Cochrane
Library

Cochrane Database of Systematic Reviews

Amnioinfusion for chorioamnionitis (Review)

Hofmeyr GJ, Kiiza JAK

Hofmeyr GJ, Kiiza JAK.
Amnioinfusion for chorioamnionitis.
Cochrane Database of Systematic Reviews 2016, Issue 8. Art. No.: CD011622.
DOI: [10.1002/14651858.CD011622.pub2](https://doi.org/10.1002/14651858.CD011622.pub2).

www.cochranelibrary.com

Amnioinfusion for chorioamnionitis (Review)

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

WILEY

TABLE OF CONTENTS

ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
SUMMARY OF FINDINGS	4
BACKGROUND	6
OBJECTIVES	7
METHODS	7
RESULTS	10
Figure 1.	11
DISCUSSION	13
AUTHORS' CONCLUSIONS	14
ACKNOWLEDGEMENTS	14
REFERENCES	15
CHARACTERISTICS OF STUDIES	16
DATA AND ANALYSES	18
Analysis 1.1. Comparison 1 Transcervical amnioinfusion versus no amnioinfusion, Outcome 1 Postpartum endometritis.	18
Analysis 1.2. Comparison 1 Transcervical amnioinfusion versus no amnioinfusion, Outcome 2 Neonatal infection.	18
Analysis 1.3. Comparison 1 Transcervical amnioinfusion versus no amnioinfusion, Outcome 3 Caesarean section.	19
Analysis 1.4. Comparison 1 Transcervical amnioinfusion versus no amnioinfusion, Outcome 4 Duration of maternal antibiotic treatment (hours).	19
Analysis 1.5. Comparison 1 Transcervical amnioinfusion versus no amnioinfusion, Outcome 5 Maternal hospitalisation (hours).	19
Analysis 1.6. Comparison 1 Transcervical amnioinfusion versus no amnioinfusion, Outcome 6 Temperature at delivery (not pre-specified) °C.	19
WHAT'S NEW	20
CONTRIBUTIONS OF AUTHORS	20
DECLARATIONS OF INTEREST	20
SOURCES OF SUPPORT	20
DIFFERENCES BETWEEN PROTOCOL AND REVIEW	20
INDEX TERMS	20

[Intervention Review]

Amnioinfusion for chorioamnionitis

G Justus Hofmeyr¹, Joseph AK Kiiza²

¹Walter Sisulu University; Centre for Evidence-based Health Care, Faculty of Medicine and Health Sciences, Stellenbosch University; and Eastern Cape Department of Health, East London, South Africa. ²Department of Obstetrics and Gynaecology, Walter Sisulu University and East London Hospital Complex, East London, South Africa

Contact: G Justus Hofmeyr, Walter Sisulu University; Centre for Evidence-based Health Care, Faculty of Medicine and Health Sciences, Stellenbosch University; and Eastern Cape Department of Health, East London, South Africa. justhof@gmail.com.

Editorial group: Cochrane Pregnancy and Childbirth Group.

Publication status and date: Edited (no change to conclusions), published in Issue 5, 2019.

Citation: Hofmeyr GJ, Kiiza JAK. Amnioinfusion for chorioamnionitis. *Cochrane Database of Systematic Reviews* 2016, Issue 8. Art. No.: CD011622. DOI: [10.1002/14651858.CD011622.pub2](https://doi.org/10.1002/14651858.CD011622.pub2).

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

Background

Chorioamnionitis is a leading cause of perinatal morbidity and mortality. Amnioinfusion aims at reducing the adverse effects of chorioamnionitis by dilution of the infective organisms or by an anti-microbial effect of the fluid infused.

Objectives

The objective of this review was to determine the effect of amnioinfusion on clinical and sub-clinical chorioamnionitis, fetal well-being, fetal heart rate characteristics and perinatal and maternal morbidity and mortality.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (6 July 2016), PubMed, [ClinicalTrials.gov](https://clinicaltrials.gov), the WHO International Clinical Trials Registry Platform (ICTRP) (6 July 2016) and reference lists of retrieved studies.

Selection criteria

Randomised clinical trials (RCTs) of amnioinfusion (treatment group) versus no amnioinfusion in women with chorioamnionitis.

We would have also considered trials comparing amnioinfusion with sham amnioinfusion; different types or volumes of amnioinfusion fluid but none were identified.

Cluster-RCTs and quasi-RCTs were eligible for inclusion but none were identified. We identified one study published in abstract form but it did not contain any numerical data and has therefore been excluded. Studies using a cross-over design are not an appropriate study design and thus were not eligible for inclusion in this review.

Data collection and analysis

Two review authors independently assessed potential studies for inclusion and assessed trial quality. Both review authors independently extracted data and data were checked for accuracy.

Main results

We included one small trial (with data from 34 participants) comparing transcervical amnioinfusion with no amnioinfusion. The trial was considered to be at a high risk of bias overall, due to small numbers, inconsistency in the reporting and lack of information on blinding. Meta-analysis was not possible. Transcervical amnioinfusion was with room temperature saline at 10 mL per minute for 60 minutes, then 3 mL per minute until delivery versus no amnioinfusion. All women received intrauterine pressure catheter, acetaminophen and antibiotics

(ampicillin or, if receiving Group B beta streptococcal prophylaxis, penicillin and gentamycin). We did not identify any trials that used transabdominal amnioinfusion.

Compared to no amnioinfusion, transcervical amnioinfusion had no clear effect on the incidence of **postpartum endometritis** (risk ratio (RR) 1.50, 95% confidence interval (CI) 0.29 to 7.87; absolute risk 176/1000 (95% CI 34 to 96) versus 118/1000; *low-quality evidence*). Nor was there a clear effect in the incidence of **neonatal infection** (RR 3.00, 95% CI 0.13 to 68.84; absolute risk 0/1000 (95% CI 0 to 0) versus 0/1000; *low-quality evidence*). The outcome of **perinatal death or severe morbidity** (such as neonatal encephalopathy, intraventricular haemorrhage, admission to intensive/high care) was not reported in the included trial.

In terms of this review's secondary outcomes, the rate of **caesarean section** was the same in both groups (RR 1.00, 95% CI 0.35 to 2.83; absolute risk 294/1000 (95% CI 103 to 832) versus 294/1000; *low-quality evidence*). There was no clear difference in the **duration of maternal antibiotic treatment** between the amnioinfusion and no amnioinfusion control group (mean difference (MD) 16 hours, 95% CI -1.75 to 33.75); nor in the **duration of hospitalisation** (MD 3.00 hours, 95% CI -15.49 to 21.49). The study did not report any information about how many babies had a **low Apgar score at five minutes after birth**.

