A full-term infant with large patent ductus arteriosus successfully closed with oral ibuprofen: a case report

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ABSTRACT

Background: Ductus arteriosus is a vascular shunt between the aorta and pulmonary artery. Within the first 24-48 hours of life, the ductus usually closes. Failure of closure is called patent ductus arteriosus (PDA). Timing for treatment is crucial. Early treatment can decrease the need for drugs or surgery, but it can cause more adverse events, such as brain hemorrhage, bowel perforation and renal dysfunction. On the other hand, late treatment can cause complications such as pulmonary hemorrhage, necrotizing enterocolitis and can render drugs to be less effective.

Case Presentation: The patient was a 2 hours old male, 39 weeks, Apgar 7/8, 3100 grams, referred to the cardiology team because of tachypnea and peripheral cyanosis. Initial echocardiographic showed large patent ductus arteriosus, coarctation aorta, patent foramen ovale and moderate tricuspid regurgitation. The patient was given 60mg of oral ibuprofen for the first day and 30mg of oral ibuprofen for the second and third days. In addition, the patient was given 2mg of furosemide, 2.5mg of spironolactone and 12.5mcg of digoxin twice daily to prevent heart failure. Echocardiographic evaluation after three days showed closure of large patent ductus arteriosus, no mild preductal coarctation aorta remains, trivial tricuspid and patent foramen ovale. No side effects were observed.

Conclusion: This case showed successful early treatment of large PDA in full-term infants with a double dose of oral ibuprofen. Adverse events were not found. As a result, ibuprofen should be considered as an early treatment for PDA in full-term infants.

Keywords: patent ductus arteriosus, ibuprofen, full-term, case report.


INTRODUCTION

Ductus arteriosus is a vascular shunt between the aorta and pulmonary artery. The ductus allows blood to circulate from the right ventricular heart to bypass pulmonary circulation into the systemic circulation. Within the first 24-48 hours of life, the ductus usually closes. Failure of closure is called patent ductus arteriosus (PDA).1,3

Clinical manifestations of PDA include murmur, tachypnea and tachycardia. Large PDA could lead to respiratory distress. Symptomatic PDA warrants immediate treatment.1,2

Timing for treatment is crucial. For example, early treatment can decrease the need for drugs or surgery, but it can cause more adverse events, such as brain hemorrhage, bowel perforation and renal dysfunction. On the other hand, late treatment can lead to complications such as pulmonary hemorrhage and necrotizing enterocolitis and can render drugs to be less effective. For large PDA, surgery is more complicated because of limited stent size and side effects such as embolization, turbulence and infection.2,4

CASE PRESENTATION

The patient was a 2 hours old male, 39 weeks, Apgar 7/8, 3100 grams, who was referred to the cardiology team because of tachypnea and peripheral cyanosis. A continuous murmur was heard at the left upper sternal border. Complete blood count results were normal. Chest radiography showed a normal cardiothoracic ratio (Figure 1). Initial echocardiographic showed a large patent ductus arteriosus, with the isthmus/amplulla measuring 5.2/7.3 mm, left to right shunt, PG 3/1 (Figure 2).

Mild preductal coarctation aorta and patent foramen ovale measured 2.3 mm, left to right shunt (Figure 3), moderate tricuspid regurgitation with pressure gradient 32 mmHg (Figure 4) were present.

Left ventricular systolic function was normal, with an ejection fraction of 71% (Figure 5). The patient was given oxygen
and 60 mg of oral ibuprofen for the first day and 30 mg of oral ibuprofen for the second and third days. The patient was given 2 mg of furosemide, 2.5 mg of spironolactone, and 12.5 mcg of digoxin to prevent heart failure. After the first day of therapy, the patient no longer had tachypnea and peripheral cyanosis.

As the condition improved, oxygen support was withdrawn. The second course of ibuprofen and heart failure prevention drugs was continued. Echocardiographic evaluation after three days showed closure of large patent ductus arteriosus (Figure 6), no mild preductal coarctation aorta remains, trivial tricuspid regurgitation (Figure 7), and patent foramen ovale measuring 1.4 mm, minimal left to right shunt (Figure 8).

Left ventricular systolic function was normal, with an ejection fraction of 78% (Figure 9). No side effects, such as oliguria, bleeding and gastrointestinal discomfort, were observed. Ibuprofen, digoxin, spironolactone and furosemide were stopped, and the patient was scheduled for an echocardiographic examination in 6 months.

