Antibiotics for meconium-stained amniotic fluid in labour for preventing maternal and neonatal infections (Review)

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[Intervention Review]

Antibiotics for meconium-stained amniotic fluid in labour for preventing maternal and neonatal infections

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ABSTRACT

Background

Chorioamnionitis is more likely to occur when meconium-stained amniotic fluid (MSAF) is present. Meconium may enhance the growth of bacteria in amniotic fluid by serving as a growth factor, inhibiting bacteriostatic properties of amniotic fluid. Many adverse neonatal outcomes related to MSAF result from Meconium Aspiration Syndrome (MAS). MSAF is associated with both maternal and newborn infections. Antibiotics may be an effective option to reduce such morbidity.

Objectives

The objective of this review is to assess the efficacy and side effects of prophylactic antibiotics for MSAF during labour in preventing maternal and neonatal infections.

Search strategy

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 September 2010).

Selection criteria

Randomized controlled trials (RCTs) comparing prophylactic antibiotics with placebo or no treatment during labour for women with MSAF.

Data collection and analysis

Two review authors independently assessed the results of the only available trial and extracted data on maternal and neonatal outcomes.

Main results

We included one study with 120 pregnant women. It compared ampicillin-salbactam (N = 60) versus normal saline (N = 60) in pregnant women with MSAF. Prophylactic antibiotics appeared to have no statistically significant reduction in the incidence of neonatal sepsis (risk ratio (RR) 1.00, 95% CI 0.21 to 4.76), neonatal intensive care unit (NICU) admission (RR 0.83, 95% CI 0.39 to 1.78) and postpartum endometritis (RR 0.50, 95% CI 0.18 to 1.38). However, significant decrease in the risk of chorioamnionitis (RR 0.29, 95% CI 0.10 to 0.82). No serious adverse effects were reported.

Authors' conclusions

Current evidence indicates that compared to placebo, antibiotics for MSAF in labour may reduce chorioamnionitis. There was no evidence that antibiotics could reduce postpartum endometritis, neonatal sepsis and NICU admission. This systematic review identifies the need for more well-designed, adequately powered RCTs to assess the effect of prophylactic antibiotics in the incidence of maternal and neonatal complications.

PLAIN LANGUAGE SUMMARY

Antibiotics for meconium-stained amniotic fluid in labour for preventing maternal and neonatal infections

Meconium-stained amniotic fluid (MSAF) is the result of waste maternal from the fetal colon passing into the mother's amniotic cavity. Its incidence increases in post-term pregnancies. Pregnant women with MSAF are more likely to develop maternal complications including inflammation of the fetal membranes caused by a bacterial infection (chorioamnionitis), postpartum inflammation of the lining of the uterus (endometritis) and neonatal complications such as neonatal sepsis and need for admission to a neonatal intensive care unit (NICU) . Fetal stress or hypoxia may trigger gasping fetal respirations, which results in the aspiration of meconium.

Our review was based on one identified randomized controlled study (involving 120 women) and found that prophylactic antibiotics may reduce the risk of intra-amniotic infection in women with MSAF. Antibiotics use did not clearly reduce neonatal sepsis, NICU admission or postpartum endometritis. Studies with much larger numbers of pregnant women with MSAF would be needed to examine these issues.

BACKGROUND

Description of the condition

Meconium-stained amniotic fluid (MSAF), as a result of the passage of fetal colonic contents into the amniotic cavity, occurs in approximately 12% of all deliveries (Cleary 1998). The incidence of intrapartum MSAF ranges from 7% to 22% for a term pregnancy but this figure increases to up to 40% in a post-term pregnancy (Katz 1992). The composition of meconium from a term fetus is primarily water (70% to 80%). Other constituents include mucopolysaccharides, cholesterol and its precursors, proteins, lipids, bile acids and salts (giving the characteristic green colour), pancreatic enzymes, interleukin-8, phospholipase A2, squamous cells, and vernix caseosa (Cleary 1998; Usta 2000).

