

# PATENT DUCTUS ARTERIOSUS

## RECOGNITION AND ASSESSMENT

### Definition

- Persistent patency of the ductus arteriosus (PDA) is a failure of functional ductal closure by 48 hr or anatomical closure by aged 3 weeks

### Factors associated with delayed closure

- Prematurity (significant PDA affects approximately 30% of very-low-birth-weight babies)
- Lack of antenatal corticosteroid prophylaxis
- Surfactant-deficient lung disease
- Hypoxaemia
- Volume overload

### Adverse effects of PDA

- Haemodynamic consequences of left-to-right shunt in preterm babies can prolong ventilatory support and are associated with mortality and morbidity [chronic lung disease, pulmonary haemorrhage, intraventricular haemorrhage, necrotising enterocolitis (NEC) and retinopathy of prematurity]
- Increased pulmonary blood flow (leading to increased work of breathing and respiratory deterioration)
- Reduced systemic blood flow (leading to acidosis and hypotension)

### Symptoms and signs

- Can be absent even in the presence of a significant duct in first 7 days of life
- A significant left-to-right shunt is suggested by:
  - bounding pulses and wide pulse pressure (i.e.  $>25$  mmHg)
  - hyperdynamic precordium (excessive movement of precordium)
  - low-pitched systolic or continuous murmur over left upper sternal edge (absence of a murmur does not exclude significant PDA)
  - signs of cardiac failure (tachypnoea, tachycardia, hepatomegaly, pulmonary oedema, generalised oedema etc.)
  - poor perfusion (hypotension, poor capillary refill, mottled skin and persistent acidosis)
  - increased or persistent ventilatory requirements

### Differential diagnosis

- Other cardiac pathology (e.g. congenital heart disease, including duct-dependent lesions, arrhythmias or cardiomyopathy)
- Sepsis

## INVESTIGATIONS

- SpO<sub>2</sub> monitoring
- Chest X-ray (cardiomegaly? pulmonary plethora?)
- Echocardiography
  - to detect duct-dependent cardiac lesions and other cardiac pathologies that are difficult to exclude clinically
  - if considering treatment with prostaglandin inhibitor
  - echocardiographic assessment of significant PDA includes:
    - size of PDA ( $>1.5$  mm)
    - volume loading of left atrium (LA/aorta ratio  $>1.5$ )
    - volume loading of left ventricle
    - velocity and flow pattern of ductal flow

## IMMEDIATE TREATMENT

### General measures

- Optimise oxygenation by appropriate ventilatory management
- Use of a higher PEEP (i.e.  $\geq 5$  cm H<sub>2</sub>O) can help minimise effects of pulmonary oedema and risk of pulmonary haemorrhage
- Treat anaemia – maintain Hb  $\geq 100$  g/L with blood transfusion (consider concurrent dose of furosemide IV)

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- Before starting medication, consider restricting fluid intake to 60–80% (e.g. from 150 mL/kg/day to 90–120 mL/kg/day)
- If fluid overload or pulmonary oedema, give 1 dose of furosemide IV in accordance with **Neonatal Formulary**

### Specific measures

- Aim to convert haemodynamically significant PDA into insignificant PDA as complete duct closure may take weeks or months

### **Pharmacological treatment with prostaglandin inhibitor to initiate closure**

Discuss with senior before starting or altering pharmacological treatment for PDA

- Ibuprofen IV is the drug of choice for this purpose – indometacin is not currently available in the UK
- **Paracetamol is often used as alternative first line**, or if ibuprofen is contraindicated - Needs discussion with consultant (see below):
  - be aware of the lack of data for long-term safety on the developing immature brain
- Pharmacological treatment is best used aged  $\leq 2$  weeks but can be effective  $\leq 6$  weeks

### **Indications for pharmacological treatment**

- Babies born  $< 34$  weeks' gestation with significant PDA – on clinical and/or echocardiographic assessment
- Includes ventilatory/CPAP dependent babies or PDA with haemodynamic effects (i.e. cardiac failure or poor perfusion)
- Monitor babies with non-significant PDA carefully and treat if becomes significant

## IBUPROFEN

### Contraindications

- Duct-dependent cardiac lesion
- Significant renal impairment: urine output  $< 1$  mL/kg/hr or creatinine  $> 120$  micromol/L
- Significant thrombocytopenia, i.e. platelet count  $< 50 \times 10^9/L$  (course started or next dose given only after platelet transfusion)
- Suspected or definite NEC or gastrointestinal perforation
- Active phase of significant bleeding (gastrointestinal or severe intracranial) – treat coagulopathy before starting course (see **Coagulopathy** guideline)

