

## Comparing the Incidence of Pulmonary Edema in Anesthesia (*with or without use of morphine and lasix*) in Children Undergoing PDA Surgery

A. Ebadi<sup>1</sup>, M. Deghani Firooz abadi<sup>2</sup>, M. Soltan zade<sup>3</sup>, A. Emmami Moghadam<sup>4</sup>, SH. Nesioonpour<sup>5</sup>, R.Akhondzadeh<sup>6</sup>, K. Behaien<sup>7</sup>, A. Ghorbani<sup>8</sup>, SH. Beladi behbahani<sup>9</sup>

1,3. Associate Professor of Cardiac Anesthesiology MD, Department of Cardiac Anesthesiology, Golestan Hospital, Ahvaz Jundishapour University, Ahvaz, Iran

2. Assistant Professor of Cardiac Anesthesiology MD JundiShapour University, Ahvaz,

5, 6- Assistant Professor of Anesthesiology MD JundiShapour University, Ahvaz.

7- Assistant Professor of JundiShapour University, Ahvaz

4- Assistant Professor of Cardiac pediatric MD, Of Jundishapour University, Ahvaz

8, 9. Resident of Anesthesiology MD of Jundishapour University, Ahvaz

**Abstract: Introduction:** Patent ductus arteriosus (PDA) is a congenital cardiovascular disorder found in patients of all ages, from tiny premature infants to older adults (1). Persistent patent ducts arteriosus often cause hemodynamic and respiratory disorders, which require use of inotropic drugs and respiratory support in the full term infants. Surgical ligation should be considered for patients when medical therapy fails (2). The aim of this study was two anesthesia techniques evaluation for pulmonary edemas reduce in PDA surgery. **Methods and Materials:** In this study, 120 patients underwent PDA surgery, Patients were divided into two groups of 60, the patients in first group received morphine and lasix during anesthesia but second group received nothing. **Results:** The average age of the patients in the case and control groups was 32.8 and 31.36 months. Frequency of Male and female in case and control groups was 38.3%, 61.7% and 45%, 55%, respectively. In control group, from 60 patients, 18.3% had pulmonary edema and 5% of them had loss of consciousness. There was significant difference between case and control groups about patients with pulmonary edema. Also, RR (0.001), Pao<sub>2</sub> (p=0.005), PH (p=0.01) and PR (P=0.003) had significant difference in cases and controls. **Conclusion:** The findings of this study suggest that the use of morphine and Lasix is useful for reduction of pulmonary edema after PDA surgery. Further studies are needed to find the better management method.

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### 1. Introduction

The patent ductus arteriosus (PDA) is a vascular structure that connects the proximal descending aorta to the roof of the main pulmonary artery near the origin of the left branch pulmonary artery. This essential fetal structure usually closes spontaneously after birth (1). Permanent closure of PDA usually occurs within a few weeks after birth however; the failure of closure within 72 hours after birth will result in persistent PDA (3).

Clinical significant and physiological damages that PDA can do depend on PDA size and patient cardiovascular status. Although PDA often diagnosed in infants, it may not be discovered until childhood or sometime even adulthood (asymptomatic PDA), therefore PDA may also be discovered by accident during Echo cardiography for other reason and it can be in different sizes (small/medium/large). Regardless of the size, it is important that pediatric and adult Cardiologist know about the clinical presentation of a PDA, pathophysiology and control of the PDA (1).

The incidence of PDA in term neonates has been estimated 1 in 2000 births (4-5) that include 5-10% of all congenital heart disease although; by considering the asymptomatic PDA the estimated incidence will rise to 1 in 500 births(6). In most report the ratio of girls to boys is 2:1. (1)

Cause permanent stay open ductus arteriosus, at 24 to 48 hours of neonatal life is not well known. Clearly premature birth, increased incidence of PDA is mostly due to physiological factors related to prematurity rather than hereditary disorder of PDA (7). In term infants often it appears to be sporadic, but increasing evidence shows that genetic factors play an important role in many patients with PDA. In addition, other factors such as prenatal infection appear to play a role in some cases. (1). Persistent patent ductus arteriosus often cause hemodynamic and respiratory disorders, which require use of inotropic drugs and respiratory support in the full term infants. When medical therapy failed, surgical ligation should be considered for patients (2). The aim of study is to assess the effect of two

anesthesia techniques on reduction of pulmonary edema in PDA surgery.