MSAF may act directly and indirectly on exposed tissue. Its effects depend on the concentration of meconium, duration of exposure, and the presence of associated stress factors (hypoxia, infection). MSAF has long been associated with potentially adverse fetal outcomes including meconium aspiration syndrome (MAS), admission to neonatal intensive care unit (NICU), neonatal sepsis, cerebral palsy, seizure and pulmonary diseases (Berkus 1994; Katz 1992; Nathan 1994). Many adverse neonatal outcomes related to MSAF result from MAS. MAS occurs in 5% of the cases of MSAF and more than 4% of infants with MAS die, accounting for 2% of all perinatal deaths (Cleary 1998; Wiswell 1990). Hypoxia is the key factor that triggers gasping fetal respirations, which results in the aspiration of meconium. Most cases of MAS probably result from in utero aspiration rather than aspiration at the time of delivery. In addition to possibly contributing to respiratory distress in the neonate, MSAF has been associated with a higher risk of neonatal infection (Romero 1991). Chorioamnionitis is a risk factor for neonatal sepsis, which results in NICU admissions and potential fetal morbidity and death (Alexander 1999). Fetal microbial invasion has been proposed to cause inflammatory brain damage through the effects of elevated cytokines (e.g. TNF alpha, IL-1 beta,and IL-6) (Hoskins 1987).

Chorioamnionitis is also more likely to occur when MSAF is present (Mazor 1995; Romero 1991; Usta 2000). The risk of clinical chorioamnionitis and histological chorioamnionitis in patients with intrapartum MSAF is significantly higher than those with clear fluid. The risk for clinically diagnosed endometritis is twofold (Markovitch 1993; Mazor 1995). Intrapartum chorioamnionitis is associated with dystocia and increased risk for operative delivery (Casey 1997; Mark 2000). Unrecognized or undertreated chorioamnionitis can lead to postpartum endomyometritis which can result in further maternal morbidity, and increased length of stay in hospital and hospital costs. MSAF is the risk factor for microbial invasion of the amniotic cavity in patients

with intact membranes and preterm labour (Romero 1991). Maternal infection is also more likely in the presence of MSAF. Patients with MSAF were almost two and a half times as likely to develop postoperative endometritis (Josephson 1984). There are statistically significant associations between MSAF and puerperal infection in term deliveries (Piper 1998). Puerperal infection rates are associated with the degree of meconium staining, with rates rising as meconium thickness increases (Tran 2003). There is a three-fold increase in positive amniotic fluid cultures in patients with MSAF compared to those with clear amniotic fluid (Mazor 1995; Romero 1991).The most common amniotic fluid isolates in MSAF are anaerobes, *Ureaplasma urealyticum, Streptococci, Escherichia coli, Candida albicans* and *Listeria monocytogenes* (Mazor 1995; Romero 1991).

Meconium may enhance the growth of bacteria in amniotic fluid by serving as a growth factor, inhibiting bacteriostatic properties of amniotic fluid, or antagonizing host defence systems, thus increasing the risk of chorioamnionitis. Generally, amniotic fluid is a poor culture medium for *Escherichia coli, Listeria monocytogenes* and *Staphylococcus aureus;* however, with enough meconium, amniotic fluid becomes an excellent culture medium (Florman 1969). Meconium may alter the zinc-to-phosphorous ratio in amniotic fluid and facilitate bacterial growth and decrease host defences (Hoskins 1987). Light and very light MSAF significantly impair mechanisms for intracellular microbial killing. Phagocytic ability of neutrophils was also significantly diminished in the presence of moderate MSAF (Clark 1995). Mechanisms of meconium associated puerperal infections include altering the antibacterial properties of amniotic fluid and enhancing bacterial growth, impairing the host immune response through the inhibition of phagocytosis and neutrophil oxidative burst (Clark 1995; Katz 1992).

Description of the intervention

One study has shown a significant reduction in the rate of clinical chorioamnionitis when the intervention ampicillin-sulbactam was administered prophylactically for the indication of MSAF (Edwards 1999).

How the intervention might work

Antibiotics can be bacteriostatic (they stop bacteria from multiplying) or bactericidal (they kill the bacteria). To perform either of these functions, antibiotics must be brought into contact with the bacteria. Antibiotics are thought to interfere with the surfactant of bacteria cells, causing a change in their ability to reproduce (Heizmann 2007). Gentamicin is an aminoglycoside antibiotic with bactericidal activity that acts at the 30S bacterial ribosomal subunit, inhibiting the synthesis of bacterial proteins (Ward 2008).