Women in the amnioinfusion group had a lower temperature at delivery compared to women in the control group (MD -0.38°C, 95% CI -0.74 to -0.02) but this outcome was not pre-specified in the protocol for this review.

The majority of this review's secondary outcomes were not reported in the included study.

Authors' conclusions

There is insufficient evidence to fully evaluate the effectiveness of using transcervical amnioinfusion for chorioamnionitis and to assess the safety of this intervention or women's satisfaction. We did not identify any trials that used transabdominal amnioinfusion. The evidence in this review can neither support nor refute the use of transcervical amnioinfusion outside of clinical trials. We included one small study that reported on a limited number of outcomes of interest in this review. The numbers included in this review are too small for meaningful assessment of substantive outcomes, where reported. For those outcomes we assessed using GRADE (postpartum endometritis, neonatal infection, and caesarean section), we downgraded the quality of the evidence to low - with downgrading decisions based on small numbers and a lack of information on blinding. The included study did not report on this review's other primary outcome (perinatal death or severe morbidity).

The reduction in pyrexia, though not a pre-specified outcome of this review, may be of relevance in terms of benefits to the fetus of reduced exposure to heat. We postulate that the temperature reduction found may be a direct cooling effect of amnioinfusion with room temperature fluid, rather than reduction of infection. Larger trials are needed to confirm and extend the findings of the trial reviewed here. These should be randomised controlled trials; participants, women with chorioamnionitis; interventions, amnioinfusion; comparisons, no amnioinfusion; outcomes, maternal and perinatal outcomes including neurodevelopmental measures.

Further research is justified to determine possible benefits or risks of amnioinfusion for chorioamnionitis, and to investigate possible benefits of reducing temperature in fetuses considered at risk of neurological damage. Research should include randomised trials to examine transcervical or transabdominal amnioinfusion compared with no infusion for chorioamnionitis and examine outcomes listed in the methods of this review.

PLAIN LANGUAGE SUMMARY

Introducing salt solution into the womb (amnioinfusion) to reduce complications associated with pregnancy fluid and sac infection (chorioamnionitis)

What is the issue?

Chorioamnionitis is an infection of the fluid and sac surrounding the baby in the womb. This is usually managed with antibiotics and by delivering the baby. An additional method suggested is to infuse a salt solution into the womb either via a needle through the mother's abdomen (transabdominal) or a catheter via the mother's vagina (transcervical). The theory is that this may have a beneficial flushing or diluting effect on the infecting organisms.

Why is this important?

Chorioamnionitis may lead to serious complications such as infection of the baby or of the mother. Any effective additional method of treatment would be useful.

What evidence did we find?

We searched for evidence on 6 July 2016 and only found one randomised controlled trial (which reported data from a total of 34 women). Data were available for 17 women who received transcervical amnioinfusion and 17 women who did not. All of the women received paracetamol and antibiotics and they also had a special type of catheter inserted into the cervix to measure information about their contractions (i.e. how often the contractions occur, how long they lasted and how strong they were).

The trial was considered to be at a high risk of bias overall, due to small numbers, inconsistency in the reporting and lack of information on blinding. Given the small sample size, the power to show differences between the two groups was thus small, and no differences were shown for the review's main outcomes: **infection of the mother's womb after the birth** (*low-quality evidence*); **infection of the baby** (*low-quality evidence*); **caesarean section** (*low-quality evidence*); **duration of antibiotic treatment**; nor **duration of hospital stay**. The **mother's temperature at delivery**, which was not a pre-defined outcome for our review, was lower in the women who received amnioinfusion, by 0.38 °C (with a likely range of 0.74 lower to 0.02 lower). The outcome **death or severe illness in the baby** was not reported, nor did the study report on the number of babies with a **low Apgar score** after they were born (a low Apgar score could indicate that the baby is in need of medical attention). Similarly, the majority of other outcomes listed in this review were not reported in the included study.

We did not identify any studies that looked at introducing the solution through the mother's abdomen (transabdominal route).

What does this mean?

There is not enough evidence to support the use of amnioinfusion for chorioamnionitis in clinical practice. We suggest that the reduction in temperature may have been in part due to a direct cooling effect of the infused fluid, and that further research is justified to determine whether such a cooling effect may be beneficial for the baby.

Further randomised controlled trials are needed in this area. Future trials should compare transabdominal or transcervical amnioinfusion with no amnioinfusion for women with pregnancy fluid and sac infection (chorioamnionitis) and report on important outcomes listed in this review.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Amnioinfusion versus no amnioinfusion for chorioamnionitis

Transcervical amnioinfusion versus no amnioinfusion for chorioamnionitis

Patient or population: pregnant women with confirmed or suspected chorioamnionitis

Setting: academic hospital based in the USA

Intervention: transcervical amnioinfusion with saline

Comparison: no amnioinfusion

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no amnioinfusion	Risk with amnioinfusion				
Perinatal death or severe morbidity (neonatal encephalopathy, intraventricular haemorrhage, admission to intensive/high care)	Outcome not reported in the included study					
Postpartum endometritis	Study population		RR 1.50 (0.29 to 7.87)	34 (1 RCT)	⊕⊕⊕⊕ LOW 1, 2	
	118 per 1000	176 per 1000 (34 to 926)				
Neonatal infection	Study population		RR 3.00 (0.13 to 68.84)	34 (1 RCT)	⊕⊕⊕⊕ LOW 1, 2	
	0 per 1000	0 per 1000 (0 to 0)				
Caesarean section	Study population		RR 1.00 (0.35 to 2.83)	34 (1 RCT)	⊕⊕⊕⊕ LOW 1, 2	
	294 per 1000	294 per 1000 (103 to 832)				
Low Apgar score at five minutes (less than seven or as defined by trial authors)	Outcome not reported in the included study					

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio.

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

---

¹ Small numbers (-1)

² Blinding not mentioned (-1)

BACKGROUND

This systematic review aims to determine the safety and efficacy of amnioinfusion for decreasing adverse outcomes in pregnancies complicated by chorioamnionitis.

Description of the condition

Chorioamnionitis is a clinical syndrome of infection of the amniotic cavity during pregnancy. In its classic form, membranes have ruptured and typical clinical signs are present. The diagnostic criteria for clinical chorioamnionitis include a fever of greater than 38°C and at least two of the following: maternal tachycardia with a pulse of more than 100/minute; fetal tachycardia of more than 160 beats/minute; foul-smelling amniotic fluid; uterine tenderness; and maternal leucocytosis (increased white blood cells (WBCs)) of more than 15,000 cells/mm² (Fishman 2012). Cases of subclinical chorioamnionitis are usually determined by amniocentesis, which remains controversial and contraindicated in the presence of HIV infection. The presence of a positive ($\geq +1$) leucocyte esterase in dipstick; glucose concentration < 15 mg/dL; > 30 WBC/mm²; and bacteria on gram stain in analysis of amniotic fluid should raise suspicion for subclinical infection.

