NCCU CLINICAL GUIDELINES
SECTION: 14

CARDIAC CONDITIONS

PATENT DUCTUS ARTERIOSUS

The ductus arteriosus is a large vessel that connects the main pulmonary trunk with the descending aorta. In utero pulmonary resistance remains high and only 7% of the combined cardiac output is directed through the right and left pulmonary arteries. The bulk of the right ventricular output travels through the ductus arteriosus maintaining flow in the descending aorta and hence placental perfusion.

At delivery a series of complex changes occur as an orchestrated continuum. With the first breath pulmonary capillaries open and resistance to pulmonary blood flow drops. This leads to further reduction in right sided pressures and directs the right ventricular output through the pulmonary circulation. As systemic pressures start to exceed pulmonary pressures, blood flow through the ductus arteriosus reverses and oxygenated blood from the systemic circulation flows into the pulmonary circulation. Final functional closure occurs by 24h of age in around half of healthy full-term infants and in all by 96h of age.

PRESENTATION

Left to right shunting across the ductus is present within a few hours of birth and echocardiographic signs are present before clinical changes. The usual presentation is on days 1 – 4 but can be later and presents as any of the following:

- Heart murmur – usually systolic and may be intermittent or continuous
- Hyperactive precordium and bounding pulses with increased pulse pressure
- Hypotension – particularly VLBW infants
- Respiratory deterioration over hours or days
- Heart failure / pulmonary oedema and haemorrhage

TREATMENT

Prophylactic treatment involves treatment of all high risk infants on the first day usually within the 1st 6 hours. Meta-analysis of trials to date shows significant reductions in both symptomatic PDA's (RR = 0.35 CI 0.26-0.27) and severe IVH (RR = 0.60 CI 0.43-0.83) and later symptomatic PDA but little effect on other morbidities particularly respiratory outcomes. The prophylactic use of indomethacin will mean many infants will be treated unnecessarily. There is no evidence that prophylactic indomethacin improves long term neurodevelopmental outcome, neither is there evidence of long term harm (TIPP trial NEJM 28 June 2001).

An alternative to prophylactic treatment is early targeted treatment of ducts that fail to constrict spontaneously. There is a lower incidence of ductal re-opening if treatment is given in the first 24 hours compared to treatment later in the first week and treatment is instituted before the majority of

duct dependent pulmonary haemorrhages. This approach relies on early ultrasound evaluation and in theory should provide the early clinical advantages of prophylaxis without exposing infants at minimal risk from PDA to unnecessary medication.

Indomethacin can thus be given either prophylactically or on a targeted basis after echocardiography or when the duct becomes clinically apparent. No one strategy has been shown unequivocally to improve outcomes.

DOSAGE OF INDOMETHACIN.

There are numerous regimes described, most of which have been evaluated at a later postnatal age. Consensus would suggest an initial dose of 0.2 mg/Kg is necessary to induce closure while a 5 dose course has benefit in preventing reopening. Indomethacin is a potent cyclo-oxygenase inhibitor having action on both the COX1 and COX2 isoforms. The drug may cause oliguria and transient renal failure, decrease cerebral, mesenteric and renal blood flow, induce gastric haemorrhage and perforation and reduce platelet adhesiveness. The drug is contraindicated in thrombocytopaenia (<50) and in active bleeding. Indonmethacin should not be given to infants with renal failure (urine output <0.5 ml/Kg/min) nor to infants suspected of having NEC.

SIGNIFICANT DUCT	**INDOMETHACIN**	
Infant remains on ventilatory support	Stat	0.2 mg / Kg
(IMV or CPAP)	12 hours	0.2 mg / Kg
and	24 hours	0.1 mg / Kg
Ductal diameter >1.5mm	48 hours	0.1 mg / Kg
and	72 hours	0.1 mg / Kg
LA or LV dilation		
	See drug manual.	

Approximately 20% of infants will fail to respond to indomethacin and a further 30-40% will reopen a ductus after initial closure. Failure is more likely in extremely premature infants.

There is insufficient evidence to make clear recommendations about fluid restriction of concomitant use of frusemide.

IBUPROFEN

There have been some trials comparing the use of Ibuprofen with indomethacin. Ibuprofen appears to induce less perturbations of cerebral blood flow but has anecdotally been associated with the onset of pulmonary hypertension. Current Cochrane reviews do not advocate its use.

SURGICAL LIGATION

The role for surgical ligation of the PDA is debated. Some centres advocate early surgical closure arguing that surgery is more effective than indomethacin, other centres resort to surgery when indomethacin is contraindicated or has failed, yet others rarely if ever ligate the ductus. There is no clear evidence to support or refute any of these approaches. We are currently proposing a randomised trail of ligation in those infants failing indomethacin.

FLOW CHART FOR MANAGEMENT OF PDA