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Original Contribution

Induction techniques for pediatric patients with congenital heart disease undergoing noncardiac procedures are influenced by cardiac functional status and residual lesion burden

Koichi Yuki, M.D.*, Sandra Lee, M.S., Steven J. Staffa, M.S., James A. DiNardo, M.D.

Department of Anesthesiology, Critical Care and Pain Medicine, Division of Cardiac Anesthesia, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, USA

Department of Anaesthesia, Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, USA

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ABSTRACT

Study objective: Appropriate agent selection in patients with congenital heart disease (CHD) undergoing cardiac surgery and catheterization have been extensively reviewed in the literature. To date, there has not been an analysis of induction drug choices made in a large group of CHD patients undergoing non-cardiac procedures and intraoperative events.

The primary objective was to characterize induction agent selection in CHD patients undergoing non-cardiac procedures and examine its association with intraoperative events.

Design: Retrospective chart review analysis.

Setting: A single center study.

Patients: Children with CHD who underwent non-cardiac procedures.

Intervention/measurement: Using the electronic preoperative anesthesia evaluation form we identified 2966 cases performed under general anesthesia. We examined the association between patient characteristics (ASA PS and CHD severity) and induction drugs using multinominal logistic regression test. We also examined the association of induction drugs with intraoperative adverse events using Fisher exact test.

Main results: Inhalational and intravenous inductions were conducted in 35.7% and 64.3% of general anesthesia cases, respectively. Sevoflurane was the main inhalation induction drug. Propofol was used as the induction agent in 54.3% of cases, while etomidate, midazolam/fentanyl, and ketamine were used as the induction agent in 18.3% 16.6%, and 10.1% of cases, respectively. ASA PS and CHD severity predicted induction drugs better than single ventricle status or ventricular function. Intraoperative inotrope use was seen more frequently in cases induced by ketamine, etomidate or opioids over sevoflurane or propofol.

Conclusions: Patients with higher ASA classes and CHD of more severity tend to be induced more with etomidate, ketamine or opioids over sevoflurane or propofol. Use of etomidate, ketamine or opioids was more associated with inotrope use, but there was not significant difference in respiratory events among different induction agents. Causative association needs to be examined in the future.

1. Introduction

Due to improved survival and life expectancy, more children with congenital heart diseases (CHD) present for treatment of non-cardiac illness, and many require non-cardiac procedures under anesthesia [1, 2]. Small, single institutional and large, multi-institutional database studies have consistently demonstrated patients with CHD undergoing non-cardiac surgery to be at increased anesthetic risk and also at high risk of morbidity and mortality [3–8]. Anesthesia induction is one of critical phases in anesthesia care, and the effects of intravenous and inhalation anesthetic induction drugs on cardiovascular physiology in patients with CHD have been extensively investigated [9–13]. However, there is no information available as to how anesthetic induction drugs were selected and if they were associated with intraoperative events in this patient cohort. The primary objective of this investigation was to characterize the choice of induction drugs in CHD patients undergoing non-cardiac procedures in our institution, and assess their association with intraoperative events.

* Corresponding author at: Department of Anesthesiology, Critical Care and Pain Medicine, Division of Cardiac Anesthesia, Boston Children's Hospital, 300 Longwood Avenue, Boston 02115, USA.

E-mail addresses: koichi.yuki@childrens.harvard.edu (K. Yuki), Steven.staffa@childrens.harvard.edu (S.J. Staffa), James.dinardo@childrens.harvard.edu (J.A. DiNardo).

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2. Methods

2.1. Data collection

This retrospective study was reviewed and approved by the institutional review committee (IRB) in Boston Children's Hospital, and consent was waived. Using the electronic preoperative anesthetic evaluation form (PAEF), we screened for and ultimately identified a list of pediatric patients with CHD who underwent non-cardiac procedures between September 2008 and August 2013 at Boston Children's Hospital. In our institution, these patients are anesthetized by pediatric anesthesiologists in the Main Operating Room Anesthesia group. Pediatric cardiac anesthesiologists provided consultative input as needed. The following information was collected; age, weight, cardiac diagnosis, procedures performed, emergent versus non-emergent status, ventricular function as assessed by echocardiogram within the preceding 6 months, American Society of Anesthesiologist (ASA) physical status (PS), and classification into three groups (minor, major or severe CHD) based on residual lesion burden and cardiovascular functional status as defined in pediatric database of the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP Pediatric) as previously described [3] (Table 1). The following characteristics related to conduct of anesthesia care were also collected: type of anesthesia (general anesthesia, monitored anesthesia care), anesthetic induction drugs and maintenance drugs. Cases, started with monitored anesthesia care, but converted to general anesthesia, were not counted as general anesthesia cases here, because our interest was on how patients were induced at the beginning of cases. Inhalation induction was performed with sevoflurane in oxygen and less commonly in combination with nitrous oxide (we consider sevoflurane as primary induction drug in this case as well). Intravenous induction was performed using propofol, ketamine, etomidate or opioid +/− benzodiazepine (categorized as opioid) only. The following intraoperative adverse events were collected: inotrope use, cardiac arrest, desaturation, difficult intubation and bronchospasm/laryngospasm. Inotrope use was defined as continuous infusion of inotrope.

