Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV) (Review)

Lumbiganon P, Thinkhamrop J, Thinkhamrop B, Tolosa JE

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ABSTRACT

Background
The incidence of chlorioamnionitis occurs in between 8 to 12 women for every 1000 live births and 96% of the cases of chlorioamnionitis are due to ascending infection. Following spontaneous vaginal delivery, 1% to 4% of women develop postpartum endometritis. The incidence of neonatal sepsis is 0.5% to 1% of all infants born. Maternal vaginal bacteria are the main agents for these infections. It is reasonable to speculate that prevention of maternal and neonatal infections might be possible by washing the vagina and cervix with an antibacterial agent for all women during labour. Chlorhexidine belongs to the class of compounds known as the bis-biguanides. Chlorhexidine has antibacterial action against a wide range of aerobic and anaerobic bacteria, including those implicated in peripartal infections.

Objectives
To evaluate the effectiveness and side-effects of chlorhexidine vaginal douching during labour in reducing maternal and neonatal infections (excluding Group B Streptococcal and HIV).

Search strategy
We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (April 2006), the Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2006, Issue 3), MEDLINE (from 1966 to 2006) and LILACS (from 1982 to 2006).

Selection criteria
Randomized or quasi-randomized trials comparing chlorhexidine vaginal douching during labour with placebo or other vaginal disinfectant to prevent (reduce) maternal and neonatal infections (excluding Group B Streptococcal and HIV).

Data collection and analysis
Two reviewers independently assessed trial eligibility and quality, extracted and entered the data into the RevMan software and interpreted the data. A third reviewer analysed and interpreted the data. The fourth reviewer also interpreted the data.

Main results
Three studies (3012 participants) were included. There was no evidence of an effect of vaginal chlorhexidine during labour in preventing maternal and neonatal infections. Although the data suggest a trend in reducing postpartum endometritis, the difference was not statistically significant (relative risk 0.83; 95% confidence interval 0.61 to 1.13).

Authors' conclusions
There is no evidence to support the use of vaginal chlorhexidine during labour in preventing maternal and neonatal infections. There is a need for a well-designed randomized controlled trial using appropriate concentration and volume of vaginal chlorhexidine irrigation solution and with adequate sample size.

PLAIN LANGUAGE SUMMARY

No evidence to support the use of 'chlorhexidine' washing of the vagina during labour for preventing maternal and neonatal infections

Bacteria live in women's vaginas and generally cause no problems. Very occasionally they infect the placenta during labour and can pass to the baby causing an infection. These infections can occasionally make the baby very ill and very occasionally the baby might die. The review of trials found there was not enough information to say whether chlorhexidine wash of the vagina during labour led to fewer infections for mothers and babies. More research is needed.

BACKGROUND

Chlorioamnionitis is an inflammatory reaction of the placental tissues in response to organism invasion. The incidence of chlorioamnionitis occurs in 8 to 12 women for every 1000 live births and 96% of the cases of chlorioamnionitis are due to ascending infection (Monif 1993). Following spontaneous vaginal delivery, 1% to 4% of women develop postpartum endometritis (Monif 1993). Although uterine infections are relatively uncommon following uncomplicated vaginal delivery, they continue to be a major problem in women delivered by caesarean section. Vaginal examinations increase the risk of inoculation and colonization of lower uterine incisions and laceration and therefore increase the risk of postpartum endometritis in patients delivered by caesarean section (Cunningham 2001).

Bacterial infection is an important cause of neonatal morbidity and mortality. A prospective study from Pakistan reported a prevalence of blood culture proven bacterial sepsis to be 5.6 per 1000 live births (Bhutta 1997). Septicemia accounted for 11.0% to 30.4% of all neonatal deaths (Boo 1994). Other forms of infection include ophthalmia neonatorum; neonatal pneumonia and neonatal meningitis. Maternal vaginal bacteria are the main agents for these infections.

