differences in cerebral tissue oxygenation secondary to induction of anesthesia with sevoflurane versus propofol.

*Methods/Study Procedures:* After institutional review board approval, the computer data of tissue cerebral oximetry of pediatric patients (1-18 years age group) undergoing non-cardiac surgeries was comparatively analyzed for changes over time between the groups of children who received sevoflurane induction versus propofol induction of anesthesia. “Hyperoxia” (“hyperoxygenation”) was defined as significant percent changes from the baseline values as recorded in tissue cerebral oximetry.

*Results:* In this case series, seven patients underwent inhalational (INH) induction with high concentrations (8%) sevoflurane with nitrous oxide in 33% oxygen and four patients underwent intravenous (IV) induction with 2 mg/kg propofol and nitrous oxide in 33% oxygen. As compared to propofol, significant cerebral tissue “hyperoxia” occurred with sevoflurane induction ( $p = 0.003$ ). This did not resolve over time.

*Conclusion:* As compared to intravenous induction with propofol, inhalational induction with “vasoparalytic” sevoflurane “hyperoxygenates” developing brains. This observation requires validation in larger trials to conclude appropriate effect on our practice of pediatric anesthesia and pediatric patient safety under anesthesia.

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## Introduction

The concerns for hyperoxia-related brain tissue injury are well known to the medical community<sup>1-3</sup> and may contribute to neuroapoptosis in developing brains of children undergoing anesthesia. The concerns include but are not limited to widespread apoptotic neurodegeneration, induction of pro-inflammatory cytokines and inhibition of growth factor signaling cascades<sup>2</sup>.

Sevoflurane, a potent cerebro-vasodilator, is the agent of choice for inhalational induction of anesthesia. The cerebro-vasodilatory properties of sevoflurane may create relative cerebral tissue “hyperoxia” during inhalational induction as compared to a propofol-based intravenous induction of anesthesia. The hyperoxia created for even a few minutes maybe detrimental<sup>3</sup>.

The objective for this case series discussion was to identify any differences in cerebral tissue oxygenation secondary to induction of anesthesia with sevoflurane versus propofol.

## Methods

After institutional review board approval, the computer data of tissue cerebral oximetry of pediatric patients (1-18 years age group) undergoing non-cardiac surgeries was analyzed. We analyzed the data for patients in whom INVOS®™ Cerebral/Somatic Oximeter (©Somanetics Corporation, Troy, Michigan, United States; ™Covidien, Mansfield, Massachusetts, United States) was used during May-June 2011 at Childrens Hospital of Michigan, Detroit Medical

Center, Detroit, Michigan, United States. Oximetry data was compared between the groups of children who received sevoflurane induction versus propofol induction of anesthesia. The changes from the baseline in the tissue cerebral oximetry were statistically compared at different points of recorded times starting from the baseline time point immediately before the induction of anesthesia to about one hour after the initiation of induction. Though computer data of tissue cerebral oximetry extended beyond one hour time-period, these extended data points were only used for graphical extrapolation because of insufficient comparative data after the one hour timeperiod.

For the purposes of this case series discussion, “hyperoxia” (“hyperoxygenation”) was defined as significant percent changes from the baseline values as recorded in tissue cerebral oximetry. Absolute tissue cerebral oximetry values were also recorded.

## Results

Cerebral tissue oximetry data was available for eleven pediatric patients. Seven patients underwent inhalational (INH) induction with high concentrations (8%) sevoflurane with nitrous oxide in 33% oxygen. Four patients underwent intravenous (IV) induction with 2 mg/kg propofol and snitrous oxide in 33% oxygen. All patients were maintained on 1.5% isoflurane with medical air in 33% oxygen. Per our analysis, as compared to propofol, significantly marked cerebral tissue “hyperoxia” occurred with sevoflurane induction ( $p = 0.003$ ). This did not resolve over time (Fig. 1). As anesthesia period progressed beyond the one-hour time-period, children who had received propofol induction showed cerebral tissue “hyperoxia” secondary to vasodilatory characteristics of isoflurane maintenance. However, the levels of “hyperoxia” never reached the levels as observed in patients who had undergone sevoflurane induction (Fig. 1). Conversely, the statistical significance was not appreciated in the absolute values ( $p = 0.687$ ) of the tissue cerebral oximetry between the two groups of patients (Fig. 2); this may have been secondary to very small number of patients, short duration of total anesthesia time studied, and higher baseline absolute oximetry values in patients who underwent propofol induction.

