Antibiotic regimens for management of intraamniotic infection (Review)

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ABSTRACT

Background
Intraamniotic infection is associated with maternal morbidity and neonatal sepsis, pneumonia and death. Although antibiotic treatment is accepted as the standard of care, few studies have been conducted to examine the effectiveness of different antibiotic regimens for this infection and whether to administer antibiotics intrapartum or postpartum.

Objectives
To study the effects of different maternal antibiotic regimens for intraamniotic infection on maternal and perinatal morbidity and mortality.

Search strategy
We searched the Cochrane Pregnancy and Childbirth Group trials register (May 2002) and the Cochrane Controlled Trials Register (The Cochrane Library, Issue 2, 2002).

Selection criteria
Trials where there was a randomized comparison of different antibiotic regimens to treat women with a diagnosis of intraamniotic infection were included. The primary outcome was perinatal morbidity.

Data collection and analysis
Data were extracted from each publication independently by the authors.

Main results
Two eligible trials (181 women) were included in this review. No trials were identified that compared antibiotic treatment with no treatment. Intrapartum treatment with antibiotics for intraamniotic infection was associated with a reduction in neonatal sepsis (relative risk (RR) 0.08; 95% confidence interval (CI) 0.00, 1.44) and pneumonia (RR 0.15; CI 0.01, 2.92) compared with treatment given immediately postpartum, but these results did not reach statistical significance (number of women studied = 45). There was no difference in the incidence of maternal bacteremia (RR 2.19; CI 0.25, 19.48). There was no difference in the outcomes of neonatal sepsis (RR 2.16; CI 0.20, 23.21) or neonatal death (RR 0.72; CI 0.12, 4.16) between a regimen with and without anaerobic activity (number of women studied = 133). There was a trend towards a decrease in the incidence of post-partum endometritis in women who received treatment with ampicillin, gentamicin and clindamycin compared with ampicillin and gentamicin alone, but this did not reach statistical significance (RR 0.54; CI 0.19, 1.49).

Authors' conclusions
The conclusions that can be drawn from this meta-analysis are limited due to the small number of studies. For none of the outcomes was a statistically significant difference seen between the different interventions. Current consensus is for the intrapartum administration of antibiotics when the diagnosis of intraamniotic infection is made; however, the results of this review neither support nor refute this although there was a trend towards improved neonatal outcomes when antibiotics were administered intrapartum. No recommendations can be made on the most appropriate antimicrobial regimen to choose to treat intraamniotic infection.

PLAIN LANGUAGE SUMMARY

Antibiotics are used to prevent life-threatening complications for mother and baby when the amniotic fluid is infected, but it is not known which antibiotic is best

Amniotic fluid is the 'water' surrounding the baby inside the womb. If this fluid becomes infected, it can be life-threatening for the mother and baby, and the baby should be born within 12 hours. Infection can come from bacteria entering the womb from the vagina, or from a medical procedure that penetrates the membranes ('bag' around baby and waters). Antibiotics reduce the risk of dangerous complications for both mother and baby. The review found there is not enough evidence from trials to show which antibiotic is best or whether it should be given before or after the baby is born.

BACKGROUND

Clinically evident intraamniotic infection (IAI) occurs in approximately one per cent of pregnancies and is potentially a serious infectious complication, leading to increased maternal and infant morbidity and mortality (Sweet 1985). Several alternative terms for intraamniotic infection are in widespread use and include chorioamnionitis, amnionitis, uterine infection and amniotic fluid infection. Intraamniotic infection occurs when there is bacterial infection of the uterine cavity and amniotic fluid and is usually a result of ascending infection from the vagina to the uterine cavity. Infection is often polymicrobial. The principal pathogens include Escherichia coli, Bacteroides species, Group B streptococci and anaerobic streptococci. Occasionally infection is due to hematogenous dissemination of bacteria such as Listeria monocytogenes (Schuchat 1992). A third mechanism for the development of intraamniotic infection is the introduction of bacteria during an invasive procedure, for example, amniocentesis, intrauterine fetal blood transfusion, and cervical cerclage (Sweet 1985). Several risk factors have been identified for the development of intrapartum intraamniotic infection. Only the duration of labor, duration of membrane rupture, use of internal fetal monitoring devices and number of vaginal examinations are independently associated with the development of intraamniotic infection (Newton 1989; Soper 1989).