Chorioamnionitis also occurs with intact membranes; severe cases are commonly caused by organisms such as *Listeria monocytogenes*, *Staphylococcus aureus* and *Streptococcus agalactiae*. Generally, causative organisms for chorioamnionitis are polymicrobial such as mycoplasma species, group B streptococcus, gram negatives and anaerobes (Gibbs 1982). The microflora of the amniotic cavity is incompletely known, since culture-based techniques have limited capacity to identify all microorganisms (DiGiulio 2012). Polymerase chain reaction (PCR) techniques have identified 30% to 50% more organisms than identified by culture methods. Microbial invasion of the amniotic cavity is said to be polymicrobial in 24% to 67% of cases (DiGiulio 2012).

Intrauterine (fetal and placental) infection may be caused by an ascending infection from the vagina (transcervical) and by an haematogenous (transplacental) route; rarely externally (transabdominal) as occurs during invasive procedures such as amniocentesis and chorionic villous sampling; and internally (trans-fallopian route).

Risk factors that predispose women to the development of chorioamnionitis include rupture of membranes (preterm or prelabour, or both); multiple digital vaginal examinations, premature labour, prolonged labour, low socio-economic status, HIV infection, nulliparity, and presence of intrauterine pressure catheters and internal fetal monitors (Newton 1989).

Chorioamnionitis is frequently associated with adverse maternal, fetal, and neonatal outcomes that result in extended hospital stay, use of intravenous antibiotics and other medications, and use of resources. Chorioamnionitis increases a woman's risk of labour abnormalities, the need for a caesarean delivery, uterine atony, postpartum haemorrhage, and intra and/or postpartum endometritis (Gibbs 1988).

Chorioamnionitis is associated with increased fetal and neonatal sepsis, morbidity and mortality (Lau 2005). It is also associated with more than a three-fold risk of cerebral palsy in term and near term

infants (Wu 2003). Neurodevelopmental outcome is also affected for preterm infants.

Induction and/or augmentation of labour is indicated in chorioamnionitis, while caesarean delivery in the presence of chorioamnionitis is reserved for obstetric indications alone (Gibbs 1988; Gilstrap 1988). Intrapartum therapy with intravenous antibiotics has been shown to decrease maternal morbidity and neonatal sepsis. Commonly, a dual antibiotic cover of ampicillin and gentamicin +/- clindamycin or cephalopen is used (Gibbs 1988; Gilstrap 1988).

Description of the intervention

Amnioinfusion is transabdominal or transcervical infusion of saline or other physiological fluid, with or without antibiotics into the amniotic cavity. Amnioinfusion has been used for several clinical indications such as midtrimester oligohydramnios (Kozinszky 2014); early (midtrimester) prelabour rupture of membranes (Roberts 2014; van Teeffelen 2014); third trimester prelabour rupture of membranes (Hofmeyr 2014); intrapartum cord compression (Hofmeyr 2012); and meconium-stained amniotic fluid (Hofmeyr 2014b).

Amnioinfusion with antibiotics has been used to treat established amnionitis. Amnioinfusion used in afebrile parturients as an irrigating or diluting measure in pregnancies complicated by preterm prelabour rupture of the membranes and amnionitis resulted in a reduced incidence of postpartum endometritis and febrile morbidity (Major 1993; Monohan 1995; Owen 1990; Parilla 1998b). Treatment of preterm premature rupture of membranes with chorioamnionitis with continuous amnioinfusion and antibiotic administrations through a subcutaneously implanted intrauterine port system has been described (Tchirikov 2015).

Two techniques for amnioinfusion exist, namely transabdominal and transcervical. Both use saline or ringers lactate under sterile conditions. The transabdominal technique is used when membranes are intact or ruptured. A needle is used under ultrasound guidance and is considered safe in women without HIV or hepatitis B infection. The transcervical technique is used in women with ruptured membranes. A catheter is introduced through the cervix below and advanced to above the presenting part into the uterine cavity. In each case, a bolus of 300 mL is usually first infused followed by an additional 20 mL to 30 mL/hour titration and the effect observed or measured.

How the intervention might work

Amnioinfusion may reduce the adverse effects of chorioamnionitis by dilution of infective organisms, or by an anti-microbial effect of the fluid infused. Previous studies of amnioinfusion in women without chorioamnionitis have found a reduction in postpartum endometritis and febrile morbidity (Major 1993; Monohan 1995; Owen 1990). In view of the high risk of endometritis in women with chorioamnionitis, it is worth investigating the possible protective effect of amnioinfusion.

Why it is important to do this review

Chorioamnionitis is an important cause of maternal and perinatal morbidity. Amnioinfusion represents a relatively simple and safe intervention (based on extensive use for other indications such as suspected fetal compromise or meconium-stained amniotic

fluid), but its effectiveness for improving outcomes related to chorioamnionitis is not known.

OBJECTIVES

To determine from the best available evidence the effect of amnioinfusion on clinical and subclinical chorioamnionitis, fetal well-being, fetal heart rate characteristics and perinatal and maternal morbidity and mortality.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised clinical trials. Trials using a cluster-randomised design were eligible for inclusion. Abstract reports were also eligible for inclusion, provided sufficient information was included in the abstract for proper assessment of the trial.

Quasi-randomised trials were eligible for inclusion but none were identified. We would have included such trials in the initial analysis and the effect of their inclusion on the results would have been determined by sensitivity analysis.

Cross-over studies are not an appropriate study design for this intervention and were therefore not eligible for inclusion.

Types of participants

Pregnant women with suspected or confirmed chorioamnionitis, as defined by trial authors.

Types of interventions

Amnioinfusion compared with no amnioinfusion or sham amnioinfusion; different types or volumes of amnioinfusion fluid.

We planned to consider transcervical and transabdominal amnioinfusion separately by subgroup analysis because of their fundamental differences, which may result in different outcomes.

