Early treatment versus expectant management of hemodynamically significant patent ductus arteriosus for preterm infants
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Background: Patent ductus arteriosus (PDA) is associated with significant morbidity and mortality in preterm infants. Nonsteroidal anti-inflammatory drugs (NSAIDs) are used to prevent or treat a PDA. There are concerns regarding adverse effects of NSAIDs in preterm infants. Controversy exists on whether early targeted treatment of a hemodynamically significant (hs) PDA improves clinical outcomes.
Objectives : To assess the effectiveness and safety of early treatment strategies versus expectant management for an hs-PDA in reducing mortality and morbidity in preterm infants.
Search methods: As per standard Cochrane search strategy. RCTs and quasi-RCTs included pharmacological treatment, defined as treatment initiated within the first seven days after birth, was compared to no intervention, placebo or other non-pharmacological expectant management strategies for treatment of an hs-PDA in preterm
(< 37 weeks' postmenstrual age) or low birth weight (< 2500 grams) infants.

ACADEMIC P.E.A.R.L.S

Pediatric Evidence And Research Learning Snippet

PDA IN PRETERM INFANTS

EARLY TREATMENT VERSUS EXPECTANT MANAGEMENT OF HEMODYNAMICALLY SIGNIFICANT PATENT DUCTUS ARTERIOSUS FOR PRETERM INFANTS

- **Results:**
- **Total 14 trial, 910 neonates** included
- Seven RCTs compared **early** treatment (< seven days) versus **expectant** management (Mx) & seven RCTs compared **very early** treatment (< 72 hours of age) versus **expectant Mx**
- **No difference** between **early treatment** versus expectant management for an hs-PDA for
  1. the primary outcome of **'all-cause mortality'** (6 studies ; n=500; RR 0.80, 95%CI 0.46 to 1.39)
  2. **surgical PDA ligation** (4 studies; n=432; RR 1.08, 95% CI 0.65 to 1.80)
  3. **chronic lung disease** (CLD) (4 studies; n=339; RR 0.90, 95% CI 0.62 to 1.29)
  4. **severe intraventricular hemorrhage** (IVH) (2 studies; n=171;l RR 0.83,95% CI 0.32 to 2.16), and
  5. **necrotizing enterocolitis** (NEC) (5 studies; n=473; RR 2.34,95% CI 0.86 to 6.41).
- **No difference** was demonstrated between very early treatment versus expectant management
  1. **all-cause mortality'** (7 studies; n=384; RR 0.94, 95% CI 0.58 to 1.53)
  2. **surgical PDA ligation** (5 studies; n=293; RR 0.88, 95% CI 0.36 to 2.17),
  3. **CLD** (7 studies; n=384 infants; RR 0.83, 95% CI 0.63 to 1.08),
  4. **severe IVH** (4 studies, n=240; RR 0.64, 95% CI 0.21 to 1.93),
  5. **NEC** (5 studies; 332 infants; typical RR 1.08, 95% CI 0.53 to 2.21) and
  6. **neurodevelopmental impairment** (1 study; n=79 infants; RR 0.27, 95% CI 0.03 to 2.31 for moderate/severe cognitive delay at 18 to 24 months; RR 0.54, 95% CI 0.05 to 5.71 for moderate/severe motor delay at 18 to 24 months; RR 0.54, 95% CI 0.10 to 2.78 for moderate/severe language delay at 18 to 24 months).
- Infants receiving very early treatment in the first 72 hours after birth were more likely to receive any PDA pharmacotherapy compared to expectant management (4 studies; n=156 infants; typical RR 1.64, 95% CI 1.31 to 2.05).
- Very early treatment, however, shortened the duration of hospitalization compared to expectant management (4 studies; 260 infants; MD -5.35 days; 95% CI -9.23 to -1.47).

EXPERT COMMENT

- Current evidence doesn't support Early or very early pharmacotherapeutic treatment of an hs-PDA as it failed to demonstrate reduction in mortality in preterm infants and no significant reduction in need for surgical PDA ligation, severe IVH or NEC (moderate-certainty evidence), and CLD or neurodevelopmental impairment (low-certainty evidence).
- Many studies were moderate to low quality and results are diluted due to open label treatment in quite a few trials.
- Conservative approach and late treatment is also not safe and associated with increased morbidity and mortality, so targeted selective treatment of duct is a safer approach. Additional large trials that specifically include preterm infants at the highest risk of PDA-attributable morbidity, which are adequately powered for patient-important are required to explore, if early targeted treatment of hs-PDA improves clinical outcomes.

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Reference

Souvik Mitra, A Scrivens et al. Early treatment versus expectant management of hemodynamically significant patent ductus arteriosus for preterm infants. Cochrane Database of Systematic Reviews Intervention. Version published: 10th December, 2020. https://doi.org/10.1002/14651858.CD013278.pub2