The usual presenting clinical manifestations of intraamniotic infection include fever associated with maternal and fetal tachycardia. Uterine tenderness and purulent amniotic fluid may be present also but are usually late manifestations. The membranes may or may not be intact and labor may or may not be present (Duff 1993).

There is a significant risk of both maternal and perinatal morbidity and mortality associated with intraamniotic infection. In addition to the initiation of labor, intraamniotic infection may lead to postpartum endometritis and also more serious infectious sequelae such as septic shock, adult respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), and acute renal failure (Westover 1995). Infected fetuses can rapidly decompensate during labor. They may be born with fulminant sepsis and subsequently die in the neonatal period or be developmentally delayed. Infants exposed to intrauterine infection can present with neonatal encephalopathy and may be at an increased risk of cerebral palsy (Hagberg 2002). Delivery is indicated once a diagnosis of intraamniotic infection is established. Few data exist, however, to indicate the optimal time frame in which to effect delivery. From the available evidence, a diagnosis to delivery interval of up to twelve hours is not associated with increased neonatal morbidity (Gibbs 1980; Hauth 1985). In both of these studies, maternal parenteral antibiotic administration was commenced at diagnosis. Whether to begin parenteral antibiotic administration immediately after making the diagnosis or after delivery has been controversial. While immediate administration of antibiotics may limit maternal sepsis, intrapartum antibiotic therapy could obscure the diagnosis of neonatal sepsis and affect the management of the infant. Side effects associated with antibiotic therapy include allergic reactions, renal toxicity, antibiotic-associated diarrhea and the consequences of the development of antimicrobial resistance. A variety of regimens, effective against the most common organisms, have been used to treat intraamniotic infection on an empirical basis. Usually treatment is with a penicillin and gentamicin with or without the addition of clindamycin, but there is no consensus on the most appropriate regimen (Sweet 1985).

OBJECTIVES

To study the effects of different maternal antibiotic regimens for intraamniotic infection on maternal and perinatal morbidity and mortality.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All trials were considered where the intention was to allocate participants randomly to one of at least two different management strategies to treat intraamniotic infection.

Types of participants

Women who were diagnosed with intraamniotic infection by the presence of fever plus at least one of: maternal tachycardia, fetal tachycardia, uterine tenderness or purulent amniotic fluid. No gestational age limit was imposed. Women were or were not in labor and the membranes were or were not intact.

Types of intervention

Trials were considered if they compared any antibiotic treatment versus no treatment, compared at least two different antibiotic drug regimens or where there was a comparison of timing of antibiotic administration (intrapartum or postpartum).

Types of outcome measures

Trials were considered if any one of the following clinical outcomes was reported, however they were defined by the authors: (i) endometritis (ii) febrile morbidity (iii) other serious infectious complication (wound infection, urinary tract infection, septic shock, adult respiratory distress syndrome, disseminated intravascular coagulation, renal failure) (iv) neonatal sepsis (v) stillbirth and neonatal death (vi) other serious neonatal infectious complication (pneumonia, respiratory distress syndrome, positive blood cultures and meningitis). In addition data were collected (where available) on adverse events of treatment (e.g. allergic reactions, antibiotic-associated diarrhea, development of bacterial resistance).

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

The primary source of studies was the review group's trials register - the Cochrane Pregnancy and Childbirth Group's Specialized Register of Controlled Trials. This review has drawn on the search strategy developed for the Cochrane Pregnancy and Childbirth Group as a whole. The full list of journals and conference proceedings as well as the search strategies for the electronic databases, which are searched by the Group on behalf of its reviewers, are described in detail in the 'Search strategies for the identification of studies section' within the editorial information about the Cochrane Pregnancy and Childbirth Group. Briefly, the Group searches on a regular basis MEDLINE, the Cochrane Controlled Trials Register and reviews the Contents tables of a further 38 relevant journals received via ZETOC, an electronic current awareness service. Relevant trials, which are identified through the Group's search strategy, are entered into the Group's Specialized Register of Controlled Trials. Please see Review Group's details for more detailed information. Date of last search: May 2002

In addition, the Cochrane Controlled Trials Register was searched (The Cochrane Library, Issue 2, 2002). The terms chorioamnionitis, amnionitis, infection, labor and intrapartum were used.

