Management of the patent ductus arteriosus in preterm infants
CPS Position Statement

Developed by Dr. Claire Wallace and Dr. Souvik Mitra for PedsCases.com.

February 9, 2022

Introduction

Hi, my name is Claire Wallace and I am a third year Pediatrics resident at Memorial University of Newfoundland. This podcast provides guidelines for appropriate management of patent ductus arteriosus in preterm infants. This podcast was created in collaboration with Dr. Souvik Mitra, a neonatologist and clinical epidemiologist at the IWK Health Center and Dalhousie University in Halifax.

Objectives

By the end of the podcast, listeners will be able to:

1. Define patent ductus arteriosus.
2. List indications for conservative management, pharmacologic treatment, procedural intervention, and prophylactic closure of a PDA.
3. Describe options for conservative management of a PDA.
4. Outline the stepwise approach to pharmacologic closure of a PDA.
5. List the procedural options for PDA closure.

Case

Let's start with a case.

Lucy is a 2-week-old baby girl who was born preterm at 28 weeks of gestation. She was diagnosed with a patent ductus arteriosus at 3 days of life based on echocardiogram. She remains dependent on respiratory support with continuous positive airway pressure (CPAP), and has poor growth. On repeat echocardiogram her PDA is large, with a significant left to right shunt.

How do you think we should manage Lucy's PDA? Is she a candidate for pharmacologic treatment? Procedural intervention? Conservative treatment? What are the potential

complications of these interventions, and what are the potential complications of leaving the PDA untreated? We will return to these questions at the end of the podcast. First, let's review some terminology and learn more about the management of patent ductus arteriosus.

Patent ductus arteriosus (PDA) is a persistent connection between the aorta and the pulmonary artery, in the neonate. The open ductus arteriosus is a normal part of the fetal circulatory system, which should close shortly after birth as the neonate transitions to extrauterine life. If the ductus arteriosus remains open, it's called a patent ductus arteriosus.

PDA is a common finding in preterm neonates. PDAs have been associated with many adverse outcomes in infants, including prolonged assisted ventilation, pulmonary hemorrhage, chronic lung disease, necrotizing enterocolitis, intraventricular hemorrhage, and death. For this reason, medical closure of PDA in preterm infants is often considered.

PDAs can either be closed prophylactically, before the patient becomes symptomatic, or they can be closed therapeutically, when a patient becomes symptomatic. They can be closed using medication or an interventional procedure. Conservative management can also be used. The question of which PDAs should be treated, when to treat them, and how to treat them, is controversial. The risks and benefits of treating a PDA must always be considered, in the context of the individual patient.

Now let’s review some of the leading questions affecting PDA management.

First of all, what is conservative management?

Conservative management means that we focus on treating the symptoms and consequences of a PDA, without actually trying to close the PDA. There is no clear consensus on what “conservative management” entails. One conservative option is to use a loop diuretic such as Furosemide. This can reduce pulmonary edema, a common complication of PDA, and improve lung function. Another option is to increase the amount of positive pressure that we give an infant via CPAP. Higher PEEP has been shown to reduce left-to-right shunting without significantly affecting cerebral perfusion or oxygenation. Another option is to restrict fluids to avoid fluid overload, although aggressive fluid restriction is not recommended.

One benefit of conservative management is that we can avoid the side effects and risks associated with pharmacologic or procedural closure. But conservative management poses its own problems. A persistent PDA can lead to a prolonged dependence on respiratory support, leading to chronic lung disease and a prolonged NICU admission.

Which preterm infants are a candidate for conservative management?

A small, asymptomatic, and hemodynamically stable PDA can be managed conservatively. Symptomatic PDAs can often be managed conservatively for the first one to two weeks of life. Most small PDAs close spontaneously before term-corrected gestation. Therefore, conservative management alone can lead to closure of the PDA in many cases. Newborns with a persistent PDA can even be discharged from hospital if they are otherwise clinically stable, growing, and can be followed by cardiology as an outpatient.

Even after term corrected gestation, a persistent low-volume PDA shunt in an otherwise stable and growing preterm infant, with no cardiorespiratory compromise, can be managed conservatively. These patients must also be followed by cardiology, as a small proportion of them are at risk of developing chronic pulmonary hypertension from prolonged exposure to PDA shunts.

What about preterm infants with a PDA who are symptomatic?

Patients with a symptomatic PDA may have a murmur, hyperdynamic precordial impulse, tachycardia, bounding pulses, widened pulse pressure, or worsening respiratory status.