**DISCUSSION**

PDA is defined as failure of closing ductus arteriosus. PDA was more common in preterm. The prevalence of PDA is around 0.03-0.08% in full-term infants. PDA mechanisms in full-term infants were unclear, but it is suspected that prostaglandin metabolism dysfunction and hypoxia induce COX production of prostaglandins. Prostaglandins, a known vasodilator, inhibit the closure of the ductus arteriosus. This patient was born in 39 gestation weeks, and the ductus was still unable to close until 24 hours after birth. Usually, full-term infants with PDA had hypoxia during prenatal, which presented clinically as a low APGAR score. Yet, this patient had an APGAR score of 7/8.

Symptomatic PDA, such as heart murmur and respiratory and hemodynamic distress, are indications for treatment. Untreated PDA can lead to heart failure, infective endocarditis and pulmonary vascular disease. In this case, due to respiratory distress, peripheral cyanosis and heart murmur, treatment for...
PDA was given.

Options for PDA treatment consist of conservative care, drugs and surgical management. There are still disputes about the timing and modality of therapy for PDA. Early treatment (during the 2-5 days after birth) can decrease the need for drugs or surgery, but it can cause more adverse events, such as brain hemorrhage, bowel perforation and renal dysfunction. Late treatment (during the second week of life) can lead to complications such as pulmonary hemorrhage and necrotizing enterocolitis and can render drugs to be less effective. As time went by, the ductus became less sensitive to drugs, and ibuprofen had higher renal clearance, making PDA more difficult to be treated.2,9,10

Drugs choice for PDA treatment consists of ibuprofen, indomethacin and paracetamol.2 Ibuprofen, a non-selective COX inhibitor, has a PDA closure rate of 60-83.8% in preterm infants and 62.1-73.3% in full-term infants.5,7,11,12 Review by Pacifici in 2016 compared oral ibuprofen and indomethacin in preterm infants. Ductal had 60% closure in the oral ibuprofen group compared to 65.7% in the indomethacin group. When the drugs were taken during the 8 days after birth, closure rates increased to 75% and 83.8%, respectively.11 A study by Pourarian et al. in 2015 showed 62.1% PDA closure after a double dose of oral ibuprofen (20mg/kg, 10mg/kg, 10mg/kg), 43.3% after the standard dose (10mg/kg, 5mg/kg, 5mg/kg) and 4.7% placebo in full-term infants.5

In 2009, Amoozgar et al. researched PDA in full-term babies. They reported 73.3% PDA closure in the treatment group (standard dose ibuprofen initially 10 mg/kg, then 5mg/kg twice 24 hours apart) versus 42.9% in the control group.7 In 2016, Alipour et al. found ductus arteriosus closure rates in full-term infants to be 62.9% in the ibuprofen group (dosage 10mg/kg, 5mg/kg, 5mg/kg) as opposed to 54.3% in the control group.12

In preterm infants, ibuprofen did not decrease renal perfusion and had less risk of necrotizing enterocolitis than indomethacin. Oral ibuprofen was the drug of choice for preterm infants with PDA.11 Oral ibuprofen had performed better in the case of PDA closure than intravenous. Higher dosage of oral ibuprofen (20mg/kg, 10mg/kg, 10mg/kg) was favored and had higher closure rates than the standard dose (10mg/kg, 5mg/kg, 5mg/kg), 70% and 30% respectively. The higher dose was not associated with a higher incidence of adverse effects.2 Systematic review and meta-analysis by Mitra et al. in 2015 reported a high dosage of oral ibuprofen leading to higher closure of hemodynamically significant PDA than standard dose of intravenous ibuprofen, indomethacin, placebo or control. The adverse event did not change significantly.9 A study by Yantie et al. in 2017 found standard dose of ibuprofen (10mg/kg, 5mg/kg, 5mg/kg) was not better than placebo. A higher dose (20mg/kg, 10mg/kg, 10mg/kg) was linked to a better chance of PDA closure and the same risk of side effects.6 For this patient, treatment started

**Figure 4.** Moderate tricuspid regurgitation with a pressure gradient of 32 mmHg

**Figure 5.** Normal left ventricular systolic function with an ejection fraction of 71%

**Figure 6.** No PDA remains
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early, within 24 hours after birth. The patient was given 60mg of oral ibuprofen for the first day and 30mg of oral ibuprofen for the second and third days. Large PDA was successfully closed after three days, and adverse events were not identified.

CONCLUSION

This case showed successful early treatment of large PDA in the full-term infant with an oral double dose of ibuprofen. Adverse events were not found. As a result, ibuprofen should be considered as an early treatment for symptomatic PDA in full-term infants.

CONFLICT OF INTEREST

There is no conflict of interest in the writing of this paper.

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ETHICAL CONSIDERATION

The patient's parents have signed the informed consent and agreed that the medical data would be published in the form of a case report in medical scientific journals.

AUTHOR’S CONTRIBUTION

All authors contributed to writing this paper, from patient examination, data collection and report writing.

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