It is reasonable to speculate that prevention of maternal and neonatal infections might be possible by washing the vagina and cervix with an antibacterial agent in women during labour. Vaginal and cervical washing is usually performed by gently introducing a catheter attached to a 50 to 60 ml syringe up to the cervix. The cervical area is flushed with 50 to 60 ml of the solution. The syringe is then refilled without removing the catheter, and a second flushing with the same amount of the solution is performed while slowly withdrawing the catheter (Gaillard 2001). This procedure can be performed within a few minutes and would not interfere with women's labour when they wish to move and adopt a position which they feel is right for them. To be clinically useful, such an agent would need to possess antimicrobial activity against a broad range of bacteria that have been implicated in peripartal infection, be non-toxic and non-irritating for mother and fetus/neonate. Ideally the agent would be inexpensive and commercially available. Chlorhexidine, a widely used medical disinfectant, satisfies these requirements.

Chlorhexidine belongs to the class of compounds known as the bis-biguanides. Because of its high cationic nature, it has a strong affinity for the cell wall of microorganisms, to which it binds, disrupting osmotic equilibrium. The disrupted cytoplasmic membrane precipitates intracellularly, preventing repair of the cell wall and eventually resulting in cell death (Davies 1973). These actions endow chlorhexidine with antibacterial action against a wide range of aerobic and anaerobic bacteria, including those implicated in peripartal infections (Emilson 1977; Hennessey 1973). This antibacterial action is achieved at very low concentration: typical minimum inhibitory concentrations are in microgram/millilitre, whereas clinically used concentrations are in milligram/millilitre. A randomized controlled trial has demonstrated that vaginal douching with chlorhexidine during labour can significantly reduce maternal and early neonatal including group B streptococcal infection (Stray-Pedersen 1999). Finally, complete resistance to chlorhexidine rarely emerges even after long-term use (Ferretti 1990).

The allergic and toxic potential of chlorhexidine is very low. For many decades, chlorhexidine has been the major medical skin and the mucous membrane disinfectant in use. Despite its widespread use, only individual cases of anaphylactic or even mild allergic reactions in exposed medical personnel have been reported (Bergqvist 1988). Chlorhexidine tends not to be absorbed by human skin and mucous membrane barrier (Johnsson 1987; Nilsson 1989). A long-term human oral safety trial has not shown any systemic or serious local side-effects after two years of continuous use (Johnsson 1987). In contrast to povidone-iodine, vaginally applied chlorhexidine was not absorbed in measurable amounts into the blood stream (Vorherr 1984).

Maternal and neonatal infections occur commonly and have serious ramifications for both mothers and newborns. Vaginal chlorhexidine douching may offer a safe, inexpensive, and theoretically sound approach to prevent maternal and neonatal infections. Vaginal disinfection during labour for reducing the risk of mother-to-child transmission (MTCT) of HIV infection is addressed in one Cochrane review which indicates that there was no evidence of an effect of vaginal disinfection on MTCT of HIV (Shey Wiysonge 2002). Another Cochrane protocol is evaluating vaginal chlorhexidine during labour to prevent neonatal group B streptococcal infection (Stade 2002).

OBJECTIVES

To evaluate the effectiveness and side-effects of chlorhexidine vaginal douching during labour in reducing maternal and neonatal infections (excluding Group B streptococcal and HIV).

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Randomized or quasi randomized trials comparing chlorhexidine vaginal douching during labour with placebo or other vaginal disinfectant to prevent (reduce) maternal and neonatal infections (excluding Group B Streptococcal and HIV).

Types of participants

All pregnant women with gestational age of greater than 28 weeks, considered to be in labour.

Types of intervention

Chlorhexidine vaginal douching during labour.

Types of outcome measures

1. ***Maternal outcomes***
(a) chorioamnionitis (variously defined by the authors);
(b) intrapartum fever;
(c) intrapartum treatment with antibiotics;
(d) postpartum endometritis (variously defined by the authors);
(e) maternal side-effects (vaginal irritation, thrush, antimicrobial resistance);
(f) serious maternal complication of treatment (e.g. anaphylaxis);
(g) laparotomy for infection;
(h) hysterectomy;
(i) maternal death;
(j) satisfaction with care;
(k) length of hospital stay;
(l) postnatal depression;
(m) successful breastfeeding (variously defined by the authors);
(n) costs of care;
(o) antimicrobial resistance.

