Prophylactic antibiotics to reduce morbidity and mortality in newborn infants with intercostal catheters (Review)
Prophylactic antibiotics to reduce morbidity and mortality in newborn infants with intercostal catheters

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ABSTRACT

Background

Intercostal catheters are commonly used for the drainage of intrathoracic collections in newborn infants, including pneumothorax and pleural effusions. Placement of an intercostal drain is a potential risk factor for nosocomial infection due to breach of the cutaneous barrier. Therefore, neonates who require intercostal drainage, especially those in high risk groups for nosocomial infection, may benefit from antibiotic prophylaxis. However, injudicious antibiotic use carries the risk of promoting the emergence of resistant strains of micro-organisms or of altering the pattern of pathogens causing infection.

Objectives

To determine the effect of prophylactic antibiotics compared to selective use of antibiotics on mortality and morbidity (especially septicaemia) in neonates undergoing placement of an intercostal catheter.

Search methods

The standard search strategy of the Cochrane Neonatal Review Group was used to search the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2011, Issue 5), MEDLINE (1948 to June 2011) and CINAHL (1982 to June 2011).

Selection criteria

Randomised controlled trials or some types of non-randomised (that is, quasi-randomised) controlled trials of adequate quality in which either individual newborn infants or clusters of infants were randomised to receive prophylactic antibiotics versus placebo or no treatment.

Data collection and analysis

We used the standard methods of the Cochrane Neonatal Review Group.

Main results

We did not find any randomised controlled trials that met the eligibility criteria.
Authors’ conclusions
There are no data from randomised trials to either support or refute the use of antibiotic prophylaxis for intercostal catheter insertion in neonates. Any randomised controlled trials of antibiotic prophylaxis would need to account for the fact that neonates who require insertion of an intercostal catheter may already be receiving antibiotics for other indications.

PLAIN LANGUAGE SUMMARY
Prophylactic antibiotics to reduce morbidity and mortality in newborn infants with intercostal catheters

There is no evidence to support or refute the use of preventive antibiotics in newborn babies with drainage tubes placed in the chest. Sick newborn babies occasionally need the insertion of a tube that is placed through the skin and into the lung space to drain air or fluid from around their lungs. Because this process involves breaching the skin barrier, there is a potential risk of infection. The group of babies most likely to need this procedure are also those that are most at risk of developing an infection during their stay in hospital. Preventive antibiotics are commonly used when there is a risk of infection, but they may have unwanted effects. The review authors found no evidence to support or refute the use of routine preventive antibiotics when intercostal catheters are inserted in newborn babies.

BACKGROUND

Description of the condition

Intercostal catheters are commonly used for the drainage of intrathoracic collections in newborn infants, including pneumothorax and pleural effusions. Placement of intercostal catheters is common in critically ill neonates, especially in infants with birthweight less than 1500 g (very low birth weight infants, VLBW). The Vermont Oxford Network Database reported an incidence of pneumothorax in VLBW infants ranging from 5.1% to 8.6% (1991 to 1996) (Horbar 2002).

As with any procedure involving breach of the cutaneous barrier, intercostal drainage is a potential risk factor for nosocomial infection. Additionally, by virtue of their underlying illness, patients requiring intercostal catheters may have impaired local and systemic defence mechanisms. Premature and low birth weight infants are particularly at risk. Retrospective data from the National Institute of Child Health and Development (NICHD) Neonatal Research Network, USA, demonstrated an incidence of pneumothorax from 1990 to 2002 of 13% in infants weighing 501 to 750 g and 6% in infants weighing 751 to 1000 g (Fanaroff 2007). In these same populations, the incidence of late-onset septicaemia was 44% and 30% respectively. Hence, the group of premature neonates most likely to require an intercostal catheter are also those most at risk of morbidity and mortality as a result of nosocomial infection.

Infection secondary to the use of intercostal catheters may cause significant morbidity and mortality. Morbidity may include prolonged duration and increased severity of respiratory illness (including chronic lung disease and the need for respiratory support) (Greenough 2005), increased length of hospital stay (Mireya 2007) and impaired neurodevelopmental outcomes (Stoll 2004). Documented complications of intercostal catheters in both pediatric and adult populations include localised cellulitis (Margau 2006) and empyema (Bailey 2000). The incidence of empyema following intercostal drainage has been reported at about 2% (Millikan 1980; Chan 1997; Bailey 2000). Potential factors to be implicated in infection of the drain site and pleural space include failure of the aseptic technique, advancement of a pre-existing drain into the pleural space and duration of intercostal drainage (Tang 2002). Factors that might affect the risk of infection, including geographic location of insertion (operating theatre, intensive care unit, retrieval site), patient acuity at the time of catheter placement, and the skill level of the operator, have been incompletely studied (Baumann 2003).