Why it is important to do this review

Cochrane reviews have addressed a number of issues about MAS including steroid therapy, endotracheal intubation, surfactant and antibiotics for neonates (Halliday 2001; Shivananda 2006; Ward 2003). Other interventions include amnioinfusion for MSAF in labour (Hofmeyr 2002). Prophylactic intravenous intrapartum ampicillin-sulbactam therapy or cefazolin infusion into the amniotic cavity during amnioinfusion in mothers with MSAF did not show any benefit in reducing chorioamnionitis, endometritis and neonatal sepsis (Adair 1996; Edwards 1999). However, the role of antibiotics for MSAF during labour has not been systematically evaluated.

OBJECTIVES

The objective of this review is to assess the efficacy and side effects of prophylactic antibiotics for meconium-stained amniotic fluid during labour in preventing maternal and neonatal infections.

METHODS

Criteria for considering studies for this review

Types of studies

We considered randomized controlled trials (RCTs) of prophylactic antibiotic administration during labour for women with MSAF. We excluded quasi-RCTs.

Types of participants

Pregnant women with a gestational age of more than 22 weeks who were in labour and had MSAF.

Types of interventions

Systemic prophylactic antibiotics started during labour in women with MSAF compared with no treatment or placebo.

Types of outcome measures

The primary outcomes were the most clinically important for the neonate, whereas the secondary outcomes also included maternal and neonatal complications.

Primary outcomes

1. Early onset neonatal sepsis (symptomatic before 72 hours of age).
2. Late onset neonatal sepsis (symptomatic after 72 hours of age).

(Definition of sepsis as defined by authors)

Secondary outcomes

Maternal

1. Intrapartum chorioamnionitis.
2. Postpartum endometritis.
3. Side effects of treatment, e.g. drug allergy, anaphylactic shock.
4. Drug resistance.

Neonatal

1. Mortality and morbidity prior to discharge, e.g. birth asphyxia, intracranial haemorrhage, intraventricular haemorrhage, necrotizing enterocolitis and admission to neonatal intensive care unit.
2. Duration of mechanical ventilation (days).
3. Duration of admission to neonatal intensive care unit/ hospital.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (30 September 2010).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

We did not apply any language restrictions.

Data collection and analysis

Selection of studies

Thitiporn Siriwachirachai (TS) and Ussanee Sangkomkamhang (US) independently assessed trials for inclusion and methodological; quality. There were no disagreements.

Data extraction and management

We designed a form to extract data. For eligible studies, TS and US independently extracted the data using the agreed form. There were no discrepancies. We entered the data into Review Manager software (RevMan 2008) and checked for accuracy. We did not contact the original study authors because the reported information was sufficient in the report.

Assessment of risk of bias in included studies

TS and US independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2009).

(1) Sequence generation (checking for possible selection bias)

We described for included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We assessed the method as:

- adequate (any truly random process, e.g. random number table; computer random number generator);
- inadequate (any non random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear.

(2) Allocation concealment (checking for possible selection bias)

We described for included study the method used to conceal the allocation sequence in sufficient detail and determine whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We assessed the methods as:

- adequate (e.g. telephone or central randomization; consecutively numbered sealed opaque envelopes);
- inadequate (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
- unclear.

(3) Blinding (checking for possible performance bias)

We described for included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We judged studies at low risk of bias if they were blinded, or if we judged that the lack of blinding could not have affected the results. We assessed blinding separately for different outcomes or classes of outcomes. We assessed the methods as:

- adequate, inadequate or unclear for participants;
- adequate, inadequate or unclear for personnel;
- adequate, inadequate or unclear for outcome assessors;

where 'adequate' is when there was blinding or where we assess that the outcome or the outcome measurement is not likely to have been influenced by lack of blinding.

(4) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)

We described for included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total randomized 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, we assessed methods as:

- adequate;
- inadequate;
- unclear.

We discussed whether missing data greater than 20% might (a) be reasonably expected (acknowledging that complete data are difficult to attain), and (b) impact on outcomes.

(5) Selective reporting bias

We described for the included trial how we investigated the possibility of selective outcome reporting bias and what we found. We assessed the methods as:

- adequate (where it is clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review have been reported);
- inadequate (where not all the study's prespecified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- unclear.

(6) Other sources of bias

We described for the included study any important concerns we have about other possible sources of bias. We assessed whether study was free of other problems that could put it at risk of bias:

- yes;
- no;
- unclear.