2. ***Neonatal outcomes***
(a) ophthalmia neonatorum;
(b) neonatal pneumonia by clinical assessment and/or chest X-ray;
(c) neonatal meningitis by clinical assessment and/or culture;
(d) blood culture confirming sepsis;
(e) neonatal sepsis (variously defined by the authors);
(f) admission to neonatal intensive care unit;
(g) length of hospital stay;
(h) perinatal mortality;
(i) abnormal neurodevelopmental assessment at follow up.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (April 2006).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:
(1) quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
(2) monthly searches of MEDLINE;
(3) handsearches of 30 journals and the proceedings of major conferences;
(4) weekly current awareness search of a further 37 journals.

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

Trials identified through the searching activities described above are given a code (or codes) depending on the topic. The codes are linked to review topics. The Trials Search Co-ordinator searches the register for each review using these codes rather than keywords.

In addition, we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2006, Issue 3), MEDLINE (from 1966 to 2006) and LILACS (from 1982 to 2006) using the following keywords and free text terms: "chlorhexidine" or "vaginal-creams-foams-and-jellies" or "vaginal gel" or "vaginal wash" or "vaginal disinfection" and "peripartum" or "maternal" or "neonatal" or "labour" or "labor" or "infant-newborn".

We searched cited references from retrieved articles for additional studies. We reviewed abstracts and letters to the editor to identify randomized controlled trials that had not been published and reviewed editorials, indicating expert opinion, to identify and ensure that no key studies were missed for consideration for inclusion in this review.

We did not apply any language restrictions.

METHODS OF THE REVIEW

Four reviewers prepared the review; three are content experts. One reviewer (P Lumbiganon (PL)) conducted the literature search with assistance from the Cochrane Pregnancy and Childbirth Group. Two reviewers (PL and J Thinkhamrop (JT)) screened

the studies identified by the search strategy described earlier, discarding the studies that were clearly ineligible but aiming to be overly inclusive rather than risk losing relevant studies. Quality assessment was based on the method of assigning participants to interventions (Higgins 2005) as follows:

- Category A - adequate allocation concealment (such as centralized or pharmacy-controlled randomization; pre-numbered or coded identical containers administered serially to participants; on-site computer system combined with allocations kept in a locked unreadable computer file that can be accessed only after the characteristics of an enrolled participant had been entered; sequentially numbered, sealed, opaque envelopes);
- Category B - uncertainty about whether the allocation was adequately concealed (for example, merely stating that a list or table was used, that sealed envelopes were used, or that the participants were randomly assigned); and
- Category C - inadequate allocation concealment: if the approach used was alternation; use of case record numbers, dates of birth, day of the week, open list of random numbers, etc.

After quality assessment, the two reviewers (PL and JT) extracted the data. We designed forms for data extraction and for requesting additional information from the investigators. In the data abstraction form, we have the review title, study reference and publication status, date of extraction, and reviewers' initials. We extracted data using the following subheadings in the form: methods (method of randomization and allocation concealment, blinding of those receiving and providing care and outcome assessors, losses to follow up and how they were handled), participants (setting, number of women randomized), interventions (disinfectant, dose, type of control group, co-interventions), outcomes, and (other) notes.

PL and JT resolved disagreements on the eligibility or quality of a trial or data extracted by discussion. J Tolosa (JET) was consulted on issues arising during the review process. We wrote to the first author of the main trial report for additional information, verification and/or updating of data extracted from the publication.

The third reviewer (B Thinkhamrop (BT)), who is a biostatistician, performed the statistical analyses. We used the relative risk and 95% confidence intervals for dichotomous data. We used a chi squared test (Q test) to test for heterogeneity, and applied a random effects or fixed effect model accordingly.

PL drafted the review which was critically reviewed by the other three reviewers.

DESCRIPTION OF STUDIES

Included studies

Three studies were included in this review.