Types of outcome measures

Primary outcomes

Baby

1. Perinatal death or severe morbidity (neonatal encephalopathy, intraventricular haemorrhage, admission to intensive/high care)
2. Neonatal infection (as defined by trial authors)

Mother

1. Postpartum endometritis/puerperal infection (as defined by trial authors)

Secondary outcomes

Baby

1. Abnormal fetal heart rate on cardiotocography, e.g. late decelerations, tachycardia, reduced variability
2. Preterm birth
3. Birthweight less than 2500 g
4. Low Apgar score at five minutes (less than seven, or as defined by trial authors)

5. Low umbilical cord arterial pH (less than 7.2, or as defined by trial authors) or high lactate levels (as defined by trial authors)
6. Fetal injury
7. Perinatal death
8. Duration of antibiotic treatment
9. Neonatal admission to intensive/high care
10. Duration of hospitalisation (neonatal)
11. Long-term neurodevelopmental outcome

Mother

1. Caesarean section
2. Instrumental vaginal delivery
3. Intrapartum maternal pyrexia: temperature more than 38°C or as defined by trial author
4. Duration of labour
5. Maternal injury
6. Placental abruption
7. Mean duration of antibiotic treatment (hours)
8. Mean duration of hospitalisation (maternal)
9. Death or severe morbidity
10. Postpartum haemorrhage (blood loss $\geq$ 500 mL, or as defined by trial authors)
11. Maternal satisfaction
12. [Non pre-specified] temperature at delivery

Health services

1. Cost

Search methods for identification of studies

The following methods section of this review is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting their Information Specialist (6 July 2016)

The Register is a database containing over 22,000 reports of controlled trials in the field of pregnancy and childbirth. For full search methods used to populate the Pregnancy and Childbirth Group's Trials Register including the detailed search strategies for CENTRAL, MEDLINE, Embase and CINAHL; the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service, please follow this link to the editorial information about the [Cochrane Pregnancy and Childbirth Group](#) in the Cochrane Library and select the '**Specialized Register**' section from the options on the left side of the screen.

Briefly, the Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by their Information Specialist and contains trials identified from:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE (Ovid);
3. weekly searches of Embase (Ovid);
4. monthly searches of CINAHL (EBSCO);

5. handsearches of 30 journals and the proceedings of major conferences;
6. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Search results are screened by two people and the full text of all relevant trial reports identified through the searching activities described above is reviewed. Based on the intervention described, each trial report is assigned a number that corresponds to a specific Pregnancy and Childbirth Group review topic (or topics), and is then added to the Register. The Information Specialist searches the Register for each review using this topic number rather than keywords. This results in a more specific search set which has been fully accounted for in the relevant review sections ([Included studies](#); [Excluded studies](#)).

In addition, the review authors searched PubMed, [ClinicalTrials.gov](#) and the WHO International Clinical Trials Registry Platform ([ICTRP](#)) for unpublished, planned and ongoing trial reports, using the term amnioinfusion. The date of the last search was 6 July 2016 and no additional studies of amnioinfusion for chorioamnionitis were found.

Searching other resources

We searched the reference lists of retrieved studies.

We did not apply any language or date restrictions.

Data collection and analysis

The following methods section of this review is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Selection of studies

Two review authors independently assessed for inclusion all the potential studies we identified as a result of the search strategy. We resolved any disagreement through discussion; if required, we planned to consult a third person.

Data extraction and management

We designed a form to extract data. For eligible studies, two review authors independently extracted the data using the agreed form. We resolved discrepancies through discussion; if required, we planned to consult a third person. We entered data into Review Manager software ([RevMan 2014](#)) and checked for accuracy.

We planned that if information regarding any of the above was unclear, we would attempt to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors independently assessed risk of bias for the included study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). We resolved any disagreement by discussion or by involving a third assessor.

(1) Random sequence generation (checking for possible selection bias)

We described for the one 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:

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

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

We described the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We assessed the methods as:

- low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
- unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

We described the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We had determined that studies would be considered at low risk of bias if they were blinded, or if we judged that the lack of blinding would be unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed the methods as:

- low, high or unclear risk of bias for participants;
- low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

We described the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed methods used to blind outcome assessment as:

- low, high or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data)

We described for the 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 and the numbers included in the analysis at each stage (compared with the total 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 planned to re-include missing data in the analyses which we undertook.

We assessed methods as:

- low risk of bias (e.g. less than 5% missing outcome data; missing outcome data balanced across groups);
- high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomisation);
- unclear risk of bias.

(5) Selective reporting (checking for reporting bias)

We described how we investigated the possibility of selective outcome reporting bias and what we found.

We assessed the methods as:

- low risk of bias (where it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported);
- high risk of bias (where not all the study's pre-specified 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 risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above)

We described any important concerns we had about other possible sources of bias.

We assessed whether the one included study was free of other problems that could put it at risk of bias:

- low risk of other bias;
- high risk of other bias;
- unclear whether there is risk of other bias.

(7) Overall risk of bias

We made explicit judgements about whether the included study was at high risk of bias, according to the criteria given in the *Handbook* (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we considered it was likely to impact on the findings. In future updates, if more studies are included, we will explore the impact of the level of bias through undertaking sensitivity analyses - see [Sensitivity analysis](#).

Assessing the quality of the body of evidence using the GRADE approach

We assessed the quality of the evidence using the GRADE approach as outlined in the [GRADE handbook](#) in order to assess the quality of the body of evidence relating to the following outcomes for the main comparison (amnioinfusion versus no amnioinfusion).

1. Postpartum endometritis
2. Perinatal death or severe morbidity (neonatal encephalopathy, intraventricular haemorrhage, admission to intensive/high care)
3. Neonatal infection
4. Caesarean section
5. Low Apgar score at five minutes (less than seven, or as defined by trial authors)

[GRADEpro](#) Guideline Development Tool was used to import data from Review Manager 5.3 ([RevMan 2014](#)) in order to create 'Summary of findings' tables. A summary of the intervention effect and a measure of quality for each of the above outcomes was produced using the GRADE approach. The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome. The evidence can be downgraded from 'high quality' by one level for serious (or by two levels for very serious) limitations, depending on assessments for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates or potential publication bias.

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals.

Continuous data

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

Unit of analysis issues

Cluster-randomised trials

Cluster-randomised trials are unlikely for this procedure. However, if we identify any cluster-randomised trials for inclusion in future updates we will include them in the analyses along with individually-randomised trials. We will adjust their sample sizes using the methods described in the *Handbook* Section 16.3.4 or 16.3.6 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. 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-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely.

We would also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

Cross-over trials

Cross-over trials are not appropriate for this intervention.

Multiple-arm trials

We did not identify any multiple-arm trials for inclusion in this review. However, if we identify such trials in future updates of this review we will include pair-wise comparison of appropriate arms in the analyses. In the event of one arm appearing twice in a single meta-analysis, the numbers will be halved to avoid double counting.

Dealing with missing data

For included studies, we noted levels of attrition. In future updates, as more data become available we will explore 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 carried out analyses, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses, and all participants were analysed 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 was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

This review includes a single study - in future updates 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 the I^2 is greater than 30% and either the T^2 is greater than zero, or there is a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

In future updates, if there are 10 or more studies in a meta-analysis, we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually. If asymmetry is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

This review contains one included study so it was not possible to combine data in meta-analysis. We carried out statistical analysis using the Review Manager software (RevMan 2014). In future updates, 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. The random-effects summary will be treated 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 considered to be clinically meaningful, we will not combine trials.

