Local Guideline

Patent Ductus Arteriosus (PDA) management in NICU

Sites where Local Guideline applies: Neonatal Intensive care Unit, JHCH
Target audience: NICU clinical staff, who provide care to neonatal patients.
Description: Guideline for clinicians to manage a patent ductus arteriosis in the neonatal period

This Local Guideline applies to:
1. Adults: No
2. Children up to 16 years: No
3. Neonates – less than 29 days: Yes

Approval gained from the Children Young People and Families Network on 24/02/15

Keywords: Ligation, NSAIDs (non-steroidal anti-inflammatory drugs), PDA (Patent ductus arteriosis), PVR (pulmonary vascular resistance), Preterm, Shunt

Replaces Existing Local Guideline and Procedure: Yes
Registration Number(s) and/or name and of Superseded Documents: Same name/no

Related Legislation, Australian Standards, NSW Health Policy Directive, NSQHS Standard/EQuIP Criterion and/or other, HNE Health Documents, Professional Guidelines, Codes of Practice or Ethics:
- Relevant Accreditation Criterion e.g. NSQHS Standards/EQuIP Criterion and/or other:
- NSW Health Policy Directive 2007_079 Clinical Procedure Safety
- NSW Health Policy PD 2005_406 Consent to Medical Treatment
- NSW Health Policy Directive PD 2007_036 Infection Control Policy

Prerequisites (if required): N/A

Local Guideline Note: This document reflects what is currently regarded as safe and appropriate practice. The guideline section does not replace the need for the application of clinical judgment in respect to each individual patient but the procedure/s requires mandatory compliance. If staff believes that the procedure/s should not apply in a particular clinical situation they must seek advice from their unit manager/delegate and document the variance in the patient’s health record.

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Date authorised: 24/02/15
This Local Guideline contains advice on therapeutics: Yes
Approval gained from Local Quality Use of Medicines Committee on 12th Feb 15

Date of Issue: 24/02/15
Review due date: 24/02/18
RISK STATEMENT

This local guideline has been developed to provide guidance to clinical staff in NICU when managing and treating neonates with a (PDA) patent ductus arteriosis and ensures that risks of harm to infants and staff during procedures and care are identified and managed.

Any unplanned event resulting in, or with the potential for injury, damage or other loss to infants or staff as a result of this management must be reported through the Incident Information Management System and managed in accordance with the Ministry of Health Policy Directive :Incident management PD2007_061. This would include unintended injury that results in disability, death or prolonged hospital stay.

RISK CATEGORY: Clinical Care & Patient Safety;

OUTCOMES

1. Infants are assessed for symptoms of a PDA and investigated using cardiac ultrasound when there is respiratory involvement

2. Infants are treated with NSAIDs according to guideline to close the PDA

3. Surgery is considered if NSAID courses x2 are unsuccessful and supportive respiratory management fails to close the PDA

ABBREVIATIONS & GLOSSARY

<table>
<thead>
<tr>
<th>Abbreviation/Word</th>
<th>Definition</th>
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<tbody>
<tr>
<td>BPD/CLD</td>
<td>Broncho pulmonary Dysplasia/Chronic Lung Disease</td>
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<tr>
<td>DETECT</td>
<td>Ductal Echocardiography Targeting &amp; Early Closure Trial-randomised placebo controlled trial of early treatment of the patent ductus arteriosus</td>
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<tr>
<td>EBM</td>
<td>Expressed breast milk</td>
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<td>ELBW</td>
<td>Extremely Low Birthweight</td>
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<tr>
<td>IV/PO</td>
<td>Intravenous/per oral</td>
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<tr>
<td>IVH</td>
<td>Intraventricular Haemorrhage</td>
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<td>LVO/RVO/LPA</td>
<td>Left ventricular Outlet/right ventricular outlet/Left pulmonary artery</td>
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<tr>
<td>NEC</td>
<td>Necrotising Enterocolitis</td>
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<td>NSAID</td>
<td>Non steroidal Anti-inflammatorys</td>
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<tr>
<td>PDA</td>
<td>Patent ductus arteriosus</td>
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<td>PPHN</td>
<td>Persistent pulmonary hypertension of the newborn</td>
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<tr>
<td>PVR</td>
<td>Pulmonary vascular resistance</td>
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<td>RDS</td>
<td>Respiratory Distress Syndrome</td>
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GUIDELINE

This Guideline does not replace the need for the application of clinical judgment in respect to each individual patient.