Eriksen 1997 reported the effectiveness of chlorhexidine vaginal wash during labour to prevent neonatal infection. The data on peripartum infections of this study were reported in the other paper (Sweeten 1997). As they are both reports of the same trial we listed them under Eriksen 1997. Participants at 36 or more weeks gestation in labour, excluding preterm labour, fetal distress, malpresentation, intra-amniotic infection, cervical dilatation greater than 6 cm and known allergy to chlorhexidine were eligible for the study. Informed consent was obtained from 1024 women who were eligible. Of these, 77 were excluded from the analysis because of incomplete records (71, 38 in the control and 33 in the study group); participants were enrolled and subsequently discharged home (3); the vaginal wash was not given (2); and there was one infant with anencephaly. Of the remaining 947 participants, 481 were randomized to the study arm and 466 served as controls. A computer software program was used to generate a random block allocation sequence to assign participants to either group. The randomization assignments were contained in sequentially numbered, opaque, sealed packets that were made up independent of the physicians managing the participants. The authors chose not to blind the study because the syringe containing chlorhexidine solution was pink and the investigators could not reproduce the colour artificially in the syringe containing the sterile water. For maternal outcomes, it is not very clear whether the intention to treat analysis was performed because it was not stated that 77 women were excluded before or after randomization. For neonatal outcomes, intention to treat analysis was not done because 24 neonatal charts in the chlorhexidine group and 13 in the control group were unavailable for review.

Rouse 1997, from USA, reported a double-blinded clinical trial to determine whether chlorhexidine vaginal irrigation prevents maternal peripartal infection. Participants were eligible if they were admitted for delivery at or beyond 24 weeks' gestation. Exclusion criteria included a contra-indication for cervical digital examination, active genital herpes, chlorioamnionitis and known or suspected allergy to chlorhexidine. The chlorhexidine and placebo bottles were randomly ordered with a computer-generated list and sequentially numbered with a peel-off study label. The active and placebo solutions were clinically indistinguishable. Among 3234 eligible participants, 1024 were randomized, 508 in chlorhexidine and 516 in placebo groups respectively. Because of incomplete or contradictory data, treatment allocation could not be determined for additional 10 women and these women were not included in the analysis. Trial analysis was restricted to 1024 women and 1030 infants (six sets of twins).

Rouse 2003 reported a clinical trial of chlorhexidine vaginal irrigation to prevent peripartal infection in nulliparas. The study was conducted in two hospitals serving predominantly publicly funded patients. Patients were eligible if they were nulliparous and admitted for delivery at or beyond 32 weeks' gestation. Exclusion cri-

teria included a contra-indication to digital cervical examination, active genital herpes, chlorioamnionitis and allergy to chlorhexidine. The chlorhexidine and placebo bottles were sequentially numbered (in groups of four) and randomly ordered based on a computer-generated list (one for each hospital). Each study bottle contained a peel-off label which, after use, was used to link participants to the correct study group. The chlorhexidine and placebo preparations were clinically indistinguishable. Four women (two women in each group) were enrolled but actually did not undergo irrigation. They are included in the intention to treat analysis.

Excluded studies
See the 'Characteristics of excluded studies' table.

METHODOLOGICAL QUALITY

Details for each trial are in the 'Characteristics of included studies' table.

All trials have adequate random allocation concealment.

RESULTS

Three studies involving 3012 women were included in this review.

Maternal outcomes
Three trials reported the incidence of chlorioamnionitis, including 1514 and 1498 participants in the chlorhexidine and placebo groups respectively. There was no statistically significant difference between the two groups (relative risk (RR) 1.10; 95% confidence interval (CI) 0.86 to 1.42). The same three trials also reported the incidence of postpartum endometritis. Although the data suggest a small reduction in the risk of postpartum endometritis with the use of the chlorhexidine vaginal wash, the difference was not statistically significant (RR 0.83; 95% CI 0.61 to 1.13). There was no report about the other maternal outcomes and side-effects of chlorhexidine in these three trials.

