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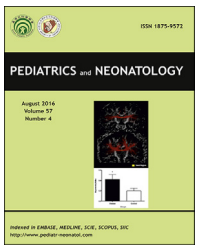

Original Article

Atropine use may lead to post-operative respiratory acidosis in neonates receiving ductal ligation: A retrospective cohort study

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Key Words
respiratory acidosis;
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patent ductus arteriosus;
ketamine

Background: Patent ductus arteriosus (PDA) is one of the most common cardiac conditions in preterm infants. Closure of the PDA in symptomatic patients can be achieved medically or surgically. Atropine is commonly administered in general anesthesia as a premedication in this age group but with limited evidence addressing the effect of its use. Our study examined the association of the use of atropine as a premedication in PDA ligation and the risk of post-operative respiratory complications.

Methods: This retrospective cohort study included 150 newborns who have failed medical treatment for PDA and received PDA ligation during 2008–2012 in a single tertiary medical center. Ninety-two of them (61.3%) received atropine as premedication for general anesthesia while 58 (38.7%) did not. Post-operative respiratory condition, the need of cardiopulmonary resuscitation and the presence of bradycardia were measured.

Results: Patients with atropine use were associated with increased odds of respiratory acidosis in both univariate analysis (22.9% vs 7.3%; OR = 3.785, 95% CI = 1.211–11.826, $p = 0.022$) and

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multivariate analysis (OR = 4.030, 95% CI = 1.230–13.202, $p = 0.021$), with an even higher odds of respiratory acidosis in patients receiving both atropine and ketamine.
Conclusion: The use of atropine as premedication in general anesthesia for neonatal PDA ligation is associated with higher risk of respiratory acidosis, which worsens with the combined use of ketamine.

1. Introduction

Closure of ductus arteriosus is a complex process at birth, but it may sometimes fail.[1] Patent ductus arteriosus (PDA) is one of the most common cardiac conditions in preterm infants with an incidence rate of between 40% and 60% depending on the estimated gestational age.[2] Intervention to close the PDA is indicated in symptomatic patients because of the increased risk in developing prolonged ventilation, pulmonary hemorrhage and bronchopulmonary dysplasia (BPD). Closure of PDA can be achieved medically or surgically. Surgical ligation of PDA is usually reserved for patients with deteriorating hemodynamic status after failing medical treatment.[3]

Neonates with PDA who require surgical intervention have higher risk of developing complications from anesthesia due to multisystem-immaturity and low birth weights.[3] The anesthetic procedures for neonatal surgeries were usually tailored individually and more challenging due to the variety in anatomy, physiological conditions, and associated congenital disorders.[4,5] For anesthesiologists, the goals are not only to improve survival rate but also to prevent long-term neurologic and pulmonary morbidities. Despite several anesthetic methods have been proposed for preterm or very-low-birth-weight infants, yet still there was no consensus of the ideal anesthetic method.[6–9]

Atropine is more commonly administered in general anesthesia as a premedication in pediatric population than in adult population, and it serves as a method to reduce cholinergic stimulation and salivary secretions.[10,11] Post-operative respiratory complications, such as having sticky secretion, as well as being prone to develop apnea and carbon dioxide retention, were sometimes noticed in neonates after PDA ligation surgery in our neonatal intensive care unit, especially in neonates who received atropine. However, there were limited studies addressing the effect of atropine use in this patient cohort. The aim of this study is to compare the post-operative outcomes and the effects of atropine use as well as the combined effect with other anesthetics in neonates receiving general anesthesia for PDA ligation.

2. Methods

2.1. Patients and study design

All neonates who received surgical ligation of PDA between 2008 and 2012 were retrospectively collected. The neonates receiving cardiovascular surgeries other than ductal ligation were excluded from our study cohort. We initially identified 215 patients, 14 of whom had other combined surgeries, and 7 of whom received atropine during surgery for bradycardia instead of the use as premedication. Forty-four patients with incomplete data were excluded. Thus, a total of 150 patients were enrolled in our study.

All patients in our study cohort were symptomatic and had failed medical treatment before going into surgery. All PDA ligation surgeries were performed by the same pediatric cardiac surgeon (Wu SJ). Peripheral intravenous access was obtained prior to anesthesia for administration of general anesthesia medications. The patients received premedication with or without atropine 0.01 mg/kg per preference of each individual anesthesiologist. The anesthesia began with ketamine 2 mg/kg and sevoflurane 2–3%, and incremental dose would be considered according to patients' responses.

Patients might be given atropine for bradycardia (HR < 100/min) during operation, but they were excluded from our study cohort. Our analysis only included those who received atropine initially. After the operation, the neonate was transferred back to neonatal intensive care unit with the standard care protocol. Capillary blood gas analysis was routinely obtained within 2 h and chest radiograph was obtained within 6 h after operation, respectively.

Demographic data, outcomes and respiratory complications of each patient were collected. Patients' outcomes and respiratory complications were also collected for analysis, including respiratory acidosis (defined as pH <7.3 and carbon dioxide retention CO_2 >50 mmHg) by capillary blood gas analysis, signs of atelectasis from chest radiograph, the need of high frequency oscillatory ventilation (HFOV), cardiopulmonary resuscitation (CPR) and the presence of bradycardia (HR < 100/min) during operation.

2.2. Statistical analysis

Categorical data were presented as event numbers and percentages and tested by Pearson's chi-square test. Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR) and tested by Student's t-test. Pre-operative atropine use and outcome analyses were tested by both univariable and multivariable logistic regression models. A two-sided p value of less than 0.05 was considered statistically significant. Statistical analysis was performed using commercially available software (Stata 13.1, StataCorp LP, College Station, Texas, USA.).

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