

## Patent Ductus Arteriosus Treatment in the Premature Newborn: Clinical and Surgical Analysis

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### Summary

**Background:** The surgical treatment of patent ductus arteriosus is indicated when the clinical intervention fails. However, this treatment may present some complications.

**Objective:** To analyze clinical and surgical aspects involved in the treatment of patent ductus arteriosus in the premature newborn.

**Methods:** Twenty-two premature newborns, submitted to surgical treatment for patent ductus arteriosus from January 2000 to June 2006, were evaluated. Of the 22 newborns, 77.3% were females, mean birth weight was 952.5 g and the mean gestational age was 27 weeks. The use of vasoactive drugs, indomethacin, echocardiographic parameters and complications were evaluated in the pre- and postoperative periods.

**Results:** In this sample, 59.1% of the patients needed intratracheal intubation at birth, 77.3% needed surfactants and 59.1% used preoperative vasoactive drugs. The mean number of indomethacin doses was 3.43, with dose ranging from 0.10 to 0.25 mg/Kg/day. The mean caliber of the patent ductus arteriosus was 1.96 mm. The surgical procedure was carried out through extrapleural access in 59.1% of the patients; the mean time of postoperative intubation was 30.9 days and 50% of the patients used postoperative vasoactive drugs. There were 18.1% of postoperative complications (non-fatal postoperative complications).

**Conclusion:** More than 50% of the patients needed intratracheal intubation at birth, surfactant use and vasoactive drugs in the preoperative period. There was a higher prevalence of the extrapleural approach during surgery. In the postoperative period, there was a lower need for vasoactive drugs and there were no deaths related to the surgical procedure. (*Arq Bras Cardiol* 2008; 90(5): 316-319)

**Key words:** Ductus arteriosus, patent; infant, premature; heart defects, congenital.

### Introduction

The arterial canal functions as a vital arterial conduit during intrauterine life that is vital for the satisfactory development of the fetus, as it diverts more than half of the cardiac output for the systemic and the umbilical-placental circulation<sup>1,2</sup>. At birth, in the presence of the blood rise of the oxygen pressure, a constriction of this canal occurs, concomitantly with the dilation of the pulmonary circulation, thus establishing a new circulatory pattern in the newborn (NB)<sup>1,2</sup>.

However, in premature NB, this mechanism of arterial canal closing does not occur in 50% of the cases, resulting in a congenital cardiac defect called patent ductus arteriosus (PDA)<sup>1-4</sup>. Therefore, there is an increase in the pulmonary flow in

detriment to the systemic perfusion, due to the left-right shunt<sup>4</sup>. This hemodynamic alteration causes a left ventricular overload, myocardial dysfunction and respiratory failure<sup>4</sup>. Additionally, severe complications that are associated or concomitant to PDA are necrotizing enterocolitis, renal failure, bronchopulmonary dysplasia and intraventricular hemorrhage<sup>4,10</sup>.

The clinical therapy of PDA is mainly based on the administration of indomethacin, an agent that is a prostaglandin-synthesis inhibitor, associated to fluid restriction and diuretics<sup>4</sup>. However, in situations where the PDA is refractory to the clinical management, its surgical ligation is indicated, aiming at attenuating its hemodynamic complications<sup>4,11-13</sup>. Although this surgical intervention presents satisfactory results, it is not complication-free. Therefore, the aim of this study is to show the clinical and surgical aspects involved in the treatment of PDA in premature newborn infants.

### Methods

A retrospective analysis of the clinical and surgical aspects of 22 newborn infants, with gestational age below 32 weeks,

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who were submitted to the surgical treatment of patent ductus arteriosus during January 2000 to June 2006 was carried out. These patients were originally from the Federal University of São Paulo – *Hospital São Paulo* and *Hospital Santa Catarina*. All NB that presented other concomitant heart diseases and/or incomplete medical files were excluded.