Neonatal outcomes
Three trials reported on neonatal outcomes, involving 1495 and 1492 neonates in the chlorhexidine and placebo groups respectively. One trial with 457 and 453 neonates in the intervention and control group respectively (Eriksen 1997) indicated that there was no significant difference in neonatal pneumonia (RR 0.33; 95% CI 0.01 to 8.09). For neonatal meningitis, one trial with 508 and 513 neonates in the intervention and control group (Rouse 1997) did not show significant difference (RR 0.34; 95% CI 0.01 to 8.29). Two trials involving 1038 and 1039 neonates in the intervention and control groups respectively (Rouse 1997; Rouse 2003) did not find significant difference in blood culture confirming sepsis (RR 0.75; 95% CI 0.17 to 3.35) and perinatal mortality (RR 1.00, 95% CI 0.17 to 5.79). For neonatal sepsis which was evaluated in three trials involving 1495 and 1492 neonates in the chlorhexidine and placebo groups respectively also did not find significant difference (RR 0.75; 95% CI 0.17 to 3.35) There was a trend that vaginal chlorhexidine during labour might lead to a higher tendency for newborns to receive antibiotics but this association is not statistically significant (RR 1.65; 95% CI 0.73 to 3.74). There was no report about the other neonatal outcomes and side-effects of chlorhexidine in these three trials.

DISCUSSION

There was no evidence of an effect of vaginal chlorhexidine during labour in preventing maternal and neonatal infections. Although all the three included trials are of high quality, one trial (Eriksen 1997) used only 20 ml of chlorhexidine or sterile water for vaginal irrigation while the other two trials (Rouse 1997; Rouse 2003) used 200 ml of chlorhexidine or sterile saline solution. The effectiveness of vaginal chlorhexidine might also depend on the volume of the solution used for irrigation. Since chlorhexidine solution is quite safe, not expensive and vaginal irrigation is not difficult to perform, there is a need for a well-designed randomized controlled trial with adequate sample size to evaluate this simple intervention. However, the investigators of future trials must use the appropriate concentration and volume of vaginal chlorhexidine irrigation solution. We have identified two ongoing studies identified from the trial registration website (Madhi 2006;Moss 2006) since the review was first published.

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence to support the use of vaginal chlorhexidine douching during labour in preventing maternal and neonatal infections.

Implications for research

There is a need for a well-designed randomized controlled trial with appropriate concentration and volume of irrigation solution and adequate sample size.

POTENTIAL CONFLICT OF INTEREST

None known.

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* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	**Eriksen 1997**
Methods	Randomized controlled trial, unblinded.
Participants	1024 term pregnant women presenting to labour and delivery. Included: 947 women (481 in chlorhexidine group (intervention) and 466 in sterile water group (control). Excluded after randomization: 77 women (71 incomplete records, 3 discharged home, 2 vaginal wash was not given, 1 anencephalic).
Interventions	Vaginal wash with 20 ml of 0.4% chlorhexidine solution versus sterile water.
Outcomes	Neonatal infection (pneumonia or sepsis) and use of antibiotics in neonates.

	Peripartal infection (intra-amniotic infection and endometritis).
Notes	The report by Eriksen 1997 provided details of the neonatal outcomes. The report by Sweeten 1997 provided details of the maternal outcomes.
Allocation concealment	A – Adequate

Study	**Rouse 1997**
Methods	Double blinded, placebo controlled randomized clinical trial.
Participants	1024 patients (508 in the chlorhexidine group and 516 in the placebo group).
Interventions	Vaginal irrigation with 200 ml of 0.2% chlorhexidine or sterile water placebo.
Outcomes	Peripartal infection (chorioamnionitis and endometritis (mutually exclusive) diagnosed) and neonatal infections.
Notes	
Allocation concealment	A – Adequate

Study	**Rouse 2003**
Methods	Double blinded, placebo controlled randomized trial.
Participants	1041 patients (525 in the chlorhexidine group and 516 in the placebo group).
Interventions	Vaginal irrigation with 200 ml of 0.2% chlorhexidine solution or sterile water every 6 hours during labour.
Outcomes	Peripartal infection (chorioamnionitis and endometritis), neonatal sepsis and perinatal death.
Notes	
Allocation concealment	A – Adequate

Characteristics of excluded studies

Study	**Reason for exclusion**
Calkin 1996	The intervention in this study was vulvar swabbing, not vaginal douching or washing during labour.
Henrichsen 1994	Participants in the control group received chlorhexidine gel during vaginal exploration. Inadequate allocation concealment - randomization was performed by changing the regimen on a weekly basis, every Monday morning at 0800.