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

Subgroup analysis and investigation of heterogeneity

In future updates we will carry out the following pre-specified subgroup analysis, if appropriate.

1. Transabdominal versus transcervical versus mixed or unclear method of amnioinfusion.
2. Amnioinfusion with versus without antimicrobials in the infused fluid.
3. Different types of antimicrobials.
4. Different types of fluids.

We will use all outcomes in the subgroup analyses.

We will assess subgroup differences by interaction tests available within RevMan (RevMan 2014) and report the results of subgroup analyses quoting the Chi^2 statistic and P value, and the interaction test I^2 value.

In future updates, if we identify substantial heterogeneity, we will investigate it using the planned subgroup analyses (above), and sensitivity analyses. We will consider whether an overall summary is meaningful, and if it is, we will use random-effects analysis to produce it.

Sensitivity analysis

In future updates, if appropriate, we will perform sensitivity analysis by excluding:

1. trials with high risk of allocation bias;
2. quasi-randomised trials;
3. trials with small sample size (less than 50 participants);

and determining the effect of such exclusion on the review results. If we include cluster-randomised clinical trials along with individually-randomised trials, we will also carry out sensitivity analysis to investigate the effect of the randomisation unit.

Planned sensitivity analysis will be restricted to this review's primary outcomes.

RESULTS

Description of studies

Results of the search

See Figure 1 for full details of search results. We found three relevant reports: two reports of one study, which was included (Parilla 1998), and one report which was excluded (Macri 1993).

Figure 1. Study flow diagram.

Included studies

One study ([Parilla 1998](#)) was included in which transcervical amnioinfusion was performed in 17 participants in the amnioinfusion group versus 19 in the control group (or 18 versus 18, the report was unclear, see [Characteristics of included studies](#)). Transcervical amnioinfusion was with room temperature saline at 10 mL per minute for 60 minutes then 3 mL per minute till delivery versus no amnioinfusion. All women received intrauterine pressure catheter, acetaminophen and antibiotics (ampicillin or, if receiving Group B beta streptococcal prophylaxis, penicillin and gentamycin).

Results were available for 17 versus 17 women. Randomisation was achieved by computer-generated random sequence, in balanced blocks of six, and allocation concealment with opaque sealed envelopes. The study took place at a University medical centre (Northwestern Memorial Hospital, Chicago, IL, USA).

The participants were at full-term gestational age (39.7 +/- 1.5 weeks in the amnioinfusion group versus 39.4 +/- 2.9 weeks in the control group). There were more nulliparous than multiparous participants: 13 versus four for the amnioinfusion group and 14 versus five for the control group. Participant numbers for the study, and therefore for this review, are small.

Outcomes reported were: mean temperature throughout labour and at delivery; postpartum endometritis (pyrexia 100.4°F or more plus uterine tenderness more than 12 hours after delivery); umbilical cord arterial pH; duration of postpartum antibiotics; duration of mother's hospital stay; neonatal infectious morbidity; time from randomisation to delivery (seven hours in the amnioinfusion group); caesarean section.

Excluded studies

One study ([Macri 1993](#)) was excluded as it was reported only as an abstract with no numerical data. We wrote to request numerical data if available (March 2016). The intervention was antibiotic amnioinfusion.

Risk of bias in included studies

The overall risk of bias for [Parilla 1998](#) was considered high due to small numbers, inconsistency in the reporting and lack of information on blinding.

Allocation

[Parilla 1998](#) was a randomised trial: randomisation was by a computer-generated series of random numbers in balanced blocks of six, in opaque envelopes (low risk of bias for sequence generation and allocation concealment).

Blinding

[Parilla 1998](#) does not mention blinding of participants and personnel, or blinding of outcome assessment. We assessed this study as being at an unclear risk of performance and detection bias.

Incomplete outcome data

The [Parilla 1998](#) study randomised 36 women and there were two losses to follow-up (2/36, 5.6%), which we regarded as low risk of attrition bias. The study reports data from 17 women in each group. However, it is not clear how many women were randomised to each

group (i.e. it is unclear whether the study examined 17 versus 19 or 18 versus 18 randomised to each group).

Selective reporting

No protocol was available for [Parilla 1998](#) and we therefore assessed this study as being at an unclear risk of reporting bias.

Other potential sources of bias

We assessed [Parilla 1998](#) as being at a high risk of 'other bias' due to inconsistency in the reporting of numbers in the trial reports. The number of participants is reported in an abstract as being 32. In the text it says that one was then lost to each group, leaving 17 in each group. Baseline data are reported as 17 in the study group (13 nulliparous, four multiparous) and 19 in the control group (14 nulliparous, five multiparous).

Effects of interventions

See: [Summary of findings for the main comparison Amnioinfusion versus no amnioinfusion for chorioamnionitis](#)

We did not identify any studies that looked at transabdominal amnioinfusion.

The results of this review are based on one small study (with data from 34 women) that examined transcervical amnioinfusion versus no amnioinfusion. Meta-analysis was not possible.

Transcervical amnioinfusion versus no amnioinfusion (one study, with data from 34 participants)

Primary outcomes

Only one trial was included (with data from a total of 34 participants). There was no clear difference in the incidence of **postpartum endometritis** between the group of women who received amnioinfusion and those who did not (risk ratio (RR) 1.50, 95% confidence interval (CI) 0.29 to 7.87; absolute risk 176/1000 (95% CI 34 to 96) versus 118/1000; *low-quality evidence* ([Analysis 1.1](#))). Similarly, there was no clear difference in **neonatal infection** between groups (RR 3.00, 95% CI 0.13 to 68.84; absolute risk 0/1000 (95% CI 0 to 0) versus 0/1000; *low-quality evidence* ([Analysis 1.2](#))). The outcome **perinatal death or severe morbidity** was not reported.

Secondary outcomes

The **caesarean section** rate was the same (5/17) in both groups (RR 1.00, 95% CI 0.35 to 2.83; absolute risk 294/1000 (95% CI 103 to 832) versus 294/1000; *low-quality evidence* ([Analysis 1.3](#))).

There was no clear difference between intervention and control groups in terms of the **duration of maternal antibiotic treatment** (mean difference (MD) 16 hours, 95% CI -1.75 to 33.75 ([Analysis 1.4](#))); or the **duration of maternal hospitalisation** (MD 3.00 hours, 95% CI -15.49 to 21.49 ([Analysis 1.5](#))).

The **temperature at delivery** was lower in the amnioinfusion group than the control group, but this outcome was not pre-specified in our protocol for this review (MD -0.38°C, 95% CI -0.74 to -0.02 ([Analysis 1.6](#))).