METHODS OF THE REVIEW

All potential trials were selected for eligibility according to the criteria specified in the protocol and data were extracted from each publication by two reviewers. Any discrepancies were resolved by discussion. In addition to the main outcome measures listed above, information on the setting of the study (country, type of population, socioeconomic status), a description of the antibiotic regimen used (drug, dose, frequency and timing), characteristics of the pregnancies (gestational age, labor, membrane status) and definitions of outcome as well as intraamniotic infection (if provided) was collected. Trials were assessed for methodological quality using the Cochrane criteria of adequacy of allocation concealment: adequate (A), unclear (B), inadequate (C), or that allocation concealment was not used (D). Subgroup analyses to examine: (1) the effect of high quality trials (defined as adequate allocation concealment), and (2) the effect of infection occurring at term versus preterm on outcomes was performed. Information on blinding of outcome assessment and loss to follow-up was collected. Where data were available, an intent to treat analysis was performed. The main comparison of treatment schemes was not stratified according to gestational age, membrane status, or presence and duration of labor. Separate comparisons of different antimicrobial regimens were made. Summary relative risks were calculated using a fixed effects model (or a random effects model if statistically significant heterogeneity among trials was observed).

DESCRIPTION OF STUDIES

Fifteen trials, published between 1956 and 1998, were examined for inclusion in the review but thirteen were excluded because they were not randomized controlled trials or did not fit the selection criteria specified in the review (for a detailed description of the reasons for exclusion, see table of 'Characteristics of excluded studies'). Both trials included in the review (Gibbs 1988; Maberry 1991) were conducted in the United States. The study by Gibbs 1988 enrolled 48 women; 133 women were included in the study by Maberry 1991. Criteria listed to define the presence of intraamniotic infection were consistent. The antimicrobial agents used in the trials included ampicillin and gentamicin with the addition of clindamycin to one of the arms in the trial by Maberry 1991. All infants in the study by Gibbs 1988 received ampicillin and gentamicin for at least 72 hours after delivery; the majority of the infants in the study from Maberry 1991received ampicillin and gentamicin for at least 48 hours after delivery. For a detailed description of studies see table of 'Characteristics of included studies'.

METHODOLOGICAL QUALITY

In the included study by Gibbs 1988, randomization by sealed

envelopes and lack of blinding weaken the study design but endpoints were well defined. The investigators and the Safety Committee agreed to stop this study after 48 patients had been enrolled based on the preliminary results; a sample size of 92 patients had been planned. Specific maternal and infant side-effects of therapy were not sought. Follow-up for infant infectious complications in the neonatal period appeared to be complete. Three of 22 women randomized to postpartum treatment were excluded from the analysis because of protocol violations: two women received intrapartum antibiotics and neonatal blood cultures were not collected in a third. An intent to treat analysis was not performed. In the included study by Maberry 1991, randomization was by a table of random numbers. There is no mention as to whether the study was blinded but again, endpoints were well-defined. All women enrolled were included in the analysis.

RESULTS

No trials were identified that compared antibiotic treatment with no treatment. Intrapartum treatment with antibiotics for intraamniotic infection was associated with a reduction in neonatal sepsis (relative risk (RR) 0.08; 95% confidence interval (CI) 0.00,1.44) and pneumonia (RR 0.15; CI 0.01, 2.92) compared with treatment given immediately postpartum, but these results did not reach statistical significance (number of women studied = 45). One neonatal death occurred in an infant whose mother received antibiotics post-partum. There was no difference in the incidence of maternal bacteremia (RR 2.19; CI 0.25, 19.48).

There was no evidence to support the use of a more broad-spectrum regimen than ampicillin and gentamicin for the treatment of intraamniotic infection. There was no difference in the outcomes of neonatal sepsis (RR 2.16; CI 0.20, 23.21) or neonatal death (RR 0.72; CI 0.12, 4.16) between a regimen with and without anaerobic activity (number of women studied = 133). There was a trend towards a decrease in the incidence of post-partum endometritis in women who received treatment with ampicillin, gentamicin and clindamycin compared with ampicillin and gentamicin alone, but this result did not reach statistical significance (RR 0.54; CI 0.19, 1.49).

DISCUSSION

The conclusions that can be drawn from this meta-analysis are limited due to the small number of studies and the early discontinuation of enrollment in one of them. For none of the outcomes was a statistically significant difference seen bbetweenthe different interventions. Current consensus within the clinical community is for the intrapartum administration of antibiotics when the diagnosis of intraamniotic infection is made; a combination of ampicillin and gentamicin is often recommended. The results of this review, however, neither supports nor confirms this approach although the trend in improved neonatal outcomes was when antibiotics were administered intrapartum. No recommendations can be made on the most appropriate antimicrobial regimen to choose to treat intraamniotic infection. The quality of evidence supporting the current approach is poor and current practice is not based on evidence from well-designed cclinicaltrials, but rather on expert opinion, descriptive studies and clinical experience.