Characteristics of ongoing studies

Study	**Madhi 2006**
Trial name or title	Preventing serious neonatal and maternal peripartum infections in developing country settings with a high prevalence of HIV infection: assessment of the disease burden and evaluation of an affordable intervention in Soweto, South Africa
Participants	Healthy female volunteers aged 15 years and above. Expected enrollment: 8000.
Interventions	0.5% chlorhexidine wipes of the birth canal during labour and of the infant at birth compared with external genitalia sterile water wipes.
Outcomes	Primary outcomes: rates of culture-confirmed or clinical neonatal sepsis, < 3 days of life; rate of vertical transmission of colonization with group B streptococcus (GBS).

Characteristics of ongoing studies (*Continued*)

	Secondary outcomes: rates of culture -confirmed or clinical neonatal sepsis (non-nosocomial), 3 to 28 days of life; rates of serious maternal per partum infections including: endometritis, culture-confirmed post-partum sepsis, and post-partum perineal wound infection; rates of neonatal hospitalization, < 3 days of life; rates of neonatal hospitalization, < 28 days of life; rates of neonatal hospitalization, suspected sepsis; rate of vertical transmission of colonization with E. coli or Klebsiella species.
Starting date	April 2004
Contact information	Clare Cutland: +27 11 9899894; cutlandc@hivsa.com Shabir Madhi: +27 11 9899894; madhis@hivsa.com
Notes	Expected completion date: May 2008. ClinicalTrials.gov identifier NCT00136370

Study	**Moss 2006**
Trial name or title	Randomized pilot trial of chlorhexidine vaginal and infant wash to reduce neonatal mortality
Participants	Healthy female volunteers aged 16 years and above. Expected total enrollment: 1000. Setting: civil hospital in Karachi, Pakistan.
Interventions	0.6% chlorhexidine solution every four hours until delivery (4 washes maximum) and one neonatal wash with the same solution compared with 200 ml of sterile physiologic saline solution.
Outcomes	Primary outcomes: neonatal death or severe sepsis at 7 days Secondary outcomes: maternal: clinical chorioamnionitis, clinical endometritis, urinary tract infection, sepsis, length of hospitalization, readmission to hospital, death; neonatals: receipt of antibiotics, duration of hospitalization, readmission to hospital
Starting date	June 2005
Contact information	Nancy Moss: mossn@mail.nih.gov
Notes	Expected completion date: June 2006. ClinicalTrials.gov identifier NCT00121394

ANALYSES

Comparison 01. Chlorhexidine vaginal wash versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Chorioamnionitis	3	3012	Relative Risk (Fixed) 95% CI	1.10 [0.86, 1.42]
02 Postpartum endometritis	3	3012	Relative Risk (Fixed) 95% CI	0.83 [0.61, 1.13]
03 Side-effects	2	2065	Relative Risk (Fixed) 95% CI	Not estimable
04 Neonatal pneumonia	1	910	Relative Risk (Fixed) 95% CI	0.33 [0.01, 8.09]
05 Neonatal meningitis	1	1024	Relative Risk (Fixed) 95% CI	0.34 [0.01, 8.29]
06 Blood culture confirming neonatal sepsis	2	2077	Relative Risk (Fixed) 95% CI	0.75 [0.17, 3.35]
07 Neonatal sepsis	3	2987	Relative Risk (Fixed) 95% CI	0.75 [0.17, 3.35]
08 Perinatal mortality	2	2071	Relative Risk (Fixed) 95% CI	1.00 [0.17, 5.79]
09 Newborn received antibiotics	1	910	Relative Risk (Fixed) 95% CI	1.65 [0.73, 3.74]

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Infective Agents, Local [*administration & dosage]; Bacterial Infections [*prevention & control]; Chlorhexidine [*administration & dosage]; Chorioamnionitis [prevention & control]; Endometritis [prevention & control]; Infant, Newborn; Labor, Obstetric; Randomized Controlled Trials; Vaginal Douching [*methods]