The majority of this review's secondary outcomes were not reported in [Parilla 1998](#) - these are listed below.

For the baby

1. Abnormal fetal heart rate on cardiotocography, e.g. late decelerations, tachycardia, reduced variability
2. Preterm birth
3. Birthweight less than 2500 g
4. Low Apgar score at five minutes (less than seven, or as defined by trial authors)
5. Low umbilical cord arterial pH (less than 7.2, or as defined by trial authors) or high lactate levels (as defined by trial authors)
6. Fetal injury
7. Perinatal death
8. Duration of antibiotic treatment
9. Neonatal admission to intensive/high care
10. Duration of hospitalisation (neonatal)
11. Long-term neurodevelopmental outcome

For the mother

1. Instrumental vaginal delivery
2. Intrapartum maternal pyrexia: temperature more than 38°C or as defined by trial author
3. Duration of labour
4. Maternal injury
5. Placental abruption
6. Death or severe morbidity
7. Postpartum haemorrhage (blood loss $\geq$ 500 mL, or as defined by trial authors)
8. Maternal satisfaction

Health services

1. Cost

DISCUSSION

Summary of main results

No data were available for the outcome of perinatal death or severe morbidity.

The one small included study found no significant effect on postpartum endometritis, neonatal infection, caesarean section, duration of antibiotic treatment or duration of hospitalisation. There was a reduction in mean maternal temperature at delivery (which was not an outcome that was pre-specified in the protocol for this review). The number of babies with a low Apgar score at five minutes after birth was not reported. Similarly, the majority of this review's secondary outcomes were not reported by [Parilla 1998](#).

The rationale for amnioinfusion for the management of amnionitis has been to treat the infection either by the diluting effect of the amnioinfusion fluid, or by the amnioinfusion of antimicrobial substances.

The reduction in pyrexia in the amnioinfusion group is considered by the trial authors ([Parilla 1998](#)) to be an indication of the effectiveness of saline amnioinfusion in reducing infection.

We postulate an alternative mechanism for temperature reduction with amnioinfusion, which is the direct cooling effect of the amnioinfusion fluid. In the study group, women received room

temperature saline at 10 mL/minute for 60 minutes then 3 mL/minute. The mean time from randomisation to delivery was seven hours, giving a mean volume infused of 1500 mL. Using simple proportion, 1500 mL amnioinfusion at 20°C might be expected to reduce the temperature of a woman weighing 60 kg by 0.42°C if distributed throughout her body. Intravenous infusion of 30 mL/kg saline at 23°C over 30 minutes to healthy afebrile volunteers caused a temporary decrease in core temperature of 0.5°C ([Moore 2008](#)). The baby's temperature would be expected to be reduced by more until the temperature stabilised.

Under normal circumstances, the baby's temperature is consistently higher than that of the mother, as metabolic heat generated by the baby can only be dissipated down a temperature gradient via the mother (85% by heat exchange in the placenta ([Asakura 2004](#))). In animal models, umbilical cord occlusion causes hyperthermia which may cause fetal damage ([Asakura 2004](#); [Gericke 1989](#)). Intrauterine temperature during labour is about 0.5°C higher than maternal tympanic temperature ([Sciscione 2001](#)). In a non-randomised observational study, the mean intrauterine temperature in afebrile women who received ambient temperature amnioinfusion (25°C) was 1.5°C lower than that of controls ([Tomlinson 2012](#)). Neonatal rectal temperatures were 1°C warmer than maternal oral temperature, and in the amnioinfusion group were reduced by 0.4°C (not statistically significant).

The neuroprotective effect of hypothermia in neonates is well-established ([Shah 2007](#)). Although not the objective of the study reviewed here, reduction of pyrexia by a direct cooling effect may be beneficial for the baby. We suggest that further investigation of the potential of amnioinfusion in chorioamnionitis both for reduction of infection and for possible benefits of a direct cooling effect in fetuses considered at risk of neurological damage, is justified.

Overall completeness and applicability of evidence

These results are inconclusive due to the small numbers of studies (one of transcervical amnioinfusion) and participants (data from 34 women and their babies). The numbers are also too small to detect rare potential adverse events. There were no studies that examined using transabdominal amnioinfusion.

Quality of the evidence

Overall, the trial was considered to be at a high risk of bias due to small numbers, inconsistency in the reporting and lack of information on blinding. When considering the individual 'Risk of bias' domains, the risk of bias was assessed as low for random sequence generation, allocation concealment and incomplete outcome data; unclear for blinding and selective reporting; and high for inconsistency in reporting of numbers randomised to each group: see [Characteristics of included studies](#).

The trial quality, assessed using GRADE, was downgraded to low because of small numbers and uncertainty regarding blinding - see [Summary of findings for the main comparison](#).

Potential biases in the review process

No potential biases identified.

Agreements and disagreements with other studies or reviews

We have not identified any other reviews of amnioinfusion for chorioamnionitis.

AUTHORS' CONCLUSIONS

Implications for practice

There is insufficient evidence to fully evaluate the effectiveness of using transcervical amnioinfusion for chorioamnionitis and to assess the safety of this intervention or women's satisfaction. There is no evidence to evaluate transabdominal amnioinfusion. The evidence in this review can neither support nor refute the use of this intervention outside of clinical trials.

Implications for research

Further research is justified to determine possible benefits or risks of amnioinfusion for chorioamnionitis with greater certainty, and to investigate possible benefits of reducing temperature in fetuses considered at risk of neurological damage. Research should include randomised controlled trials:

1. participants: women with chorioamnionitis;
2. intervention: transcervical or transabdominal amnioinfusion;
3. comparison: no amnioinfusion;
4. outcomes: endometritis; neonatal infection; perinatal death or severe morbidity; neurodevelopmental outcomes; caesarean section; maternal temperature at birth; neonatal temperature; other measures of maternal and perinatal morbidity.

ACKNOWLEDGEMENTS

We thank Cochrane Pregnancy and Childbirth's editorial base for technical support.

As part of the pre-publication editorial process, this review has been commented on by three peers (an editor and two referees who are external to the editorial team) and the Group's Statistical Adviser.

This project was supported by the National Institute for Health Research, via Cochrane Infrastructure funding to Cochrane Pregnancy and Childbirth. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.

REFERENCES

References to studies included in this review

Parilla 1998 {published data only}

McDermott TM, Parilla BV. Amnioinfusion as a therapy to reduce post partum endometriosis after chorioamnionitis. *American Journal of Obstetrics and Gynecology* 1998;**178**(1 Pt 2):S212.

* Parilla BV, McDermott TM. Prophylactic amnioinfusion in pregnancies complicated by chorioamnionitis: a prospective randomized trial. *American Journal of Perinatology* 1998;**15**(12):649-52.