AUTHORS' CONCLUSIONS

Implications for practice

The results of this review neither support nor refute the current approach to the clinical management of intraamniotic infections.

Implications for research

Future research should be directed at recognizing the risk factors for the development of intraamniotic infection and clarifying what interventions and preventative strategies can be effective in reducing the incidence of infection. Although the trend was towards improved neonatal outcomes when antibiotics were administered intrapartum, adverse neonatal events associated with antibiotic administration were not specifically sought. Further trials should be designed to look at longer term outcomes, including the consequences of neonatal cerebral damage, provide a thorough understanding of the pharmcokinetic profile of the drugs administered intrapartum and evaluate more comprehensively the effectiveness of different regimens.

POTENTIAL CONFLICT OF INTEREST

None known.

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SOURCES OF SUPPORT

External sources of support

- No sources of support supplied

Internal sources of support

- No sources of support supplied

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TABLES

Characteristics of included studies

Study	**Gibbs 1988**
Methods	Randomized study. Study period: May 5, 1987 to November 8, 1987. Not intention to treat.
Participants	Inclusion criteria: maternal fever > 100 degrees F and ruptured membranes plus two or more of: maternal or fetal tachycardia, uterine tenderness, purulent or foul amniotic fluid or maternal leukocytosis. Exclusion criteria: < 34 weeks gestation, cervix < 4 cm at the time of diagnosis.
Interventions	Group 1: Intrapartum treatment with ampicillin 2g iv q6h and gentamicin 1.5 mg/kg iv q8h. Group 2: Postpartum treatment with above regimen.
Outcomes	Neonatal sepsis (positive blood culture): Group 1: 0/26 vs Group 2: 4/19. Neonatal pneumonia: Group 1: 0/26 vs Group 2: 2/19. Neonatal Death: Group 1: 0/26 vs Group 2: 1/19. Maternal Bacteremia: Group 1: 3/26 vs Group 2: 1/19.
Notes	Power calculation for alpha error 0.05 required 46 in each arm; interim analysis forced closure of study.
Allocation concealment	A – Adequate

Study	**Maberry 1991**
Methods	Women admitted between December 1987 and January 1989 with intraamniotic infection were randomized to one of two arms.
Participants	Inclusion criteria: laboring patients, gestational age > 24 weeks, amniotic infection diagnosed based on maternal fever > 38 degrees C plus one of: fetal or maternal tachycardia, uterine tenderness, foul amniotic fluid. Exclusion criteria: penicillin allergy, on antibiotics at time of admission.
Interventions	Group 1: ampicillin/gentamicin/clindamycin. Group 2: ampicillin and gentamicin.
Outcomes	Endometritis (fever > 38 degrees C on two occasions: Group 1: 5/64 vs 10/69. Neonatal death: Group 1: 2/64 vs Group 2: 3/69. Neonatal sepsis: Group 1: 2/64 vs Group 2: 1/69. Respiratory Distress Syndrome: Group 1: 5/64 vs Group 2: 6/69. Intraventricular Hemorrhage: Group 1: 0/64 vs Group 2: 2/69.
Notes	No cases of wound infection, pelvic abscesses, septic pelvic vein thrombophlebitis, or necrotizing enterocolitis. No stratification for gestational age. Average stay in hospital 4 days for both groups.
Allocation concealment	A – Adequate