## 2. Methods

120 children from 1 to 12 years old with PDA and pulmonary hypertensions participate in this study. The children were divided into two groups of 60; surgical ligation of PDA was performed in the operating room of Golestan Hospital. Following drugs used for induction of anesthesia in all patients:

- I. Midazolam: 0.1 mg/kg
- II. fentanyl 3-5µg/kg
- III. Sodium thiopental: 4-6 mg/kg
- IV. Atracurium 0.5 mg/kg

Then anesthesia was maintained with intermittent doses of fentanyl (0.5-1.5 µg/kg). During anesthesia monitoring of ABG, urinary Out put control and aggressive control of BP was performed for all patients. The first group as prophylaxy for pulmonary edema received morphine (0.1 mg / kg) and lasix (0.5 mg / kg) with regard to the hemodynamic after clamping off the ductus.

At the end of operation intubated patients transferred to ICU and specific parameters like Blood Pressure, ABG changes, Heart rate, intubation time and level of consciousness were recorded.

Then, the classic stages of extubation from IPPV to SIMV mode and afterwards Spontaneous mode with monitoring vital signs and Controlling ABG and heating patients were Wean until 24 hours after extubation (When the patient is in ICU), symptoms like dyspnea, pulmonary rales and reduce and control Out put together the results of both groups were compared.

## 3. Results

The average age of the patients in the case and control groups was 32.8 and 31.36 months. Frequency of Male and female in case and control groups was 38.3%, 61.7% and 45%, 55%, respectively. In the control group, 11 out of the 60 patients (18.3%) had pulmonary edema and 5% of them had loss of consciousness. Only 1 patient from those patients who had pulmonary edema required re-intubation and 5% of them were suffering from decreased level of consciousness. Significant differences between groups was found in terms of developing pulmonary edema after closure of PDA, ( $P = 0.0001$ ). Also significant differences between groups in terms of respiratory rate ( $p = 0.001$ ), arterial oxygen ( $p = 0.005$ ), PH ( $p = 0.01$ ) and heart rate ( $P = 0.003$ ) was found. However, there was not significant different between the two groups in the mean arterial pressure ( $P = 0.839$ ), mean pressure in ICU ( $P = 0.096$ ) and after extubation ( $P = 0.238$ ).

One case of death in patients with pulmonary edema was observed. Average transfer time from the ICU for case group was 24 hours after surgery and for control group was 36.5 hours which has significant different with case group ( $p = 0.01$ ).

## 4. Discussion

During intrauterine life, 10% of cardiac output passes through the lungs and 90% shunt through the ductus arteriosus to the aorta and systemic circulation. After birth, most of right ventricle outflow should be able to pass through the lungs for gas exchange, thus ductus arteriosus should be closed right after the birth in full term infants.

In 80% of full term infants ductus arteriosus close within 48 hours after birth and in 100% of them close in 96 hours after birth. Failure of ductal closure causes special problems in infants are pre term (10, 8, and 9).

From hemodynamic point of view, significant shunt of PDA present in 40% of infants with weight less 1 kg and in 20% of infants with weight between 1-5/1 kg (10, 8, and 9).

Pre-term infant with respiratory distress syndrome requires surfactant and ventilation, usage of surfactant itself associated with an increased risk of PDA development. The indomethacin and ibuprofen are used for treatment of PDA (11, 12) PDA treatment has negative correlation with fetal age and birth weight (10, 8, and 9). Surgical indications include contraindications for medical therapy and failure of the second indomethacin course. Two forms of surgical therapy are performed for closure of PDA, the traditional surgical approach, Thoracotomy or Video-assisted thoracoscopic surgery (VATS) (13). Shunting blood form systemic to pulmonary circulation because congestive heart failure that associates with widened pulse pressure and bounding peripheral pulses. Overload of lung blood vessels, leading to pulmonary edema / hemorrhage and predispose the Infant to chronic lung disease. (10, 8, and 9).

