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Paracetamol for the Treatment of Pre-term Patent Ductus Arteriosus - A Systematic Review and Meta-analysis

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Introduction: Ibuprofen is commonly used to close arterial ducts (PDA) in preterm neonates. In order to help determine if Paracetamol offered similar efficacy, a systematic review and meta analysis was performed to compare outcomes in significant PDA in neonates <37 weeks gestation. Primary outcome was PDA closure after one or two courses (3 or 6 days) of medication.

Methods: Medline, Scopus, Embase and Google scholar were searched. Manual screening of results revealed six completed trials. Data regarding the risk of selection, detection, attrition and reporting bias were collected and studies were evaluated using the Cochrane collaboration tools for their risk of bias. Using a predesigned data extraction form, the PDA closure rates, as well as rates of complications were extracted, including gastrointestinal bleeding; oliguria; necrotising enterocolitis; Brochopulmonary dysplasia; and mortality. The mean post treatment serum creatinine; aspartate transaminase; and alanine aminotransferase level were also extracted. Data from studies were entered into Stat version 13.0 and compared using the Metan functions.

Results: 733 neonates from six studies were randomised for PDA closure after one course of study medication (371 to Paracetamol, 362 to Ibuprofen). 646 from five studies were randomised for PDA closure after two courses (327 to Paracetamol, 319 to Ibuprofen). The relative risk of PDA closure with Paracetamol compared to Ibuprofen was 1.07 (95% CI 0.98-1.17, p=0.124) and 1.05 (95% CI 0.99-1.11, p=0.129) after one and two courses respectively. The relative risk of gastrointestinal bleeding was 0.27 (95% CI=0.11-0.67, p=0.005) compared to those treated with Ibuprofen. There was a non significant trend towards lower rates of oliguria with Paracetamol (relative risk=0.46 95% CI 0.2-1.1, p=0.083).

Conclusion: The effectiveness of Paracetamol for PDA closure in pre-term neonates appears to be similar to that of ibuprofen. It confers a lower risk of gastrointestinal bleeding and may reduce the incidence on oliguria. Paracetamol should be considered as a first line medication for haemodynamically or clinically significant PDA closure in pre-term neonates.