A symptomatic PDA may also be hemodynamically significant, if there is a large volume PDA shunt. An echocardiogram should always be used to confirm the presence of a left-to-right PDA shunt before treating a PDA.

The majority of large, hemodynamically significant PDAs, especially in clinically unstable extremely preterm infants (<26 weeks GA) may require early medical management in order to prevent complications. This is because these infants have higher rates of mortality when left with a persistently symptomatic PDA.

So how do we medically treat PDA?

PDA can be treated with pharmacotherapy, or procedural intervention. Our pharmacotherapy options include three cyclo-oxygenase (COX) inhibitor drugs; ibuprofen, indomethacin, and acetaminophen. Of the COX inhibitor drugs, ibuprofen should be used as the first line pharmacotherapy for PDA closure. It is safer than indomethacin and more effective than acetaminophen, especially in very low birth weight infants. The usual ibuprofen regimen is one dose of 10 mg/kg followed by two doses of 5 mg/kg at 24 hour intervals. A higher dose of ibuprofen may be considered for preterm infants beyond the first 3 to 5 days of age.

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What happens if the PDA remains open after one course of medication?

If the PDA remains open after a course of medication, a second course of COX-inhibitor medication can be used. The second treatment can be done using ibuprofen or indomethacin. The second treatment course has been shown to significantly improve overall PDA closure rates without an increase in adverse effects. If the second course of medications is not effective, a third treatment course may be used, while planning for procedural PDA closure. Acetaminophen is the safest and most effective medication to use in the third course. Ibuprofen or indomethacin should not be used for more than 2 courses.

What happens when a patient fails medical treatment altogether?

If a patient fails 2-3 courses of medical therapy, or if pharmacotherapy is contraindicated for the infant, procedural closure may be used. Procedural closure of a PDA is controversial. It is reserved for infants with significant symptoms, who have a large shunt volume and pulmonary over-circulation on echocardiogram.

What methods are available for procedural closure of a PDA?

There are two methods for procedural closure of a PDA: surgical closure and closure via percutaneous catheter. Percutaneous closure is becoming more popular, although it has not replaced surgical closure as the main method of procedural closure of PDA.

Finally, is there a way treat PDA before it causes symptoms?

Prophylactic closure of a known PDA in an asymptomatic patient may be considered in extremely low birth weight (ELBW) infants (< 1000g) who are at high risk for severe intraventricular hemorrhage (IVH). Indomethacin is the best medication in this case.

There are several potential benefits of early PDA closure in this population. Early closure can significantly reduce the rates of severe IVH, procedural PDA closure, and symptomatic PDA in ELBW infants. However, early closure does not improve rates of chronic lung disease, severe neurodevelopmental impairment, or cerebral palsy among survivors. It is important to weigh the risks and benefits of early treatment for each patient. The risks of treatment may only outweigh the benefits in patients at high risk of severe IVH. Prophylactic closure with ibuprofen, or acetaminophen is not recommended in ELBW infants.

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Now that we've learned about the management of PDA's let's review our case…

Lucy is a 2-week-old preterm baby girl with a large, symptomatic and hemodynamically significant PDA that is causing her to remain dependent on respiratory support. The PDA is also impacting her growth.

After reviewing the risks and benefits, the decision is made treat her PDA medically with a three-dose course of ibuprofen. On repeat echocardiogram, her PDA is closed. Over the next several days, she tolerates a wean off her respiratory support. She gains weight steadily over the next 6 weeks and is discharged home from the NICU.

Let's finish by reviewing the key learning points from this podcast:

1. Echocardiography should be used to confirm the presence of a left-to-right PDA shunt before considering treatment
2. Conservative management may be considered in the first 1 to 2 weeks of life in clinically stable preterm infants
3. Ibuprofen is the medication of choice for symptomatic PDA treatment
4. A second course of pharmacotherapy should be considered over invasive management for a persistent, symptomatic PDA
5. Procedural closure may be considered for infants with persistent PDA even after two courses of pharmacotherapy, or for those with contraindications to pharmacotherapy, especially when their clinical symptoms are significant and echocardiography shows signs of large shunt volume and pulmonary overcirculation
6. Percutaneous transcatheter PDA closure may be considered as an alternative to surgical PDA ligation when institutional expertise is available and patient characteristics are appropriate.
7. Patients discharged home with a persistent PDA should be followed by cardiology
8. Selective prophylaxis with intravenous indomethacin may be considered for ELBW infants at high risk for severe IVH.

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