Patent Ductus Arteriosus (PDA) Management in NICU - One Page Summary and Checklist

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Background

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Treatment Options

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Treatment

Follow up

Background

The ductus arteriosus is an artery joining the aorta and pulmonary artery that normally closes functionally soon after birth. A patent ductus arteriosus (PDA) results from failure of the ductus arteriosus to close or from reopening after functional closure. Failure of ductal closure, coinciding with the normal postpartum fall in pulmonary vascular resistance (PVR), results in a left-to-right transductal shunt. The consequences may include pulmonary over-perfusion and/or systemic hypoperfusion.

Diagram showing normal anatomy

Showing Ductus Arteriosis between aorta & pulmonary artery
Incidence

The incidence of a PDA is not uniformly reported, as it is dependent on the definition used (clinical signs and/or ultrasound parameters) and at what postnatal age this is measured. In preterm infants with no significant respiratory disease, more than 90% of the ducts are closed at day 3.

Spontaneous closure happens in 70% of the infants of 29 weeks gestation, but with decreasing gestational age, the spontaneous closure rate drops to approximately 30%. Risk factors for a PDA are lower gestational age, lack of antenatal steroids and the need for mechanical ventilation. The introduction of exogenous surfactant therapy has altered both the incidence and the presentation of the PDA. Although surfactant has no effect on the contractile behavior of the ductus, its effects on pulmonary vascular resistance, the improvement in PaO2 and reversal of respiratory acidosis leads to an earlier clinical presentation of the left-to-right shunt.

Clinical Consequences of a PDA

The clinical impact of a PDA is dependent on the magnitude of the shunt and the ability of the infant to initiate compensatory mechanisms. Shunt magnitude is dependent on PDA diameter and the pressure difference between the pulmonary and systemic ends.

A PDA is associated with hypotension during transition, intraventricular hemorrhages, pulmonary hemorrhage, necrotizing enter colitis and chronic lung disease. Early studies on the PDA have shown significant hemodynamic changes in ventilated preterm animals, with increased pulmonary blood flow and significantly decreased organ blood flow. The effect of a PDA on systemic blood flow during and after the immediate transition could not be reproduced in recent studies incorporating current treatment approaches that tend to reduce the need for mechanical ventilation, including routine antenatal steroid use, early selective surfactant and improved respiratory strategies.

Treatment options

NSAIDS

Trials designed to close the PDA provide insight into the contribution of the PDA to morbidity as well as the efficacy of therapy. If the PDA is related to morbidity in a causal relationship, closure should reduce the incidence of the morbidity. An overview of meta-analyses evaluating different treatment approaches to close the PDA on major morbidities is presented in the table below.

<table>
<thead>
<tr>
<th></th>
<th>IVH</th>
<th>NEC</th>
<th>BPD</th>
<th>Neuro-development</th>
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<tr>
<td>Prophylactic closure</td>
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<td>Pre-symptomatic closure</td>
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<td>Symptomatic closure</td>
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<tr>
<td>Surgical ligation</td>
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No approach has proven to be superior. Prophylactic treatment in ELBW infants reduced the incidence of IVH, but did not improve neuro-developmental outcome to 2 years of age. The few available pre-symptomatic and symptomatic trials reduced oxygen days, but not mechanical ventilation days nor BPD. The recent DETECT trial showed that early targeted treatment in infants < 29 weeks gestation could reduce the number of infants with pulmonary hemorrhage from 23 to
9%, however, such a strategy would need the availability of a 24/7 ultrasound service. It seems that most meta-analysis of trials showed no improvement in clinical outcomes, even though PDA was reduced. It is possible that the treatment received is causing more harm than benefit or treatment is being directed at the wrong patient subgroups. No randomized trials have truly explored the possibility of not treating the PDA, as practically all earlier studies provided open label (non-randomised) treatment in the placebo group at a later stage.

**Surgical ligation**

PDA ligation as a definitive form of treatment is associated with reduced mortality, but surviving infants are at increased risk of adverse outcomes like BPD and impaired neuro-developmental outcome. However, there is a lack of studies addressing survival bias and confounding by indication.

Spontaneous closure rate is >70% in a cohort of infants < 28 week gestation at an average 51 days of life. Ligation should be reserved for infants with a PDA and significant cardiorespiratory failure at advanced postnatal age not responding to optimal conservative management.

**Supportive care**

Supportive care can be instituted with, without or after NSAID treatment. The aim would be to maintain an optimal pulmonary condition with the known increased pulmonary volume load. Respiratory support for improvements in oxygenation and lung compliance can be achieved by increasing the positive end expiratory pressure (PEEP) to levels that maintain optimal recruitment and minimize atelectasis-induced lung injury.

