

Systematic review and network meta-analysis of IV indomethacin versus IV Ibuprofen versus oral Ibuprofen versus oral acetaminophen versus placebo for treatment of symptomatic patent ductus arteriosus in preterm infants

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Citation

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Review question

Systematic review and network meta-analysis comparing indomethacin, ibuprofen, acetaminophen with placebo for treatment of Patent Ductus Arteriosus in preterm infants.

Searches

A systematic literature search would be conducted from the following electronic databases:

Cochrane Central Register of Controlled Trials (CENTRAL)

MEDLINE

PubMed

EMBASE

In addition, we will seek registered details of selected trials in the U.S. National Institutes of Health resource Clinicaltrials.gov. We would obtain information by personal communication, review the reference lists of relevant articles, abstracts and conference proceedings (Society for Pediatric Research, European Society for Paediatric Research 1990–2015) and seek results of unpublished trials. No language restrictions would be imposed.

The following keywords would be used to build our search strategy for each electronic database

1. Population:

Newborn Ductus

Ductus Arteriosus, Patent

Ductus (free term)

PDA

Persistent fetal circulation

AND

Newborn (free term)

Infant

Neonate

Preterm

Premature

2. Intervention and Control:

Indomethacin

Ibuprofen

paracetamol

placebo

Acetaminophen

Cox inhibitor

Prostaglandin synthetase inhibitor

NSAID (free)

Ant-Inflammatory Agents, Non-steroidal [Mesh]

3. Design:

Randomized controlled trials as a topic [Mesh]

Randomized Controlled trial [Publication type]

Clinical Trial

Randomized Controlled trial

Types of study to be included

Randomized controlled trials

Condition or domain being studied

Management of patent ductus arteriosus (PDA) in preterm infants is one of the most controversial topics in neonatal medicine. It is associated with a number of co-morbidities like necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD) and intraventricular hemorrhage (IVH). The management dilemmas have mainly centered on when to treat and with what to treat. To increase the complexity of matters, these two aspects of PDA management are not mutually exclusive, with the modality of treatment often being dictated by the timing of treatment. There have been a large number of published studies, meta-analyses, reviews, and editorials focusing on different aspects of management dilemmas. Regarding the timing of treatment, prophylactic therapy has gradually fallen out of favor and neonatal units have shifted towards a more conservative approach by treating only the clinically and echocardiographically significant PDAs. However, the big dilemma that still persists among neonatologists is what to use as the primary modality of treatment.

Participants/population

Preterm infants with hemodynamically significant PDA

Intervention(s), exposure(s)

1. Intravenous Indomethacin

or

2. Intravenous Ibuprofen

or

3. Oral Ibuprofen

or

4. Oral Acetaminophen

or

5. IV acetaminophen

Inclusion criteria: trials included in our review will have 1) Indomethacin or Ibuprofen or Acetaminophen being used for the treatment of clinically and/or echocardiographically determined hemodynamically significant PDA ; 2) have randomized infants to two intervention arms using the above mentioned drugs or an intervention arm using one of the above mentioned drugs and a control arm.

Exclusion criteria: use of any intervention for prophylaxis

Comparator(s)/control

Any of the interventions or placebo

Primary outcome(s)

Closure of PDA

Secondary outcome(s)

Incidence of necrotizing enterocolitis

Incidence of oliguria

Duration of ventilatory support

Data extraction (selection and coding)

Risk of bias (quality) assessment

GRADE guidelines will be used for risk of bias assessment

Strategy for data synthesis

Network meta-analysis will be done

Data will be analyzed as aggregate

Quantitative synthesis is planned

Analysis of subgroups or subsets

None planned

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Organisational affiliation of the review

McMaster University

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None

Conflicts of interest

None known

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English

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England, Canada, Colombia

Stage of review

Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Acetaminophen; Cyclooxygenase Inhibitors; Ductus Arteriosus, Patent; Humans; Ibuprofen; Indomethacin; Infant, Newborn; Infant, Premature

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Revision note for this version

Details of search strategies including keywords and database sources have been specified on section # 16

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

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Versions

30 June 2015

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