Fig. 1

Mean Percent Changes in Cerebral Tissue Oximetry over Time

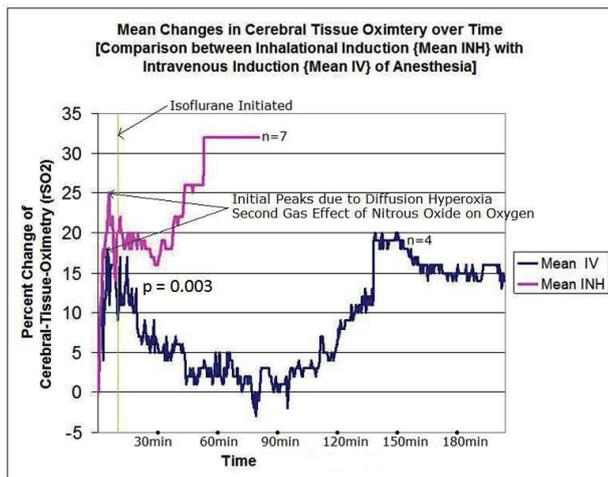
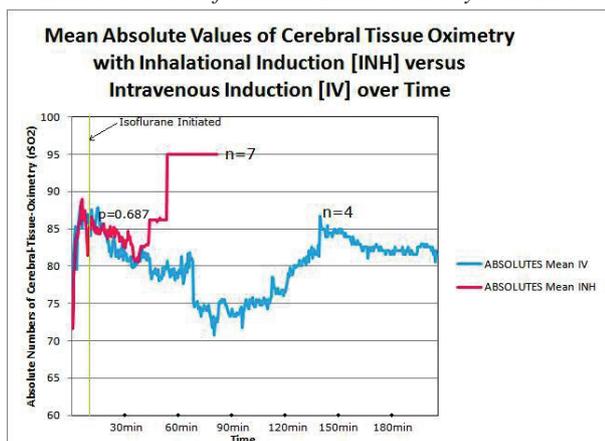


Fig. 2

Absolute Values of Cerebral Tissue Oximetry over Time



## Discussion

The safety of anesthesia for children has gained limelight because animal studies have reported neuroapoptotic properties of most anesthetic agents. The only differences elicited in those studies are the possible differences in the severity of the neuroapoptosis induced by the different anesthetic agents<sup>4-7</sup>. Additionally, the concerns for hyperoxia-related brain tissue injury are not new to the medical community<sup>1,8-10</sup>. The only paradigm shift is that hyperoxia-related tissue injury (most common to lungs and brain) may be a continuum of spectrum. Hyperoxia-related lung injury occurs more often at normobaric conditions and hyperoxia-related cerebral injury occurs more often at hyperbaric conditions<sup>10</sup>.

However, this continuum cannot rule out the possibility of the hyperoxia-related cerebral injury at normobaric conditions. The ideal anesthetic technique and choice of agents used differ in pediatric anesthesia. The inhalational induction of anesthesia is often standard of care in the pediatric anesthesia work environments where avoidance of needle sticks often precludes intravenous induction of anesthesia. Sevoflurane (the agent of choice for inhalational induction) decreases cerebral metabolic rate despite being a cerebral vasodilator. Conversely, propofol (the agent of choice for intravenous induction) decreases cerebral blood flow as well as the cerebral metabolic rate. Therefore, sevoflurane creates a potential physiological dilemma for the cerebral tissues due to increased ratio of oxygen supply to oxygen demand as compared to propofol. As cerebral tissue oximetry may provide an estimate of tissue oxygen tension<sup>11</sup> or saturation, the dilemmatic physiological phenomenon of luxury oxygenation was reflected in our case series as the significantly different changes in the cerebral tissue oximetry incurred by sevoflurane induction (Fig. 1). Additionally, nitrous oxide (used during induction of anesthesia for ‘second gas’ effect<sup>12</sup> on sevoflurane-induction and for reducing propofol injection pain) induces transient diffusion hyperoxia secondary to ‘concentrating effect’ or ‘second gas’ effect on oxygen<sup>13-14</sup> that was reflected as the initial V-shaped peaks in the graphical presentation of changes in cerebral tissue oximetry (Fig. 1).

There are few study limitations for this case series. Firstly, it is difficult to interpret these observations in regards to quantifying potential neuroapoptotic or hyperoxia cerebral injury because this case series had a very small number of patients with short duration of observation period without any short-term or long-term follow up to quantifiably assess the abovementioned obscure injuries. Secondly, higher baseline absolute values of cerebral tissue oximetry were observed in the intravenous induction group (Fig. 2) because these patients had pre-existing intravenous access and were well rehydrated with maintenance infusions; and they received intravenous induction of anesthesia only because of their pre-existing intravenous access as inpatients. In contrast to these inpatients, the fasting outpatients had received inhalational induction of anesthesia per universal practice protocols based on prevailing patient/provider choices. Reciprocally, the

difference in the baseline absolute values of cerebral tissue oximetry may be suggestive that fasting patients are exposed to starvation induced hypovolemia<sup>15</sup> and its deleterious effects on cerebral tissue environments and it may be uncertain how these hyperosmolar and susceptible environments respond to sudden luxury oxygenation with sevoflurane induction. Finally, as the cerebral tissue oximetry has been primarily quantified to indirectly and non-invasively assess the degree of cerebral ischemia/cerebral hypoxia, the higher values of cerebral tissue oximetry have not been quantified to appropriately reflect the degree of cerebral “hyperoxia” that may be cumulative reflection of increased oxygen delivery (cerebral vasodilation), and/or decreased oxygen extraction (increased anesthetic depth) and/or increased oxygen content (cerebral hypoxemia). Based on these limitations, the future projects should assess (a) whether the results of this small case series can be validated in larger retrospective and prospective trials (b) whether sevoflurane induction would have increased the oximetry levels if patients were well hydrated before induction of anesthesia, (c) whether the higher doses of sevoflurane (8%) required to

rapidly achieve induction of anesthesia is the major contributing factor for the changes observed in our case series.

## **Conclusion**

As compared to intravenous induction with propofol, inhalational induction with “vasoparalytic” sevoflurane “hyperoxygenates” developing brains. This observation requires validation in larger trials to conclude appropriate effect on our practice of pediatric anesthesia and pediatric patient safety under anesthesia.

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