High daily fluid intake contributes to ductal patency. A modest fluid restriction (140-150 ml/kg/day) might help reduce the increased pulmonary fluid burden.

Early studies on the use of frusemide in RDS showed a transient improvement in pulmonary function without increasing ductal patency, although the pulmonary effects were not consistently present in all studies. Concerns were raised about prolonging ductal patency with frusemide, as it can stimulate prostaglandin E2 synthesis. Again, this could not consistently be found in the studies. Hydrochlorothiazide does not increase prostaglandin E2 production and is a good alternative to treat fluid overload in preterm infants with a PDA.

**Investigations (Indications for cardiac ultrasound)**

Clinical signs of pulmonary volume overload (need at least one)

- Increased number of apnea’s over the last few days
- Persistent (>12-24 hours) increase in FiO₂
- Increase in mean airway pressure
- Increasing respiratory distress (respiratory rate, work of breathing) not otherwise explained
- Unable to wean off respiratory support
- The need for mechanical ventilation for which no other cause can be found

Although a murmur and bounding pulses are common findings in patients with a PDA, these signs do not indicate pulmonary volume overload or predict further respiratory compromise. However, cardiac ultrasound can be indicated to exclude congenital heart disease.
Cardiac ultrasound signs of pulmonary volume overload include enlargement of the left heart and parameters of increased pulmonary blood flow. The parameters indicating pulmonary volume overload most used in our department are

- M mode derived LA/Ao ratio > 1.5
- 2D derived LA/Ao ratio > 1.9
- LPA end diastolic velocity > 20 cm/s
- LVO:RVO ratio > 1.25

Treatment

Treatment with NSAIDs is recommended when all 3 criteria of hemodynamic significance are met:

Clinical signs of pulmonary volume overload

AND
PDA diameter > 1.5 mm

AND
Cardiac ultrasound parameters of pulmonary volume overload

The therapeutic goals of PDA treatment are to improve the pulmonary symptoms. This can be achieved with ductal constriction or closure. Contradictory to this therapeutic goal, NSAID treatment commonly increases FiO₂ demand.

**IBUPROFEN (IV, PO)**
Starting dose 10 mg/kg, subsequent doses 5 mg/kg
One course is a total of 3 doses (1<sup>st</sup> dose =10 mg/kg; 2<sup>nd</sup> dose = 5 mg/kg; 3<sup>rd</sup> dose = 5 mg/kg) at 24 hour intervals (total course = 3 days)
Side effects: renal impairment, (rare) sudden severe PPHN if used in first 24 hours after birth

**INDOMETHACIN (IV, PO)**
Starting dose 0.2 mg/kg, subsequent doses 0.2 mg/kg
One course is a total of 3 doses (1<sup>st</sup> dose = 0.2 mg/kg; 2<sup>nd</sup> dose = 0.2 mg/kg; 3<sup>rd</sup> dose = 0.2 mg/kg) at 12 hour intervals (total course = 1 ½ days) [Overmeire, B et.al 2001]
Side effects: renal impairment (more likely than Ibuprofen)

**Absolute NSAID contra-indications**
- Active haemorrhage

**Relative NSAID contra-indications**
- Poor renal function (oliguria <0.5 ml/kg/hr or creatinine > 110 micromol/L). Consult with Neonatologist: consider lower dose or longer interval between doses
- Bleeding disorders
- Thrombocytopenia (< 50 x 10<sup>9</sup>/L). Even though NSAIDs reduce platelet aggregation and not total platelet number, this relative contra-indication is mentioned in almost every PDA study performed. Consider platelet transfusion before starting NSAIDs

**Monitoring during NSAID treatment**
- Urine output, fluid balance
- Serum electrolytes (daily)
- Review infant prior to each dose, ensure urine output >0.5-1ml/kg/hour
- Gastrointestinal function: there is no need to routinely stop enteral feeds (EBM or Formula) when starting NSAIDs. Close monitoring of feed intolerance is needed and enteral feeds should be adjusted accordingly
Follow-up after NSAID treatment

- Evaluate treatment effect with a repeat ultrasound at least 24 hours after the last dose was given
- Repeat medical treatment course if necessary. A maximum of 2 courses is recommended, but further doses can be considered at clinicians discretion
- Supportive care after failure to close should include optimal airway pressure, careful fluid management, and the use of diuretics
- Indication for surgical closure is decided per individual case and can be complex, best decided after team consultation

References


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FEEDBACK

Any feedback on this document should be sent to the Contact Officer listed on the front page.