### Dose

- Calculate carefully and prescribe individually on single dose part of prescription chart so that contraindications checked before each dose
- Administer IV in accordance with **Neonatal Formulary**

### Monitoring during treatment

- Check the following before each dose:
  - creatinine ( $< 120$  micromol/L)
  - urine output ( $> 1$  mL/kg/hr)
  - platelet count ( $\geq 50 \times 10^9/L$  with platelet infusions if needed)
- If any parameter abnormal withhold dose until it normalises

## PARACETAMOL

### Contraindications

- Duct dependent cardiac lesion

### Dose

- **Dose and regimen as per local trust policy or formulary**
- IV loading dose 15–20 mg/kg followed by IV maintenance dose 6–8 hrly. Lower IV cumulative dose 40–50 mg/kg/day have been found to be effective and safe in RCTs
- **Paracetamol 15 mg/kg 6-hrly oral (total cumulative dose 60 mg/kg/day) has also been shown to be safe and effective in RCTs – consider this route if IV access difficult**
- Repeat echo 3–5 days after commencing treatment
- Duration of treatment is 3 days but can be extended by a maximum of 3 more days if PDA remains significant (based on clinical or echo evaluation)

### Monitoring during treatment

- Serum paracetamol trough levels (pre-dose levels) and frequency/dose of paracetamol medication adjusted as per local trust policy e.g. serum paracetamol trough levels before 3<sup>rd</sup> and 6<sup>th</sup> maintenance doses, and before every 3<sup>rd</sup> dose after any changes in frequency/dose
- therapeutic range 15–25 mg/L
  - if levels >25 mg/L, reduce frequency/dose of paracetamol medication and recheck the pre-dose level before every 3<sup>rd</sup> dose after the change
- LFTs before treatment, then daily for 6 days
- Echo day 3–5 of treatment

### SUBSEQUENT MANAGEMENT (both drugs)

- Aim to avoid concomitant nephrotoxic drugs e.g. gentamicin or vancomycin. Monitor levels or use an alternative drug
- Observe for signs of feed tolerance (feeds cautiously initiated or continued during treatment – briefly stopped during actual infusion)
- Monitor clinical signs of PDA and baby's progress
- Echocardiography (if clinically indicated), repeated after 2–3 days of completion
- Fluid gradually liberalised after treatment based on:
  - daily weight (weight gain suggests fluid retention)
  - serum sodium (dilutional hyponatraemia common)

### Persistence or recurrence of asymptomatic PDA

- **Persistence of murmur does not necessarily indicate return of PDA**
- Echocardiogram sometimes demonstrates physiological branch pulmonary stenosis
- If baby with asymptomatic murmur is making progress, plan echocardiography before discharge to decide follow-up

### Persistent significant PDA and surgical referral

- If PDA significant after 48 hr of completion of first course of prostaglandin inhibitor, use second course of ibuprofen
- If PDA still significant but baby making progress (i.e. can be extubated or come off CPAP):
  - commence regular diuretics (furosemide + amiloride/spironolactone) to help control haemodynamic effects/cardiac failure – in accordance with **Neonatal Formulary**
  - monitor closely
- If PDA still significant and baby ventilatory or CPAP/high flow dependent, discuss with **cardiac centre** for surgical ligation when:
  - prostaglandin inhibitor contraindicated
    - if ibuprofen contraindicated, use paracetamol
  - prostaglandin inhibitor not indicated (≥34 weeks with cardiac failure not controlled by diuretics)
  - prostaglandin inhibitor ineffective (usually after giving second course). Paracetamol used as 3<sup>rd</sup> course if not used before, while considering surgical ligation
- Discuss further cardiac assessment and surgical ligation of PDA with cardiologist at **regional cardiac centre and transport team – follow local care pathway (e.g. West Midlands PDA Ligation Referral Pathway)**
- After surgical ligation, keep baby nil-by-mouth for 24 hr before gradually building up feeds (because of risk of NEC)

### DISCHARGE POLICY FOR PERSISTENT PDA

- If PDA persistent clinically or echocardiographically at discharge or at 6 weeks follow-up, arrange further follow-ups in cardiac clinic (**locally or at cardiac centre depending on local practice**)
- If PDA reviewed locally still persistent at aged 1 yr or if clinically significant during follow-up (cardiac failure or failure to thrive), refer to **paediatric cardiologist** at **regional cardiac centre** to consider closure (first option is usually catheter closure)

**Medical treatment of persistent PDA <34 weeks' gestation**