(7) Overall risk of bias

We made explicit judgements about whether studies are at high risk of bias, according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2009). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. We did not explore the impact of the level of bias through undertaking sensitivity analyses because we included only one study.

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented results as summary risk ratios (RR) with 95% confidence intervals (CIs) .

Continuous data

For continuous data, we used the mean difference if outcomes were measured in the same way between trials. We used the standardized mean difference to combine trials that measure the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomized trials

We included only one RCTs. In future updates, if we identify cluster-randomized trials, we will include these in the analyses along with individually randomized trials. We will adjust their sample sizes using the methods described in the *Handbook* using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population (Higgins 2009). If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both

cluster-randomized trials and individually-randomized trials, we plan to synthesize the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and we consider the interaction between the effect of intervention and the choice of randomization unit to be unlikely.

We will also acknowledge heterogeneity in the randomization unit and perform a subgroup analysis to investigate the effects of the randomization unit.

Dealing with missing data

For the included study, we noted levels of attrition. We explored the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis.

For all outcomes, we have carried out analyses, as far as possible, on an intention-to-treat basis; i.e. we attempted to include all participants randomized to each group in the analyses, and analyze all participants in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial is the number randomized minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

This review did not include meta-analysis. In future updates, as more data become available, we will assess statistical heterogeneity in each meta-analysis using the T^2, I^2 and Chi^2 statistics. We will regard heterogeneity as substantial if T^2 is greater than zero and either I^2 is greater than 30% or there is a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

In subsequent updates of this review, if there are 10 or more studies in the meta-analysis we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually, and use formal tests for funnel plot asymmetry. For continuous outcomes we will use the test proposed by Egger 1997, and for dichotomous outcomes we will use the test proposed by Harbord 2006. If asymmetry is detected in any of these tests or is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2008). This review only included one RCT so we did not pool any data. In future updates, if more data become available, we will use fixed-effect meta-analysis for combining data where it is reasonable to assume that studies are estimating the same underlying treatment effect: i.e. where trials are examining the same intervention, and the trials' populations and methods are judged sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, we will use random-effects meta-analysis to produce an overall summary if an average treatment effect across trials is considered clinically meaningful. We will treat the random-effects summary as the average range of possible treatment effects and we will discuss the clinical implications of treatment effects differing between trials. If the average treatment effect is not clinically meaningful we will not combine trials.

If we use random-effects analyses, we will present the results as the average treatment effect with its 95% confidence interval, and the estimates of T^2 and I^2.

Subgroup analysis and investigation of heterogeneity

In future updates of this review, when sufficient data become available, we plan to carry out the following subgroup analyses:

1. intact versus rupture membrane;
2. single versus combine antibiotic regimens;
3. duration of antibiotics less than 24 hours versus more than 24 hours.

We will use the following outcomes in subgroup analysis:

- early onset neonatal sepsis (symptomatic before 72 hours of age);
- late onset neonatal sepsis (symptomatic after 72 hours of age).

For fixed-effect inverse variance meta-analyses we will assess differences between subgroups by interaction tests. For random-effects and fixed-effect meta-analyses using methods other than inverse variance, we will assess differences between subgroups by inspection of the subgroups' confidence intervals; non-overlapping confidence intervals indicate a statistically significant difference in treatment effect between the subgroups.

Sensitivity analysis

In subsequent updates we also plan to conduct a sensitivity analysis comparing the results using all studies and using only those of high methodological quality.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

We identified four publications as potentially eligible for inclusion in this review.

Included studies

This review includes one RCT (Adair 1996) in which 120 pregnancies were randomized and analyzed; *see* Characteristics of included studies.

Excluded studies

We assessed and excluded two retrospective cohort studies (Adair 1998; Edwards 1999) and one conference abstract (Adair 1999); *see* Characteristics of excluded studies.

Risk of bias in included studies

We have summarized the risk of bias of the included study (Adair 1996) in Figure 1 and Figure 2. We classified it as a trial with low risk of bias because it had 'clear' allocation concealment, blinding and no withdrawal.