MeSH check words

Adult; Female; Humans; Pregnancy

COVER SHEET

Title	Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV)
Authors	Lumbiganon P, Thinkhamrop J, Thinkhamrop B, Tolosa JE
Contribution of author(s)	Pisake Lumbiganon (PL) wrote the protocol. Jadsada Thinkhamrop (JT), Bandit Thinkhamrop (BT) and Jorge Tolosa (JET) commented on the early drafts and approved the published version. PL and JT conducted the review. BT assisted in the data analysis. PL drafted the review. JT, BT and JET gave significant intellectual comments on the review and approved the final version.
Issue protocol first published	2003/1
Review first published	2004/4
Date of most recent amendment	08 November 2006
Date of most recent SUBSTANTIVE amendment	01 July 2004
What's New	April 2006 We have identified two ongoing studies from the trial registration website (Madhi 2006; Moss 2006) and another report for Rouse 2003. There are no additional relevant data available yet.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	27 April 2006
Date authors' conclusions section amended	Information not supplied by author
Contact address	Prof Pisake Lumbiganon Professor Department of Obstetrics and Gynaecology Faculty of Medicine Khon Kaen University Khon Kaen 40002 THAILAND E-mail: pisake@kku.ac.th Tel: +66 43 8719030 Fax: +66 43 348395
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GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Chlorhexidine vaginal wash versus placebo, Outcome 01 Chorioamnionitis

Review: Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV)

Comparison: 01 Chlorhexidine vaginal wash versus placebo

Outcome: 01 Chorioamnionitis

Study	Chlorhexidine wash n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Eriksen 1997	25/481	21/466		20.6	1.15 [0.65, 2.03]
Rouse 1997	27/508	32/516		30.7	0.86 [0.52, 1.41]
Rouse 2003	63/525	50/516		48.7	1.24 [0.87, 1.76]
Total (95% CI)	1514	1498		100.0	1.10 [0.86, 1.42]
Total events: 115 (Chlorhexidine wash), 103 (Placebo)					
Test for heterogeneity chi-square=1.43 df=2 p=0.49 I^2 =0.0%					
Test for overall effect z=0.76 p=0.4					

Analysis 01.02. Comparison 01 Chlorhexidine vaginal wash versus placebo, Outcome 02 Postpartum endometritis

Review: Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV)

Comparison: 01 Chlorhexidine vaginal wash versus placebo

Outcome: 02 Postpartum endometritis

Study	Chlorhexidine wash n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Eriksen 1997	9/481	9/466		10.7	0.97 [0.39, 2.42]
Rouse 1997	24/508	37/516		43.1	0.66 [0.40, 1.09]
Rouse 2003	38/525	39/516		46.2	0.96 [0.62, 1.47]
Total (95% CI)	1514	1498		100.0	0.83 [0.61, 1.13]
Total events: 71 (Chlorhexidine wash), 85 (Placebo)					
Test for heterogeneity chi-square=1.36 df=2 p=0.51 I^2 =0.0%					
Test for overall effect z=1.19 p=0.2					

Analysis 01.03. Comparison 01 Chlorhexidine vaginal wash versus placebo, Outcome 03 Side-effects

Review: Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV)

Comparison: 01 Chlorhexidine vaginal wash versus placebo

Outcome: 03 Side-effects

Study	Chlorhexidine wash n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Rouse 1997	0/508	0/516		0.0	Not estimable
× Rouse 2003	0/525	0/516		0.0	Not estimable
Total (95% CI)	1033	1032		0.0	Not estimable
Total events: 0 (Chlorhexidine wash), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Analysis 01.04. Comparison 01 Chlorhexidine vaginal wash versus placebo, Outcome 04 Neonatal pneumonia

Review: Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV)

Comparison: 01 Chlorhexidine vaginal wash versus placebo

Outcome: 04 Neonatal pneumonia

Study	Chlorhexidine wash n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Eriksen 1997	0/457	1/453		100.0	0.33 [0.01, 8.09]
Total (95% CI)	457	453		100.0	0.33 [0.01, 8.09]
Total events: 0 (Chlorhexidine wash), 1 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.68 p=0.5					