Of the patients that were included in the study, 5 (22.7%) were males and 17 (77.3%) were females; the mean gestational age at birth was 27 weeks (ranging from 23 to 32 weeks) and mean weight was 952.5 g (ranging from 485 to 1,765 g). Birth by normal delivery had occurred in 4 (18.1%) cases and the diagnosis of PDA was carried out clinically in 8 (36.3%) and by echocardiogram in 14 (63.7%) cases.

The mean diameter of the arterial canal was 1.96 mm (0.2 – 3.2 mm). Of all the patients, only 4 (18.1%) did not undergo the clinical management with indomethacin, considering that their clinical condition required immediate surgical approach. The mean number of indomethacin applications was 3.4, with the dose varying from 0.1 to 0.25 mg/Kg/day, administered orally. However, this drug was not effective in any of the cases of this surgical series, regarding the closing of the canal.

Based on the reviewed data, information on the pre-, intra- and postoperative periods of each patient were obtained. These data included the need for orotracheal intubation (OTI) and ventilation parameters, surfactant administration, use of vasoactive drugs, access pathway and surgical technique, postoperative complications, re-operations, hospital stay duration and deaths.

All these reviewed parameters were evaluated under the aspect of analyses of prevalence.

## Results

The surgical procedure was carried out exclusively at the surgical center, with the patient under general anesthesia. The surgical access of choice was the left posterolateral thoracotomy and the intrapleural approach was used in 9 (40.9%) of the patients, with a mean operation time of 58 minutes (20 to 120 minutes). In this series, only one patient was submitted to the arterial canal clamping, whereas the others were submitted to its ligation.

The complications observed in this series were bronchopulmonary dysplasia in 2 patients, congestive heart failure and surgical wound infection in 1 patient. No cases of renal failure or necrotizing enterocolitis were observed; however, all patients presented intraventricular hemorrhage, although there were no consequences for the central nervous system. Three deaths, which were unrelated to the surgical procedure, occurred due to septic shock with a pulmonary infectious source and 1 patient needed to be re-operated due to clamping loosening. The mean time of OTI during the hospital stay was 30.9 days (1 to 91 days) and the mean duration of hospital stay was 89 days (17 to 332 days). The chest drain in the patients with an intrapleural approach was removed after a mean time of 1.8 days (1 to 2 days) after the surgery. Complementary data of the results are shown in charts 1 and 2.

## Discussion

The decrease in the mortality rates of premature, low-weight newborn infants is one of the milestones of modern Medicine and reflects the development and the quality of assistance given during the pregnancy and labor management. It is known that a premature patient, even when free of other comorbidities, presents neuropsychomotor development (NPMD) retardation, which requires a stringent follow-up by the healthcare team<sup>14</sup>.

However, it is also known that this group of patients presents an increased risk of malformations and congenital diseases, mainly cardiovascular ones. The study by Rivera et al<sup>15</sup>, published in 2007, shows a prevalence of congenital heart disease of 13.2:1,000 live births, which is higher than that reported by Guitti<sup>16</sup>, in 2000, of 5.5:1,000 live births. In premature infants, the presence of heart disease significantly impairs the NPMD, in addition to failure to thrive. It is under these considerations that one must analyze the patent ductus arteriosus.

Our cohort shows a predominance of the female sex (77.3%), which corresponds with the prevalence of PDA described in the literature. Due to lung immaturity, surfactant was administered to 77.3% of the patients and OTI was carried