Figure 1. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

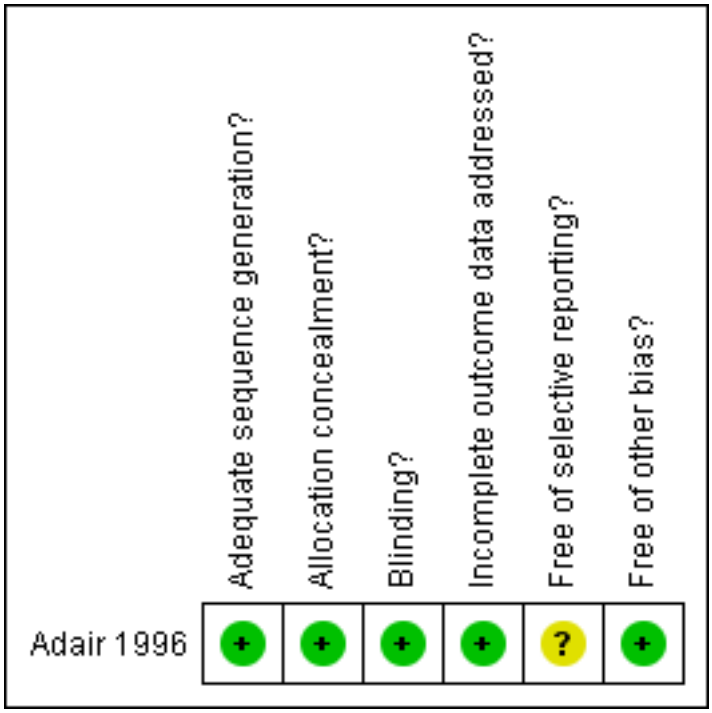
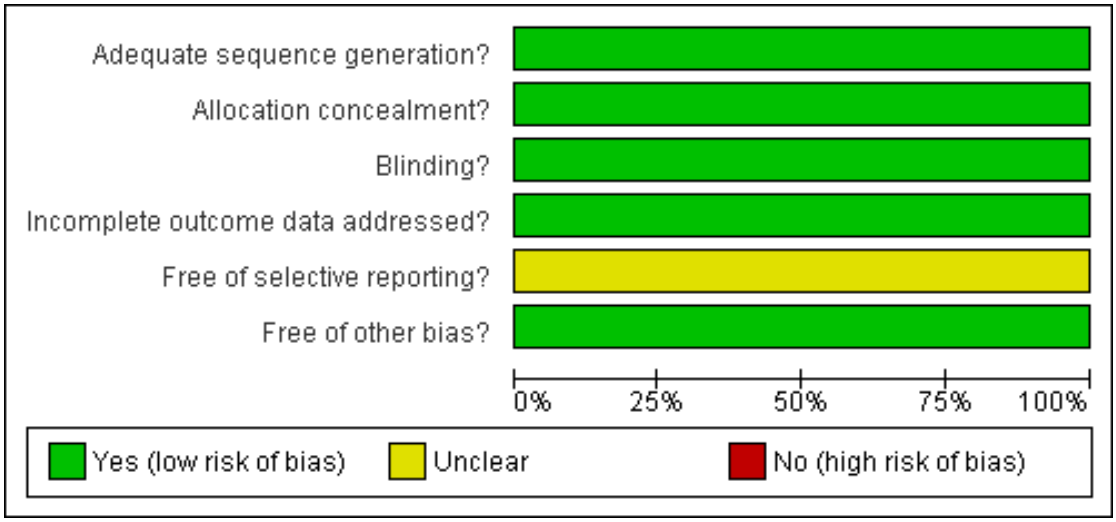


Figure 2. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.



Allocation

The trial reported clear information of allocation concealment. The randomization schedule was generated and kept in an area away from the clinical area and was unavailable to caregivers (Adair 1996).

Blinding

Participants and all caregivers were thoroughly blinded until the study was completed. Interventions were identically prepared in 100 ml fluid bags and issued by one of two research nurses, independent to the trial investigators. The outcome assessors were also blinded to the randomization status**.**

Incomplete outcome data

No withdrawals occurred and analysis could be done based on intention-to-treat basis.

Selective reporting

We do not have access to this study protocol; therefore we could not evaluate this risk of bias..

Other potential sources of bias

None.

Effects of interventions

Results are based on one RCT (120 pregnancies/120 newborns).

Antibiotic versus placebo

Primary outcomes

There was no significant reduction in the incidence of neonatal sepsis (RR 1.00, 95% CI 0.21 to 4.76), *see* Analysis 1.1. The authors (Adair 1996) did not report their results in terms of early and late onset neonatal sepsis.