2.2. Data analysis

Categorical variables were expressed as number and percentage, and continuous variables were expressed as median and interquartile percentages. Normality was measured using the Shapiro-Wilk test. Statistical analysis was performed using multinomial logistic regression analysis to examine the relationship between patient characteristics and the choice of induction drugs. The Akaike information criterion (AIC) was used as an estimator of the relative quality of statistical models for a given set of data [14]. The preferred model is the one with lower AIC value. We also examined the relationship between anesthetic induction agents and intraoperative adverse events for patients with CHD of different severity using Fisher exact test. Lastly, the correlation between ASA PS class and severity of CHD was evaluated using Spearman's correlation coefficient. Data were analyzed using statistical software STAT13 (StataCorp LLC, College Station, TX, USA). In order to reduce the risk of Type I statistical error due to multiple testing with five induction drugs (one drug as a reference), we have implemented a Bonferroni correction in which we consider the two-sided alpha level of $p < 0.01$ (0.05/4) for statistical significance.

Table 1
Congenital heart disease classification.

Classification	Definition
Minor CHD	• Cardiac condition with or without medication and maintenance (e.g., ASD, small to moderate VSD without symptoms) • Repair of CHD with normal cardiovascular function and no medication
Major CHD	• Repair of CHD with residual hemodynamic abnormality with or without medications (e.g., TOF with free PR, HLHS including Stage 1 repair)
Severe CHD	• Uncorrected cyanotic CHD • Patients with any documented pulmonary hypertension • Patients with ventricular dysfunction requiring medications • Listed for heart transplantation

Table 2
Services involved in procedures.

ORL	26.1%
Radiology	14.0%
General surgery	13.2%
Orthopedics	10.5%
Gastroenterology	10.0%
Urology	5.9%
Dental	4.5%
Plastics	3.1%
Hematology	2.7%
Ophthalmology	2.7%
Neurosurgery	2.6%
Pulmonary	1.2%
Maxillofacial	0.6%
Dermatology	0.3%
Others	2.6%

3. Results

Among all the cases, 2966 cases were performed under general anesthesia. Services involved in these cases were shown in Table 2. Also syndromes were seen in 40.4% of cases, and Down syndrome was the most prevalent one (16.4% of cases). 1060 cases were subject to inhalation induction, and 1906 cases were induced intravenously (Table 3). Inhalation induction was exclusively performed using sevoflurane. For intravenous induction, propofol was used in 54.3% of cases, while etomidate, midazolam/fentanyl, and ketamine were used as induction agents in 18.3% 16.6%, and 10.1% of cases, respectively. The association of choice of induction drugs with various parameters was summarized in Table 4. We performed multinomial logistic regression analysis to assess the association between the choice of induction drugs and various patient characteristics (**Supplemental Table 1**). Sevoflurane was used as a reference induction drug. Etomidate, ketamine and opioid induction was performed more in ASA

Table 3
Patient characteristics between inhalational and intravenous induction.

	IV induction (1060)	Inhalational induction (1906)
Age (months)	60 (15, 168)	46.5 (20, 84)
ASA class		
ASA I	24 (2.3)	81 (4.2)
ASA II	238 (22.4)	699 (36.7)
ASA III	603 (56.9)	1012 (53.1)
ASA IV	191 (18.0)	112 (5.9)
ASA V	4 (0.4)	2 (0.1)
Emergency	64 (6.0)	14 (0.7)
ACS CHD classification		
Minor CHD	658 (62.1)	1489 (78.1)
Major CHD	313 (29.5)	356 (18.7)
Severe CHD	89 (8.4)	61 (3.2)
Single V	123 (11.6)	61 (3.2)
Non-single V	937 (88.4)	1845 (96.8)
PreBDG	27 (2.5)	14 (0.7)
BDG	26 (2.5)	20 (1.0)
Fontan	66 (6.2)	26 (1.4)
BiV	4 (0.4)	1 (0.1)
Echo < 6 month	838 (79.1)	1409 (73.9)
Not available	222 (21.0)	495 (26.0)
Normal fxn	744 (70.2)	1342 (70.4)
Mild-mod dysfxn	84 (7.9)	64 (3.4)
Severe dysfxn	10 (0.9)	3 (0.2)