g = gram
iv = intravenous
mg/kg = milligram per kilogram

q6h = every 6 hours
q8h = every 8 hours
vs = versus

Characteristics of excluded studies

Study	Reason for exclusion
Berry 1992	No criteria are listed to define the diagnosis of intraamniotic infection.
Creatsas 1980	This was a randomized trial examining the concentration of ampicillin and gentamicin in maternal serum, amniotic fluid and cord serum.
Gibbs 1980	A retrospective chart review. All patients were managed with the same antibiotic regimen.
Gillstrap 1988	This was a retrospective chart review, not a randomized trial. Also, the diagnosis of intraamniotic infection was based only on the presence of fever > 38 degrees C in labor.
Hauth 1985	This is a retrospective chart review. It contains no information on antibiotic regimens utilized.
Koh 1979	This is a retrospective study. There is no information on antibiotic drug regimens utilized.
Krohn 1998	This is a retrospective case control study. The study was examining demographic and lifestyle characteristics in women diagnosed with intraamniotic infection.
McCredie-Smith 1956	This is a quasi-randomized trial. The criteria for intraamniotic infection included fetal tachycardia alone, which probably led to women being included who were not infected. This would make detection of a difference with treatment difficult. Further, the antibiotics used in this trial can cause maternal and neonatal toxicity and are not utilized by obstetricians today.
Mitra 1997	This study does not compare two different antibiotic regimens for the management of intraamniotic infection. Women were treated postpartum with the same drug regimen (gentamicin and clindamycin) but with either once daily or three times daily gentamicin.
Scalambrino 1989	The authors do not define the parameters upon which the diagnosis of intraamniotic infection is based. In fact, they refer only to the presence of fever > 38 as their inclusion criteria and list 'cure' as their main outcome, defined as defervescence and disappearance of all signs and symptoms of infection.
Sperling 1987	This is a prospective cohort study, not a randomized trial. Also, the criteria to diagnose intraamniotic infection included only a maternal fever > 100 F.
Stovall 1988	This is retrospective case control study examining whether or not a short course of parenteral antibiotics without the addition of an oral agent is comparable to then-standard extended parenteral treatment regimens.

ANALYSES

Comparison 01. Intrapartum versus postpartum ampicillin and gentamicin for intraamniotic infection

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Neonatal sepsis	1	45	Relative Risk (Fixed) 95% CI	0.08 [0.00, 1.44]
02 Neonatal pneumonia	1	45	Relative Risk (Fixed) 95% CI	0.15 [0.01, 2.92]
03 Neonatal death	1	45	Relative Risk (Fixed) 95% CI	0.25 [0.01, 5.75]
04 Maternal bacteremia	1	45	Relative Risk (Fixed) 95% CI	2.19 [0.25, 19.48]

Comparison 02. Intrapartum ampicillin, gentamicin and clindamycin vs ampicillin and gentamicin for intraamniotic infection

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Neonatal sepsis	1	133	Relative Risk (Fixed) 95% CI	2.16 [0.20, 23.21]
02 Neonatal death	1	133	Relative Risk (Fixed) 95% CI	0.72 [0.12, 4.16]
03 Respiratory distress syndrome	1	133	Relative Risk (Fixed) 95% CI	0.90 [0.29, 2.80]
04 Postpartum endometritis	1	133	Relative Risk (Fixed) 95% CI	0.54 [0.19, 1.49]

INDEX TERMS

Medical Subject Headings (MeSH)

*Amnion; Anti-Bacterial Agents [*therapeutic use]; Bacterial Infections [*drug therapy]; Placenta Diseases [*drug therapy]; Randomized Controlled Trials

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

Title	Antibiotic regimens for management of intraamniotic infection
Authors	Hopkins L, Smaill F
Contribution of author(s)	Laura Hopkins was responsible for designing the protocol, assessing eligibility of studies, data abstraction and writing the first draft of the review. Fiona Smaill assisted with assessing eligibility of studies, data abstraction, writing the first draft of the review and revising it in response to the editorial feedback. The published version has not been approved by Laura Hopkins.
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Date new studies found and included/excluded	Information not supplied by author
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GRAPHS AND OTHER TABLES

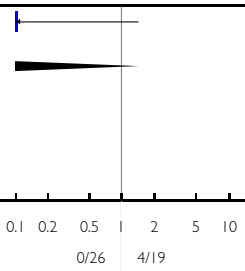
Analysis 01.01. Comparison 01 Intrapartum versus postpartum ampicillin and gentamicin for intraamniotic infection, Outcome 01 Neonatal sepsis

Review: Antibiotic regimens for management of intraamniotic infection

Comparison: 01 Intrapartum versus postpartum ampicillin and gentamicin for intraamniotic infection

Outcome: 01 Neonatal sepsis

Study	Intrapartum n/N	Postpartum n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Gibbs 1988	0/26	4/19		100.0	0.08 [0.00, 1.44]
Total (95% CI)	26	19		100.0	0.08 [0.00, 1.44]
Total events: 0 (Intrapartum), 4 (Postpartum)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.71 p=0.09					