Secondary outcomes

There was a significant reduction in the incidence of chorioamnionitis in the ampicillin-sulbactam group compared with placebo (RR 0.29, 95% CI 0.10 to 0.82), *see* Analysis 1.2. There was no significant reduction in the incidence of endometritis (RR 0.50, 95% CI 0.18 to 1.38), *see* Analysis 1.3 or neonatal intensive care unit admission (RR 0.83, 95% CI 0.39 to 1.78), *see* Analysis 1.4. No serious adverse effects were reported.

DISCUSSION

Summary of main results

There was a significant reduction in the incidence of chorioamnionitis in mothers who received ampiciline-sulbactam compared to placebo. Neonatal sepsis was not differentiated into 'early' or 'late' onset but there was no difference in the incidence of neonatal sepsis between the two groups. Endometritis was not statistically reduced. There was no information about adverse effects.

Overall completeness and applicability of evidence

Only one RCT from a developed country was found by this review and it did not report the primary outcome 'neonatal sepsis' in terms of early or late onset. The evidence may be insufficient to evaluate the efficacy and side effects of prophylactic antibiotics for meconium-stained amniotic fluid in labour for preventing neonatal sepsis.

Quality of the evidence

The included trial is of high methodological quality based on adequate random allocation concealment. However, the sample size was not adequate to make any firm conclusion.

Potential biases in the review process

We followed the process of review as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* Higgins 2009. We also did an exhaustive search which included many clinical trial registries.

Agreements and disagreements with other studies or reviews

There are no other reviews and studies related to the efficacy and side effects of prophylactic antibiotics for MSAF during labour in preventing maternal and neonatal infections.

AUTHORS' CONCLUSIONS

Implications for practice

There is insufficient evidence to support the use of prophylactic antibiotics in women with MSAF during labour because the rates of neonatal sepsis were not different in the two groups.

Implications for research

This systematic review has identified the need for more well-designed, adequately powered RCTs to assess the benefits and harms of antibiotic prophylactic in MSAF during labour for preventing neonatal sepsis. The trials should include clinical outcomes of neonatal sepsis.

ACKNOWLEDGEMENTS

As part of the pre-publication editorial process, this review has been commented on by two peers (an editor and referee who is external to the editorial team), a member of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Adair 1996

Methods	Randomized trial with allocation concealment using computer-generated randomization list. All participants, caregivers and outcome assessors were blinded to the treatment regimen.
Participants	Intervention group: 60 pregnant women (mean age 24.5, SD 6.3) with gestational age more than 24 weeks (mean 39.8, SD 1.0). Control group: 60 pregnant women (mean age 25.9, SD 6.3), (mean gestational age 39.9, SD 1.2). Inclusion criteria: gestational age more than 24 weeks with MSAF complicating the intrapartum. Exclusion criteria: patients with penicillin and/or cephalosporin allergy, evidence of active infection, presence of intrauterine death, GA < 24 weeks, or history of antibiotics use in 7 days. Location: North Carolina, United States.
Interventions	**Intervention**: ampicillin-sulbactam 3.0 g intravenous prepared in 100 ml fluid bags, and was repeated every 6 hours until delivery. **Control**: normal saline infused as an IV bolus.
Outcomes	**Mother** Chorioamnionitis. Postpartum endometritis. **Neonatal** Number of NICU admissions. Incidence of sepsis (not defined), and adverse outcomes including enterocolitis and respiratory distress.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Randomization was performed by a computer-generated list.
Allocation concealment?	Yes	Adequate: there was randomization by computer-generated list and both IV preparations were prepared by 1 of 2 research nurses who were not involved in this study.

Adair 1996 (*Continued*)

Blinding? All outcomes	Yes	Adequate: there was blinding of participants, caregivers and outcome assessor.
Incomplete outcome data addressed? All outcomes	Yes	Adequate: there was no withdrawal.
Free of selective reporting?	Unclear	Unclear, because we don't have access to this trial's outcomes.
Free of other bias?	Yes	Study appeared to be free of other sources.

GA: gestational age
IV: intravenous
MSAF: meconium-stained amniotic fluid
NICU: neonatal intensive care unit
RCT: randomized controlled trial
SD: standard deviation

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Adair 1998	Not a RCT, this was a retrospective cohort study.
Adair 1999	This is a conference abstract.
Edwards 1999	Intervention not of interest to systematic review, it is not systematic prophylactic antibiotics.