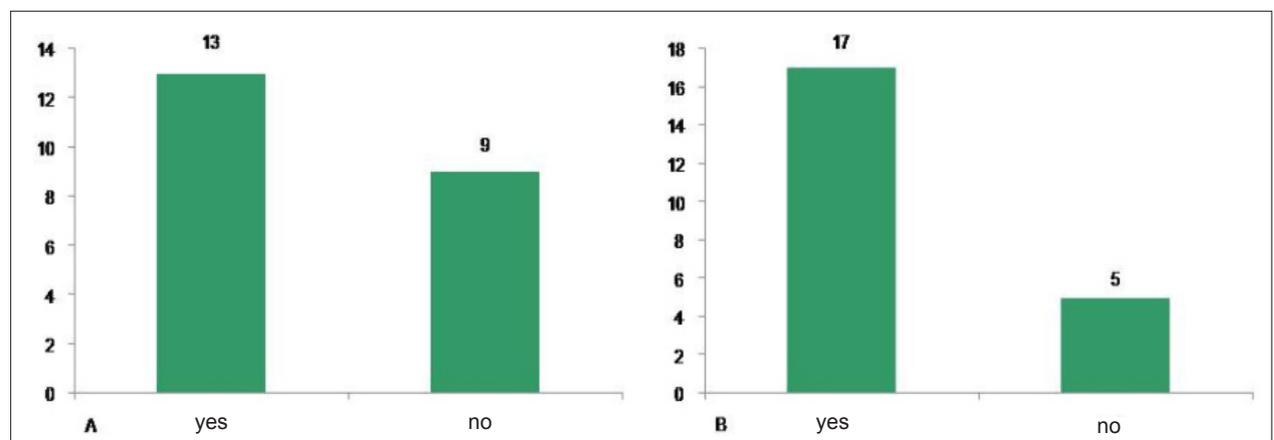


Chart 1 - A. Orotracheal intubation at birth. B. Surfactant administration.

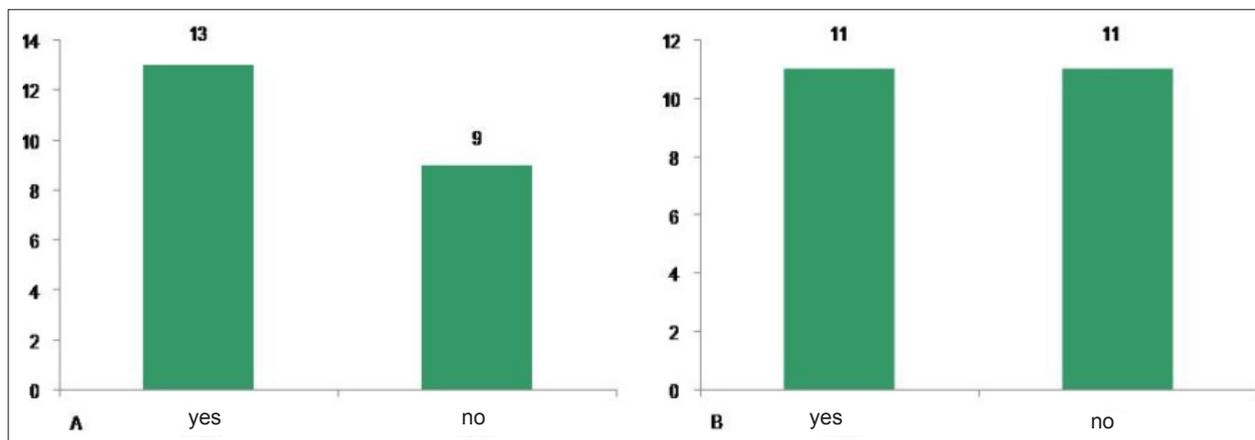


Chart 2 - A. Preoperative use of vasoactive drugs. B. Postoperative use of vasoactive drugs.

out in 59.1% of the cases. It is known that PDA influences adequate pulmonary function; however, Van Woerkom et al, in a study of low-weight NB infants submitted to PDA ligation, did not observe short-term improvement in the patients' ventilation parameters<sup>17</sup>. This fact was confirmed by Carboni & Ringel<sup>18</sup>, Farstad & Bratlid<sup>19</sup> in their results.

The mean diameter of the PDA was 1.96 mm. Literature data show that PDA severity can be expressed as a ratio between the sizes of the left atrium and aortic root > 1.47 or a transversal diameter of the largest canal > 1.5 mm, in the presence of a left-right shunt<sup>20,21</sup>.