Analysis 01.02. Comparison 01 Intrapartum versus postpartum ampicillin and gentamicin for intraamniotic infection, Outcome 02 Neonatal pneumonia

Review: Antibiotic regimens for management of intraamniotic infection

Comparison: 01 Intrapartum versus postpartum ampicillin and gentamicin for intraamniotic infection

Outcome: 02 Neonatal pneumonia

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Gibbs 1988	0/26	2/19		100.0	0.15 [0.01, 2.92]
Total (95% CI)	26	19		100.0	0.15 [0.01, 2.92]
Total events: 0 (Treatment), 2 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.26 p=0.2					

Analysis 01.03. Comparison 01 Intrapartum versus postpartum ampicillin and gentamicin for intraamniotic infection, Outcome 03 Neonatal death

Review: Antibiotic regimens for management of intraamniotic infection

Comparison: 01 Intrapartum versus postpartum ampicillin and gentamicin for intraamniotic infection

Outcome: 03 Neonatal death

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Gibbs 1988	0/26	1/19		100.0	0.25 [0.01, 5.75]
Total (95% CI)	26	19		100.0	0.25 [0.01, 5.75]
Total events: 0 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.87 p=0.4					

Analysis 01.04. Comparison 01 Intrapartum versus postpartum ampicillin and gentamicin for intraamniotic infection, Outcome 04 Maternal bacteremia

Review: Antibiotic regimens for management of intraamniotic infection

Comparison: 01 Intrapartum versus postpartum ampicillin and gentamicin for intraamniotic infection

Outcome: 04 Maternal bacteremia

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Gibbs 1988	3/26	1/19		100.0	2.19 [0.25, 19.48]
Total (95% CI)	26	19		100.0	2.19 [0.25, 19.48]
Total events: 3 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.70 p=0.5					

Analysis 02.01. Comparison 02 Intrapartum ampicillin, gentamicin and clindamycin vs ampicillin and gentamicin for intraamniotic infection, Outcome 01 Neonatal sepsis

Review: Antibiotic regimens for management of intraamniotic infection

Comparison: 02 Intrapartum ampicillin, gentamicin and clindamycin vs ampicillin and gentamicin for intraamniotic infection

Outcome: 01 Neonatal sepsis

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Maberry 1991	2/64	1/69		100.0	2.16 [0.20, 23.21]
Total (95% CI)	64	69		100.0	2.16 [0.20, 23.21]
Total events: 2 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.63 p=0.5					

Analysis 02.02. Comparison 02 Intrapartum ampicillin, gentamicin and clindamycin vs ampicillin and gentamicin for intraamniotic infection, Outcome 02 Neonatal death

Review: Antibiotic regimens for management of intraamniotic infection

Comparison: 02 Intrapartum ampicillin, gentamicin and clindamycin vs ampicillin and gentamicin for intraamniotic infection

Outcome: 02 Neonatal death

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Maberry 1991	2/64	3/69		100.0	0.72 [0.12, 4.16]
Total (95% CI)	64	69		100.0	0.72 [0.12, 4.16]
Total events: 2 (Treatment), 3 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.37 p=0.7					

Analysis 02.03. Comparison 02 Intrapartum ampicillin, gentamicin and clindamycin vs ampicillin and gentamicin for intraamniotic infection, Outcome 03 Respiratory distress syndrome

Review: Antibiotic regimens for management of intraamniotic infection

Comparison: 02 Intrapartum ampicillin, gentamicin and clindamycin vs ampicillin and gentamicin for intraamniotic infection

Outcome: 03 Respiratory distress syndrome

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Maberry 1991	5/64	6/69		100.0	0.90 [0.29, 2.80]
Total (95% CI)	64	69		100.0	0.90 [0.29, 2.80]
Total events: 5 (Treatment), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.18 p=0.9					

Analysis 02.04. Comparison 02 Intrapartum ampicillin, gentamicin and clindamycin vs ampicillin and gentamicin for intraamniotic infection, Outcome 04 Postpartum endometritis

Review: Antibiotic regimens for management of intraamniotic infection

Comparison: 02 Intrapartum ampicillin, gentamicin and clindamycin vs ampicillin and gentamicin for intraamniotic infection

Outcome: 04 Postpartum endometritis

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Maberry 1991	5/64	10/69		100.0	0.54 [0.19, 1.49]
Total (95% CI)	64	69		100.0	0.54 [0.19, 1.49]
Total events: 5 (Treatment), 10 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.19 p=0.2					