References to studies excluded from this review

Macri 1993 {published data only}

Macri C, Paek J, Greenspoon J, Paul R. Antibiotic amnioinfusion does not decrease maternal morbidity in term pregnancy complicated by amnionitis. *American Journal of Obstetrics and Gynecology* 1993;**168**:414.

Additional references

Asakura 2004

Asakura H. Fetal and neonatal thermoregulation. *Journal of Nippon Medical School* 2004;**71**(6):360-70.

DiGiulio 2012

DiGiulio DB. Diversity of microbes in amniotic fluid. *Seminars in Fetal & Neonatal Medicine* 2012;**17**(1):2-11.

Fishman 2012

Fishman SG, Gelber SE. Evidence for the clinical management of chorioamnionitis. *Seminars in Fetal & Neonatal Medicine* 2012;**17**(1):46-50.

Gericke G1989

Gericke GS, Hofmeyr GJ, Laburn H, Isaacs H. Does heat damage fetuses?. *Medical Hypotheses* 1989;**29**(4):275-8.

Gibbs 1982

Gibbs RS, Blanco JD, St Clair PJ, Castaneda YS. Quantitative bacteriology of amniotic fluid from women with clinical intraamniotic infection at term. *Journal of Infectious Diseases* 1982;**145**(1):1-8.

Gibbs 1988

Gibbs RS, Dinsmoor MJ, Newyon ER, Ramamurthy RS. A randomised trial of intrapartum versus immediate postpartum treatment of women with intra-amniotic infection. *Obstetrics & Gynecology* 1988;**72**(6):823-8.

Gilstrap 1988

Gilstrap LC 3rd, Leveno KJ, Cox SM, Burris JS, Mashburn M, Rosenfeld CR. Intrapartum treatment of acute chorioamnionitis: impact on neonatal sepsis. *American Journal of Obstetrics and Gynecology* 1988;**159**(3):579-83.

Higgins 2011

Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Hofmeyr 2012

Hofmeyr GJ, Lawrie TA. Amnioinfusion for potential or suspected umbilical cord compression in labour. *Cochrane Database of Systematic Reviews* 2012, Issue 1. [DOI: [10.1002/14651858.CD000013.pub2](https://doi.org/10.1002/14651858.CD000013.pub2)]

Hofmeyr 2014

Hofmeyr GJ, Eke AC, Lawrie TA. Amnioinfusion for third trimester preterm premature rupture of membranes. *Cochrane Database of Systematic Reviews* 2014, Issue 3. [DOI: [10.1002/14651858.CD000942.pub3](https://doi.org/10.1002/14651858.CD000942.pub3)]

Hofmeyr 2014b

Hofmeyr GJ, Xu H, Eke AC. Amnioinfusion for meconium-stained liquor in labour. *Cochrane Database of Systematic Reviews* 2014, Issue 1. [DOI: [10.1002/14651858.CD000014.pub4](https://doi.org/10.1002/14651858.CD000014.pub4)]

Kozinszky 2014

Kozinszky Z, Sikovanyecz J, Pásztor N. Severe midtrimester oligohydramnios: treatment strategies. *Current Opinion in Obstetrics & Gynecology* 2014;**26**(2):67-76.

Lau 2005

Lau J, Magee F, Qiu Z, Houbé J, Von Dadelszen P, Lee SK. Chorioamnionitis with a fetal inflammatory response is associated with higher neonatal mortality, morbidity, and resource use than chorioamnionitis displaying a maternal inflammatory response only. *American Journal of Obstetrics and Gynecology* 2005;**193**(3 Pt 1):708-13.

Major 1993

Major CA, de Veciana M, Morgan MA, Henry JA. The impact of amnioinfusion on maternal and neonatal morbidity in pregnancies complicated by pre-term premature rupture of membranes and amnionitis. *American Journal of Obstetrics and Gynecology* 1993;**168**(1 Pt 2):SPO Abstract no: 383.

McDermott 1998

McDermott TM, Parilla BV. Amnioinfusion as a therapy to reduce post partum endometriosis after chorioamnionitis. *American Journal of Obstetrics and Gynecology* 1998;**178**(1 Pt 2):S212.

Monohan 1995

Monahan E, Katz V, Cox R. Amnioinfusion for preventing puerperal infection. *Journal of Reproductive Medicine* 1995;**40**(10):721-3.

Moore 2008

Moore TM, Callaway CW, Hostler D. Core temperature cooling in healthy volunteers after rapid intravenous infusion of cold and room temperature saline solution. *Annals of Emergency Medicine* 2008;**51**(2):153-9.

Newton 1989

Newton ER, Prihoda TJ, Gibbs RS. Logistic regression analysis of risk factors for intra-amniotic infection. *Obstetrics & Gynecology* 1989;**73**(4):571-5.

Owen 1990

Owen J, Henson BV, Hauth JC. A prospective randomized study of saline solution amnioinfusion. *American Journal of Obstetrics and Gynecology* 1990;**162**(5):1146-9.

Parilla 1998b

Parilla BV, McDermott TM. Prophylactic amnioinfusion in pregnancies complicated by chorioamnionitis: a prospective randomized trial. *American Journal of Perinatology* 1998;**15**(12):649-52.

RevMan 2014 [Computer program]

The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Roberts 2014

Roberts D, Vause S, Martin W, Green P, Walkinshaw S, Bricker L, et al. Amnioinfusion in preterm premature rupture of membranes (AMIPROM): a randomised controlled trial of amnioinfusion versus expectant management in very early preterm premature rupture of membranes - a pilot study. *Health Technology Assessment* 2014;**18**(21):1-136.

Sciscione 2001

Sciscione AC, Zainia T, Leet T, Winn JN, Winn HN. A new device for measuring intrauterine temperature. *American Journal of Obstetrics and Gynecology* 2001;**184**(7):1431-4.

Shah 2007

Shah PS, Ohlsson A, Perlman M. Hypothermia to treat neonatal hypoxic ischemic encephalopathy: systematic review. *Archives of Pediatrics & Adolescent Medicine* 2007;**161**(10):951-8.

Tchirikov 2015

Tchirikov M, Zhumadilov Z, Winarno AS, Haase R, Buchmann J. Treatment of preterm premature rupture of membranes with oligo-/anhydramnion colonized by multiresistant bacteria with continuous amnioinfusion and antibiotic administrations through a subcutaneously implanted intrauterine port system: a case report. *Fetal Diagnosis and Therapy* 2015;**epub**:epub.