Therefore, most of the patients in the present study presented disease with important clinical and/or hemodynamic implication. However, the patients with a transversal diameter < 1.5 mm, although they did not have severe PDA, according to the aforementioned criteria, presented unfavorable clinical conditions, which also represented high risk.

The number of doses of indomethacin used in this study is in accordance with the doses administered in other studies<sup>4,22</sup>. However, the closing of the arterial canal was not observed following this treatment protocol. This might be explained by the fact that, in the present study, indomethacin was administered orally, which has been proven to be less effective than the intravenous administration of the drug.

Additionally, this drug has also been studied as prophylaxis for intraventricular hemorrhage in patients with PDA<sup>23,24</sup>. A meta-analysis designed by Fowlie et al, in 2003<sup>14</sup>, showed the efficacy of indomethacin in preventing this complication. Nevertheless, whether the prophylactic effect in intraventricular hemorrhage is secondary to the closing of PDA by indomethacin is debatable<sup>22</sup>.

All of the patients presented intraventricular hemorrhage, a fact that, in literature, is associated to the presence of PDA<sup>4,10</sup>. However, this fact might be simply due to prematurity itself, as this group of patients is more susceptible to this type of brain injury, regardless of other morbidities<sup>14</sup>. Hence, we agree with the results by Brooks et al<sup>22</sup>, when they state they did not observe an association between PDA and intraventricular hemorrhage and other comorbidities.

The surgical procedure was carried out at the surgical center,

in all patients, without any intercurrent events. It is known that this surgical procedure can be performed at the Intensive Care Unit (ICU); however, the risks of infection and complications, which are inherent to the operative intervention, are in fact better controlled and prevented at the surgical center<sup>4</sup>. Similar results were reported by Gould et al<sup>4</sup>, in a study where the authors compared interventions performed at the ICU and those performed at the surgical center<sup>4</sup>. The study results were based on the possible complications inherent to the transportation of the NB to the operating room.

In addition to the conventional surgery, i.e., the left posterolateral or axillary thoracotomy with canal ligation, the thoracoscopy can be employed, as well as the mini-thoracotomy with extrapleural access and the interventionist catheterism<sup>25-30</sup>.

In fact, the development of several techniques for the treatment of PDA aims at attaining the least trauma, risk, cost and higher effectiveness than the conventional treatment.

The extrapleural approach is the access of choice for reaching the arterial canal, as it prevents the need for introducing a chest drain and thus, results in a lower risk of postoperative infection and pain. However, considering the anatomical variability of the parietal pleural thickness, even when the dissection is performed very carefully, many times it is not possible to preserve its integrity and the intrapleural access is followed.

The chest drain, when employed, remained in our patients for a mean period of 1.8 days. This is in accordance with the information reported by Gould et al<sup>4</sup>. However, these authors do not discuss the type of surgical access was employed, whether it was intra or extrapleural.

Among the observed postoperative complications, the main one was bronchopulmonary dysplasia, which presented as a consequence of the PDA, although some studies do not show such association<sup>4,20</sup>. The deaths described were not due to the surgical procedure, as they occurred 30 days after the intervention, but they reflect the severity of the picture in the newborn. The mortality rate of 13.6% is in accordance with that reported in literature, with similar data<sup>4,20</sup>.

In summary, the data presented here show the experience

of our Service in the treatment of PDA, explicating the clinical and surgical management. In fact, the inclusion criteria are restricted and well-delimited, so if anything is lost regarding the number of patients, it is gained in terms of sample homogeneity. However, it is important to mention that, as demonstrated by our experience, when treating a newborn patient with PDA, one must keep in mind that a prolonged postoperative period should be expected, with a mean intubation time > 3 weeks and, therefore, with a higher risk of hospital infection and sepsis.

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## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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There were no external funding sources for this study.

## Study Association

This study is not associated with any graduation program.