



## Patent Ductus Arteriosus Closure Treatment: Ibuprofen or Acetaminophen, Which One Do You Prefer?

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### Editorial

The Ductus Arteriosus is a vascular structure that is responsible for the union of the pulmonary artery with the descending aorta during fetal life [1]. At the time of birth, with the beginning of breathing and separation of the placenta, the ductus is closed. This closure is carried out in two phases. During the first twelve hours of life, contraction and migration of the smooth muscle of the duct occurs, which causes a longitudinal shortening and a circumferential narrowing. This process generates an occlusion of the vascular structure that occurs at functional closure. At 2-3 weeks of age, the fibrosis phase of the medial and intimal layers is terminated and the ductus arteriosus is closed. It is estimated that in 90% of full-term newborns, the ductus arteriosus is closed at eight days of age [2].

The persistence of the ductus arteriosus is considered a congenital heart disease with a high prevalence in preterm patients [3], which represents 5-10% of congenital cardiopathies. In addition, its frequency being twice as high among females [4]. In newborn infants, it is considered that delayed closure is due to prematurity while in term infants it has been associated with environmental causes (rubella exposure trisomy 21 or 18, alcohol, anticonvulsants or amphetamines). The

symptoms generated by the patent ductus arteriosus are variable and depend above all on the size of the defect [5].

The ductus arteriosus of small size generates null or few symptoms, but when the patent ductus arteriosus presents a moderate size, a short circuit occurs from left to right and symptoms such as tachypnea, irritability, and difficulty in feeding and growth retardation appear. The symptoms become more evident from the second and third month of life. To compensate for the short circuit, a myocardial hypertrophy occurs that causes an improvement in the clinical situation.

The medical treatment used so far has been based on the administration of the most commonly used drugs for this purpose: cyclooxygenase inhibitors (Ibuprofen) or inhibitors of the prostaglandin synthase (Acetaminophen also known as Paracetamol) [6].

The current pharmacological treatment is based on the administration of Ibuprofen (first-line therapy), the latter being the one of choice [7]. These therapies have shown an effectiveness of 70-80% [8]. Although they have high closure rates, they have been associated with multiple adverse reactions: interventricular hemorrhage, thrombocytopenia, necrotizing enterocolitis, renal failure

and hyperbilirubinemia. Due to the amount of side effects that appeared with nonselective COX inhibitors, other therapies were used like Acetaminophen with fewer side effects: higher renal safety [9] or low or absent hepatic toxicity in neonates due to the existence of a large therapeutic serum concentration range for Acetaminophen.

In the last published papers: Dang et al, Eleven et al, Bagheri et al, and Al-Iawama et al [10-13] compared the use of ibuprofen and acetaminophen orally for the closure of the persistent ductus arteriosus. The purpose of these studies was to verify the superiority of some of these

drugs in terms of percentages of closure and adverse effects. After the first treatment cycle, two studies [10,12] observed a higher rate of closure with acetaminophen compared to two other studies that observed a higher rate of closure with ibuprofen [11,13]. The final closure result was higher with the treatment of acetaminophen in three of the four studies that compared both drugs [10-12]. There were significant differences in the rate of adverse effects in the study by Dang et al, in which a number of cases of gastrointestinal hemorrhage and hyperbilirubinemia were reported in preterm infants who received ibuprofen significantly higher than those treated with acetaminophen.

Study	Ductus arteriosus closure with paracetamol (%)	Ductus arteriosus closure with ibuprofen (%)
D.Dang <i>et al.</i>	81,2%	78,7%
Oncel <i>et al.</i>	97,7%	95,5%
M.Bagheri <i>et al.</i>	91%	90%
M.Al-Iawama <i>et al.</i>	92,3%	100%

Table 1: Percentage of success in the closure of persistent ductus arteriosus with acetaminophen and with ibuprofen.

Acetaminophen can be considered an effective for the treatment of patent ductus arteriosus closure in preterm neonates [14,15] due to the low percentage of adverse effects that appear and the high success rate of ductus arteriosus closures after its administration. Although ibuprofen is also effective for the treatment of patent ductus arteriosus closure in preterm neonates because the success rate closures is similar to the acetaminophen treatment [16]. But with the success rates of ductus arteriosus closure, it cannot be concluded that acetaminophen is more effective than ibuprofen in the treatment of this pathology. Because most authors agree with the necessity of more trials to establish the safer dose in preterms and its efficacy, to establish acetaminophen as first-line therapy for patent ductus arteriosus treatment [17].

### Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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