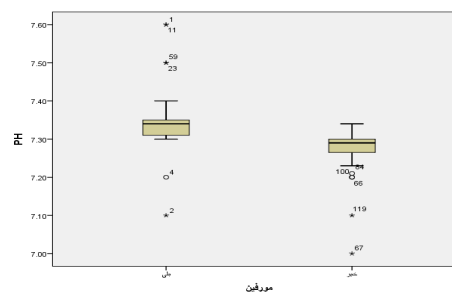
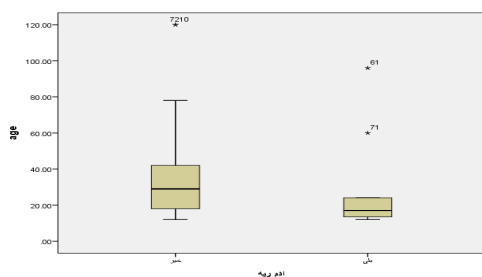


Figure 1: Comparison of PH and control groups



**Figure 2: Average age of patients developing pulmonary edema**

Although morphine has been used for years in treatment of acute pulmonary edema but its mechanism of this action are still largely unknown. Studies on animals show that morphine is significantly causes venous dilatation and that moves the blood from the central to the peripheral circulation 'medical phlebotomy' term describes this phenomenon. (14). There are several definitions on beneficial results of morphine administration in pulmonary edema:

1. *Morphine to calm anxiety and agitation by central venous pressure helps.*
2. *In respiratory distress, Intrathoracic negative pressure causes alveolar collapse and impaired blood vessel formation is oxygen, morphine eliminates this condition by maintaining normal breathing (15).*

Morphine effects on the peripheral venous system in patients with pulmonary edema may be quite different. These patients had increased venous capacity, which is caused by sympathetic nervous system activity, Shown that the vasodilatation caused by morphine in normal cases, secondary to reduced sympathetic nervous system activity, probably is at the level of central system.(14)

Lasix (furosemide) is a loop diuretic that lower blood pressure (16). In acute pulmonary edema it is given as single dose of intravenous or intramuscular (1mg/kg). If the diuretic response to the initial dose is not satisfactory and edema resist, dosage may be increased by 1 mg/kg (18, 17).

In 2008 a study was conducted by Andrew and colleagues, in their study 23patients With PDA participated, divided into two groups, underwent surgical PDA ligation without any mortality (19). But in our study we had one case death and it was due to pulmonary edema.

Janvier and colleagues in 2010 studied the anesthesia techniques and postoperative outcomes in full term

infants. These infants had PDA ligation surgery. This study was conducted at the University of Montreal, Canada.

All infants underwent surgery within 21 months period and they were studied retrospectively, altogether 33 infants were examined. Average weights of infants were  $0.29 \pm 1.031$  kg. All infants, except one, during the operation, had received the opioid. Unstable breathing period after surgery and postoperative hypotension were the variables that were studied in all infants. The study found that 8 patients after surgery have shown unstable postoperative respiratory course (UPRC). Average fentanyl dose in patients with UPRC,  $2.6 \pm 5.3$   $\mu\text{g} / \text{kg}$  and in patients without UPRC,  $16.6 \pm 22.6$   $\mu\text{g} / \text{kg}$ , respectively. This study reveals that proper dose of opioid associated with diuretic has significant effect in reduction of pulmonary edema.

Afzali and colleagues in 2009 studied the patients with patent ductus arteriosus in Golestan Hospital, Ahwaz University of Medical Sciences. In Golestan Hospital in Ahwaz 107surgical PDA ligation performed from January 1995 to January 1999, from 107 patients 70% were female and 30% male the age range of 4 months to 38 years with a mean of 8.5 years (21). In our study female to male ratio was 2:1 (1) which is same compare to above however, the average age of patients in our study is 3.5 years less than average age above study.

In a study conducted in 1976 by Lewis and colleagues, the effect of morphine on the reduction of pulmonary edema was studied. Following injection of morphine, dyspnea of patients and their respiratory rates improved and decreased from  $24.3 \pm 2.5$  to  $17.2$  per min (22). In our study group also those patients who had received morphine during surgery, compared to control group, had significantly lower respiratory rate per minute ( $p = 0.01$ ).

## 5. Conclusion

Very few studies have been conducted on beneficial effect of morphine and lasix administration during PDA ligation surgery. To achieve more definitive results and gaining more solid evidence there is need of doing more research in this field. In this study the use of morphine and Lasix has been supported as part of treatment. This technique appears to be safe and effective in reduction of pulmonary edema after surgery. (23)

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**Contact us:**

JundiShapour University of Medical Sciences,  
Golestan Hospital Cardiovascular Anesthesia,  
Ahwaz, Khuzestan, IRAN,  
Dr Ahmad Ebadi Telephone: 09161110099  
Work Fax: 06113743017  
E-mail: [Ebadi1959@ajums.ac.ir](mailto:Ebadi1959@ajums.ac.ir)

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