There are currently no published recommendations on the use of prophylactic antibiotics for intercostal catheters for non-traumatic indications. In adult chest trauma patients requiring intercostal drainage, several studies have found evidence of benefit from single-dose antimicrobial prophylaxis (Grover 1977; LeBlanc 1985; Demetriades 1991) and published evidence-based guidelines for chest trauma make a level III recommendation (based on class I and II data) for up to 24 hours of cover with a first generation cephalosporin (Luchette 2000). However, for non-traumatic indications across all age groups there remains variability in practice, including the timing, target population and choice of antibiotics.
Description of the intervention

Antibiotic prophylaxis is the administration of antibiotics with the goal of reducing the risk of bacterial infection (Antibiotic Expert Group 2006). In practice, antibiotic prophylaxis is used where there is an increased risk of infection or where the consequence of infection would be significant. The specific choice of antibiotic is determined by the known or likely target organisms.

How the intervention might work

With any invasive procedure, including insertion of an intercostal catheter, there is a risk of the introduction of colonising bacteria into the systemic circulation (Dear 2005). The use of antibiotic prophylaxis against known or likely target organisms would potentially reduce pathogen load and, therefore, minimise local and systemic infection related to intercostal catheter use.

Why it is important to do this review

There are significant public health implications for failure of judicious antibiotic use (CDC 2004). Antimicrobial prophylaxis, while potentially preventing intercostal catheter-related soft tissue and bloodstream infection, may have the undesirable effect of promoting the emergence of resistant strains of micro-organisms (Freij 1999) or of altering the pattern of pathogens causing infection (Viudes 2002). At the individual level, there is a risk of adverse effects associated with antibiotic use including ototoxicity and nephrotoxicity (Fanos 1999; Contopoulos-Ioannidis 2004). Any policy of antimicrobial prophylaxis must take these potential risks into account.

Recent Cochrane systematic reviews on the use of prophylactic antibiotics for neonates with umbilical artery catheters (Inglis 2007), umbilical venous catheters (Inglis 2005) and central venous catheters (Jardine 2008) demonstrated that there was no evidence to either support or refute the use of antimicrobial prophylaxis during the use of such catheters in newborn infants. The following systematic review evaluated the use of prophylactic antibiotics for neonates with intercostal catheters.

OBJECTIVES

To determine the effects of prophylactic antibiotics compared to selective use of antibiotics on mortality and morbidity (especially sepsis) in neonates undergoing placement of an intercostal catheter.

Pre-specified subgroup analyses:

1. term (≥ 37 weeks gestation) versus preterm (< 37 weeks gestation);
2. type of antibiotic (e.g., penicillins, macrolides, aminoglycosides, cephalosporins, or combinations);
3. indication for catheter (e.g., pneumothorax (not post-operative), pleural effusion, post-operative indications);
4. type of prophylaxis (e.g., single dose(s) with insertion, ongoing prophylaxis for the life of the catheter);
5. whether infant was on antibiotics at the time of study entry.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) or some types of non-randomised (that is, quasi-randomised) controlled trials of adequate quality in which either individual newborn infants or clusters of infants (such as separate neonatal units) were randomised to receive prophylactic antibiotics versus placebo or no treatment.

Types of participants

Neonates with intercostal catheters: full term infants less than 28 days old; preterm infants up to 44 weeks post-menstrual age.

Types of interventions

Any systemic antibiotic (not including antifungals) or combination of antibiotics, either as a single dose or ongoing prophylaxis, versus placebo or no treatment given at the time of catheter insertion. We did not specifically exclude any study that enrolled babies who were or were not receiving a treatment course (or dose or doses) of antibacterial antibiotics.

Types of outcome measures

Primary outcomes

- Mortality (neonatal mortality, mortality prior to discharge, or however defined in individual studies)
- Proven bacterial sepsis (blood culture positive), suspected sepsis, or clinical sepsis.
Secondary outcomes

- Incidence of cellulitis (local soft tissue infection causing inflammation)
- Incidence of empyema (a collection of pus in the pleural space)
- Chronic lung disease (oxygen requirement at 36 weeks post-menstrual age)
- Duration of ventilation (hours or days)
- Duration of respiratory support (hours or days)
- Duration of oxygen therapy (hours or days)
- Duration of hospital stay (days)
- Number of resistant organisms (i.e., species) causing infection, identified per time period per infant or per cluster unit (resistance however defined in individual studies)
- Number of resistant organisms (i.e., species) colonising infants in the study, identified per time period per infant (resistance however defined in individual studies)
- Number of resistant organisms (i.e., species) colonising all infants identified per time period per cluster unit (resistance however defined in individual studies)
- Neurodevelopmental outcome (cerebral palsy, sensorineural hearing loss, visual impairment or developmental delay) at one year, 18 months, two years, or five years.