Analysis 01.05. Comparison 01 Chlorhexidine vaginal wash versus placebo, Outcome 05 Neonatal meningitis

Review: Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV)

Comparison: 01 Chlorhexidine vaginal wash versus placebo

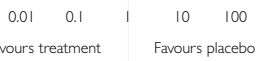
Outcome: 05 Neonatal meningitis

Study	Chlorhexidine wash n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Rouse 1997	0/508	1/516		100.0	0.34 [0.01, 8.29]
Total (95% CI)	508	516		100.0	0.34 [0.01, 8.29]

Total events: 0 (Chlorhexidine wash), 1 (Placebo)

Test for heterogeneity: not applicable

Test for overall effect z=0.66 p=0.5



Analysis 01.06. Comparison 01 Chlorhexidine vaginal wash versus placebo, Outcome 06 Blood culture confirming neonatal sepsis

Review: Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV)

Comparison: 01 Chlorhexidine vaginal wash versus placebo

Outcome: 06 Blood culture confirming neonatal sepsis

Study	Chlorhexidine wash n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Rouse 1997	2/512	2/518		49.7	1.01 [0.14, 7.15]
Rouse 2003	1/526	2/521		50.3	0.50 [0.05, 5.45]
Total (95% CI)	1038	1039		100.0	0.75 [0.17, 3.35]

Total events: 3 (Chlorhexidine wash), 4 (Placebo)

Test for heterogeneity chi-square=0.20 df=1 p=0.65 I^2 =0.0%

Test for overall effect z=0.37 p=0.7

Analysis 01.07. Comparison 01 Chlorhexidine vaginal wash versus placebo, Outcome 07 Neonatal sepsis

Review: Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV)

Comparison: 01 Chlorhexidine vaginal wash versus placebo

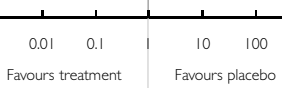
Outcome: 07 Neonatal sepsis

Study	Chlorhexidine wash n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Eriksen 1997	0/457	0/453		0.0	Not estimable
Rouse 1997	2/512	2/518		49.7	1.01 [0.14, 7.15]
Rouse 2003	1/526	2/521		50.3	0.50 [0.05, 5.45]
Total (95% CI)	1495	1492		100.0	0.75 [0.17, 3.35]

Total events: 3 (Chlorhexidine wash), 4 (Placebo)

Test for heterogeneity chi-square=0.20 df=1 p=0.65 I^2 =0.0%

Test for overall effect z=0.37 p=0.7



Analysis 01.08. Comparison 01 Chlorhexidine vaginal wash versus placebo, Outcome 08 Perinatal mortality

Review: Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV)

Comparison: 01 Chlorhexidine vaginal wash versus placebo

Outcome: 08 Perinatal mortality

Study	Chlorhexidine wash n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Rouse 1997	0/508	1/516		59.7	0.34 [0.01, 8.29]
Rouse 2003	2/526	1/521		40.3	1.98 [0.18, 21.78]
Total (95% CI)	1034	1037		100.0	1.00 [0.17, 5.79]

Total events: 2 (Chlorhexidine wash), 2 (Placebo)

Test for heterogeneity chi-square=0.75 df=1 p=0.39 I^2 =0.0%

Test for overall effect z=0.00 p=1

Analysis 01.09. Comparison 01 Chlorhexidine vaginal wash versus placebo, Outcome 09 Newborn received antibiotics

Review: Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV)

Comparison: 01 Chlorhexidine vaginal wash versus placebo

Outcome: 09 Newborn received antibiotics

Study	Chlorhexidine wash n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Eriksen 1997	15/457	9/453		100.0	1.65 [0.73, 3.74]
Total (95% CI)	457	453		100.0	1.65 [0.73, 3.74]

Total events: 15 (Chlorhexidine wash), 9 (Control)

Test for heterogeneity: not applicable

Test for overall effect z=1.21 p=0.2