Tomlinson 2012

Tomlinson TM, Schaecher C, Sadovsky Y, Gross G. Intrauterine temperature during intrapartum amnioinfusion: a prospective observational study. *BJOG: an international journal of obstetrics and gynaecology* 2012;**119**(8):958-63.

van Teeffelen 2014

van Teeffelen AS, van der Ham DP, Willekes C, Al Nasiry S, Nijhuis JG, van Kuijk S, et al. Midtrimester preterm prelabour rupture of membranes (PPROM): expectant management or amnioinfusion for improving perinatal outcomes (PPROMEXIL - III trial). *BMC Pregnancy and Childbirth* 2014;**14**:128.

Wu 2003

Wu YW, Escobar GJ, Grether JK, Croen LA, Greene JD, Newman TB. Chorioamnionitis and cerebral palsy in term and near-term infants. *JAMA* 2003;**290**(20):2677-84.

References to other published versions of this review

Kiiza 2015

Kiiza JAK, Hofmeyr GJ. Amnioinfusion for chorioamnionitis. *Cochrane Database of Systematic Reviews* 2015, Issue 6. [DOI: [10.1002/14651858.CD011622](https://doi.org/10.1002/14651858.CD011622)]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Parilla 1998

Methods	Randomised controlled trial.
Participants	Women in labour with pyrexia 100.1°F or more (n = 36). Exclusion criteria: cervical dilation > 8 cm; multiple pregnancy; placental abruption; non-reassuring fetal heart rate tracing.
Interventions	Transcervical amnioinfusion with room temperature saline at 10 mL per minute for 60 minutes then 3 mL per minute till delivery; versus no amnioinfusion. All women received intrauterine pressure catheter, acetaminophen and antibiotics (ampicillin or, if receiving Group B beta streptococcal prophylaxis, penicillin and gentamycin). Data available for 17 women in each group. Unclear whether 17 versus 19 or 18 versus 18 were randomised to each group.
Outcomes	Primary: mean temperature throughout labour and at delivery. Secondary:

Amnioinfusion for chorioamnionitis (Review)

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Parilla 1998 (Continued)

- postpartum endometritis (pyrexia 100.4°F or more plus uterine tenderness more than 12 hours after delivery);
- umbilical cord arterial pH;
- duration of postpartum antibiotics;
- duration of mother's hospital stay;
- neonatal infectious morbidity;
- time from randomisation to delivery (7 hours in the amnioinfusion group);
- caesarean section.

Notes Recruitment 1 June 1996 to 31 March 1997. Setting: academic hospital in the USA.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated series of random numbers in balanced blocks of 6.
Allocation concealment (selection bias)	Low risk	Opaque envelopes.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not mentioned.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not mentioned.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 2/36 (5.6%), but it is not clear which group the losses were from (see 'other bias').
Selective reporting (reporting bias)	Unclear risk	No published protocol.
Other bias	High risk	Interim analysis with 32 participants reported in conference abstract (McDermott 1998). Inconsistency in numbers. In the text it states 1 in each group lost to follow-up leaving 17 in each group. Baseline data report 17 in study group (13 nulliparous plus 4 multiparous) and 19 in control group (14 plus 5).

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Macri 1993	No quantitative data given in the published abstract. 46 women with chorioamnionitis were 'prospectively randomised' to amnioinfusion with 1 g ampicillin in 500 mL saline versus no amnioinfusion. All women received intravenous ampicillin and gentamycin. There were no differences in caesarean section, postpartum febrile morbidity nor wound infections.

DATA AND ANALYSES

Comparison 1. Transcervical amnioinfusion versus no amnioinfusion

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Postpartum endometritis	1	34	Risk Ratio (M-H, Fixed, 95% CI)	1.5 [0.29, 7.87]
2 Neonatal infection	1	34	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 68.84]
3 Caesarean section	1	34	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.35, 2.83]
4 Duration of maternal antibiotic treatment (hours)	1	34	Mean Difference (IV, Fixed, 95% CI)	16.0 [-1.75, 33.75]
5 Maternal hospitalisation (hours)	1	34	Mean Difference (IV, Fixed, 95% CI)	3.0 [-15.49, 21.49]
6 Temperature at delivery (not pre-specified) °C	1	34	Mean Difference (IV, Fixed, 95% CI)	-0.38 [-0.74, -0.02]

Analysis 1.1. Comparison 1 Transcervical amnioinfusion versus no amnioinfusion, Outcome 1 Postpartum endometritis.

Analysis 1.2. Comparison 1 Transcervical amnioinfusion versus no amnioinfusion, Outcome 2 Neonatal infection.

Analysis 1.3. Comparison 1 Transcervical amnioinfusion versus no amnioinfusion, Outcome 3 Caesarean section.

Analysis 1.4. Comparison 1 Transcervical amnioinfusion versus no amnioinfusion, Outcome 4 Duration of maternal antibiotic treatment (hours).

Analysis 1.5. Comparison 1 Transcervical amnioinfusion versus no amnioinfusion, Outcome 5 Maternal hospitalisation (hours).

Analysis 1.6. Comparison 1 Transcervical amnioinfusion versus no amnioinfusion, Outcome 6 Temperature at delivery (not pre-specified) °C.

WHAT'S NEW

Date	Event	Description
9 May 2019	Amended	Edited Declarations of interest

CONTRIBUTIONS OF AUTHORS

JAK wrote the first draft of the protocol and did the initial assessment of studies for inclusion, data extraction and analysis.

GJH reviewed the protocol, carried out duplicate assessment of studies for inclusion and data extraction, conducted the GRADE analysis and wrote the final discussion and conclusions.

DECLARATIONS OF INTEREST

G Justus Hofmeyr - receives royalties from UpToDate for chapters related to [breech pregnancy](#), [delivery of a baby in breech presentation](#) and [external cephalic version](#). UpToDate is an electronic publication by Wolters Kluwer to disseminate evidence-based medicine (such as Cochrane reviews).

Joseph AK Kiiza: none known.

SOURCES OF SUPPORT

Internal sources

- CEBHC Stellenbosch University, South Africa.

Centre for Evidence-based Health Care, Department of Interdisciplinary Health, Faculty of Medicine and Health Sciences, Stellenbosch University: support to GJH

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There are some differences between this review and our published protocol ([Kiiza 2015](#)) for this review.

1. Methods/outcomes - we have added a new secondary outcome - mean temperature at delivery.
2. We have used the GRADE approach to assess the quality of the evidence and we have prepared a 'Summary of findings' table.

INDEX TERMS

Medical Subject Headings (MeSH)

*Amniotic Fluid; Anti-Bacterial Agents [administration & dosage]; Cervix Uteri; Cesarean Section [statistics & numerical data]; Chorioamnionitis [*therapy]; Endometritis [epidemiology]; Infections [epidemiology]; Length of Stay; Perinatal Death

MeSH check words

Female; Humans; Infant, Newborn; Pregnancy