Search methods for identification of studies

We used the standard methods of the Cochrane Neonatal Review Group.

Electronic searches

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library, Issue 5, 2011), MEDLINE (1948 to June 2011) and CINAHL (1982 to June 2011) using the following strategy.

MeSH search terms “Thoracostomy” OR “Chest Tubes” OR the textwords (“intercostal” OR “inter-costal”) AND “cathet$”) OR “ICC” OR “ICTD” OR “chest drain” OR “chest tube” OR “tube thoracostomy” OR “tube thoracotomy” AND MeSH search term “Infant, newborn” OR the textwords “neonat$” OR “infant” AND MeSH search term “Anti-Bacterial Agents” OR the textword “antibiotic” AND MeSH search terms “Chemoprevention” OR “Antibiotic Prophylaxis” OR the textword “prophyl$”.

Searching other resources

We also searched previous reviews (including cross references). We did not restrict the searches to publications in the English language or published data. We planned to contact authors for additional or missing information.

Data collection and analysis

The review authors planned to separately extract, assess and code all data for each study using a form that was designed specifically for this review. It was planned to replace any standard error of the mean with the corresponding standard deviation (SD = se X square root N). Any disagreement was to be resolved by discussion. For each study, final data would be entered into RevMan by one review author and then checked by a second review author. Any disagreements would be addressed by a third review author.

Selection of studies

We planned to include all randomised, quasi-randomised controlled trials or cluster trials fulfilling the selection criteria described in the previous section. Two of the review authors (AS and PK) independently searched for and assessed trials for inclusion and methodological quality. We planned to resolve any disagreement by discussion.

Data extraction and management

We planned to employ the standard methods of the Cochrane Neonatal Review Group. Data for any included studies were to be extracted independently by at least two of the review authors for each of the available outcomes, as listed above, and the data entered into Revman 5.

Assessment of risk of bias in included studies

It was intended that two of the review authors would independently assess risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008). Any disagreement was to be resolved by discussion with or by involving a third review author.

The methodological quality of the studies was to be assessed using the following criteria.

1) Sequence generation (evaluating possible selection bias). For each included study, description of the method used to generate the allocation sequence as: low risk (any truly random process e.g., random number table, computer random number generator); high risk (any non-random process e.g., odd or even date of birth, hospital or clinic record number); or unclear risk.
2) Allocation concealment (evaluating possible selection bias). For each included study, description of the method used to conceal the allocation sequence as: low risk (e.g., telephone or central randomisation, consecutively numbered sealed opaque envelopes);
high risk (open random allocation, unsealed or non-opaque envelopes, alternation, date of birth); or unclear risk.

3) Blinding (evaluating possible performance bias). For each included study, we planned to provide a description of the methods used to blind study participants and personnel from knowledge of which intervention a participant received. Blinding was to be assessed separately for different outcomes or classes of outcomes. We planned to assess the methods as: low risk, high risk or unclear risk for participants; low risk, high risk or unclear risk for personnel; and low risk, high risk or unclear risk for outcome assessors.

4) Incomplete outcome data (evaluating possible attrition bias through withdrawals, dropouts, protocol deviations). For each included study, and for each outcome, we planned to describe the completeness of data including attrition and exclusions from the analysis. We planned to state whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total number of randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported or could be supplied by the trial authors, we intended to re-include missing data in the analyses that we undertook. We planned to assess methods as: low risk (<20% missing data); high risk (≥20% missing data); or unclear risk.

5) Selective reporting bias. For each included study, we planned to describe how we investigated the possibility of selective outcome reporting bias and what we found. Methods would be assessed as: low risk (where it was clear that all of the study’s pre-specified outcomes and all expected outcomes of interest to the review had been reported); high risk (where not all the study’s pre-specified outcomes had been reported, one or more of the reported primary outcomes were not pre-specified, outcomes of interest were reported incompletely and so could not be used, study failed to include results of a key outcome that would have been expected to have been reported); or unclear risk.

6) Other sources of bias. For each included study, we planned to describe any important concerns we had about other possible sources of bias (e.g., whether there was a potential source of bias related to the specific study design or whether the trial was stopped early due to some data-dependent process). It was planned to assess each study as to whether it was free of other problems that could put it at risk of bias as: yes; no; or unclear.

Assessment of heterogeneity
We planned to assess heterogeneity using the I² statistic test of heterogeneity where sufficient included studies were available.

Data synthesis
We planned to perform the analysis using Review Manager software (RevMan 5) supplied by The Cochrane Collaboration, if meta-analysis was judged to be appropriate. We planned to report weighted mean differences (WMD) for pooled results of continuous variables, and 95% confidence intervals. We planned to use the Mantel-Haenszel method for estimates of a typical relative risk and risk difference. We planned to use the inverse variance method for measured quantities. All meta-analyses were to be done using the fixed-effect model.