RCT: randomized controlled trial

DATA AND ANALYSES

Comparison 1. Antibiotic versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Neonatal sepsis	1	120	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.21, 4.76]
2 Chorioamnionitis	1	120	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.10, 0.82]
3 Postpartum endometritis	1	120	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.18, 1.38]
4 Neonatal intensive care admissions	1	120	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.39, 1.78]

Analysis 1.1. Comparison 1 Antibiotic versus placebo, Outcome 1 Neonatal sepsis.

Review: Antibiotics for meconium-stained amniotic fluid in labour for preventing maternal and neonatal infections

Comparison: 1 Antibiotic versus placebo

Outcome: 1 Neonatal sepsis

Study or subgroup	Antibiotic n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Adair 1996	3/60	3/60		100.0 %	1.00 [0.21, 4.76]
Total (95% CI)	**60**	**60**		**100.0 %**	**1.00 [0.21, 4.76]**
Total events: 3 (Antibiotic), 3 (Placebo)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					

Analysis 1.2. Comparison 1 Antibiotic versus placebo, Outcome 2 Chorioamnionitis.

Review: Antibiotics for meconium-stained amniotic fluid in labour for preventing maternal and neonatal infections

Comparison: 1 Antibiotic versus placebo

Outcome: 2 Chorioamnionitis

Study or subgroup	Antibiotic n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Adair 1996	4/60	14/60		100.0 %	0.29 [0.10, 0.82]
Total (95% CI)	**60**	**60**		**100.0 %**	**0.29 [0.10, 0.82]**
Total events: 4 (Antibiotic), 14 (Placebo)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.33 (P = 0.020)					

Analysis 1.3. Comparison 1 Antibiotic versus placebo, Outcome 3 Postpartum endometritis.

Review: Antibiotics for meconium-stained amniotic fluid in labour for preventing maternal and neonatal infections

Comparison: 1 Antibiotic versus placebo

Outcome: 3 Postpartum endometritis

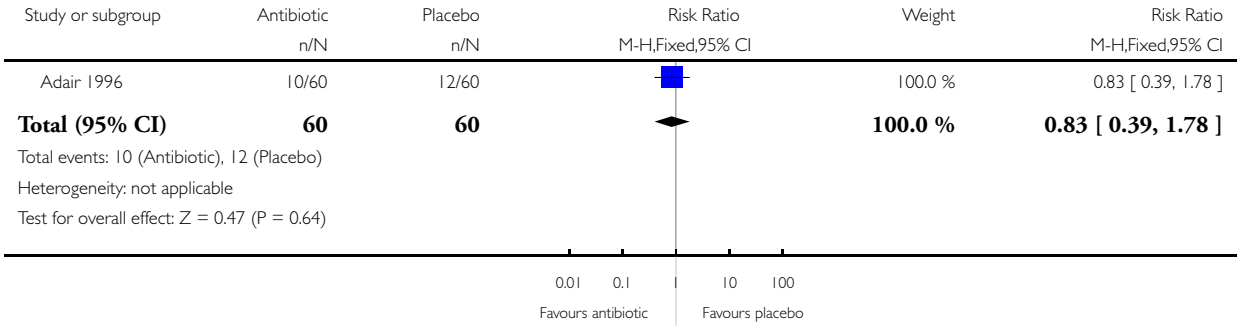
Study or subgroup	Antibiotic n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Adair 1996	5/60	10/60		100.0 %	0.50 [0.18, 1.38]
Total (95% CI)	**60**	**60**		**100.0 %**	**0.50 [0.18, 1.38]**
Total events: 5 (Antibiotic), 10 (Placebo)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.34 (P = 0.18)					

Analysis 1.4. Comparison 1 Antibiotic versus placebo, Outcome 4 Neonatal intensive care admissions.

Review: Antibiotics for meconium-stained amniotic fluid in labour for preventing maternal and neonatal infections

Comparison: 1 Antibiotic versus placebo

Outcome: 4 Neonatal intensive care admissions



HISTORY

Protocol first published: Issue 2, 2009

Review first published: Issue 12, 2010

CONTRIBUTIONS OF AUTHORS

Thitiporn Siriwachirachai and Ussanee Sangkomkamhang drafted the review, Pisake Lumbiganon and Malinee Laopaiboon revised and approved the final version of the review.

DECLARATIONS OF INTEREST

None known.

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