Subgroup analysis and investigation of heterogeneity
Data permitting, subgroup analysis was to be done in order to determine whether results differed by:

1. term (≥37 weeks gestation) versus preterm (<37 weeks gestation);
2. type of antibiotic (e.g., penicillins, macrolides, aminoglycosides, cephalosporins, or combinations);
3. indication for catheter (e.g., pneumothorax (not post-operative), pleural effusion, post-operative indications);
4. type of prophylaxis (e.g., single dose(s) with insertion, ongoing prophylaxis for the life of the catheter);
5. whether infant was on antibiotics at the time of study entry.

Sensitivity analysis
Given availability of sufficient data, a sensitivity analysis was planned to see if results differed by the quality of the included studies (for example, adequacy of randomisation, quasi-randomised versus randomised).

RESULTS

Description of studies
See: Characteristics of excluded studies.

Results of the search
One study was retrieved using the above search strategy, but was not eligible for inclusion in this review.
Included studies
No studies met the criteria for inclusion in this review.

Excluded studies
See: Characteristics of excluded studies
Patel 2009 was a retrospective observational study of antibiotic use in neonatal intensive care units. It was a non-randomised controlled trial which did not meet our inclusion criteria for study design.

Risk of bias in included studies
No studies met the criteria for inclusion in this review.

Effects of interventions
No studies met the criteria for inclusion in this review.

DISCUSSION
We did not find any randomised controlled trials that assessed the effects of antibiotic prophylaxis on mortality and morbidity in neonates with intercostal catheters. Although it is plausible that premature neonates who require insertion of an intercostal catheter are likely to be at high risk of nosocomial infection and might therefore benefit from antibiotic prophylaxis, there are no data available to indicate whether antibiotic prophylaxis in this patient group reduces mortality and morbidity.

The only published randomised prospective trials of antibiotic prophylaxis for intercostal catheter insertion have been performed in adult chest trauma populations. Grover 1977 and LeBlanc 1985 found evidence of benefit from prophylaxis, and Demetriades 1991 found single-dose prophylaxis to be as effective as prolonged prophylaxis. There are no published studies addressing the use of antibiotic prophylaxis for intercostal catheters for non-traumatic indications in any age group. Nonetheless, the use of antibiotic prophylaxis for intercostal catheter insertion in the neonatal population has been reported (Patel 2009) and, in the absence of any evidence of benefit, concerns remain regarding the role of this practice in the development of antimicrobial resistance (CDC 2004; Patel 2009).

AUTHORS’ CONCLUSIONS
Implications for practice
There are no data from randomised trials to either support or refute the use of antibiotic prophylaxis for intercostal catheter insertion in neonates.

Implications for research
A large randomised controlled trial would be needed for an unbiased assessment of the effect of antibiotic prophylaxis in neonates with intercostal catheters and would need to account for the fact that neonates who require insertion of an intercostal catheter may already be receiving antibiotics for other indications. For this reason it is unlikely such a trial would be practical. In addition, clinicians do not commonly attribute nosocomial infection to the presence of an intercostal catheter and there may be little enthusiasm for such a trial.

REFERENCES

References to studies excluded from this review
Patel 2009 (published data only)

Additional references
Antibiotic Expert Group 2006

Bailey 2000

Baumann 2003

CDC 2004

Chan 1997
Chan L, Reilly K, Henderson C, Kahn F, Salluzzo RF.

Contopoulos-Ioannidis 2004

Dear 2005

Demetriades 1991

Fanaroff 2007

Fanos 1999

Freij 1999

Greenough 2005

Grover 1977

Higgins 2008

Horbar 2002

Inglis 2005

Inglis 2007

Jardine 2008

LeBlanc 1985

Luchette 2000

Margau 2006

Millikan 1980

Mireya 2007

Stoll 2004

Tang 2002

Viudes 2002

* Indicates the major publication for the study
## Characteristics of excluded studies

[ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
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<tr>
<td>Patel 2009</td>
<td>Multicentre retrospective observational study of antibiotic use in neonatal intensive care units. Not a RCT, did not meet inclusion criteria</td>
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DATA AND ANALYSES

This review has no analyses.

HISTORY

Protocol first published: Issue 4, 2009
Review first published: Issue 4, 2012

CONTRIBUTIONS OF AUTHORS

AS and PK searched for and assessed studies for inclusion.
AS wrote the review.
GDT, LA, PK and MWD co-wrote the review.

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources
- Grantley Stable Neonatal Unit, Royal Brisbane and Women's Hospital, Brisbane, Australia.
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INDEX TERMS
Medical Subject Headings (MeSH)

*Antibiotic Prophylaxis; Chest Tubes [*adverse effects]; Cross Infection [etiologic; *prevention & control]; Infant, Newborn; Sepsis [*prevention & control]

MeSH check words

Humans