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Maternal oxygen administration for fetal distress (Review)

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[Intervention Review]

Maternal oxygen administration for fetal distress

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ABSTRACT

Background

Maternal oxygen administration has been used in an attempt to lessen fetal distress by increasing the available oxygen from the mother. This has been used for suspected fetal distress during labour, and prophylactically during the second stage of labour on the assumption that the second stage is a time of high risk for fetal distress.

Objectives

The objective of this review was to assess the effects of maternal oxygenation for fetal distress during labour and to assess the effects of prophylactic oxygen therapy during the second stage of labour on perinatal outcome.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (22 October 2012) and searched reference lists of retrieved studies.

Selection criteria

Randomized trials comparing maternal oxygen administration for fetal distress during labour and prophylactic oxygen administration during the second stage of labour with a control group (dummy or no oxygen therapy).

Data collection and analysis

Both review authors assessed eligibility and trial quality. Data were extracted, checked and entered into Review Manager software. For dichotomous data, we calculated relative risks (RR) and 95% confidence intervals (CI). For continuous data, we calculated weighted mean differences and 95% CI.

Main results

We located no trials addressing maternal oxygen therapy for fetal distress. We included two trials which addressed prophylactic oxygen administration during labour. Abnormal cord blood pH values (less than 7.2) were recorded significantly more frequently in the oxygenation group than the control group (RR 3.51, 95% CI 1.34 to 9.19). There were no other statistically significant differences between the groups. There were conflicting conclusions on the effect of the duration of oxygen administration on umbilical artery pH values between the two trials.

Authors' conclusions***Implications for practice***

There is not enough evidence to support the use of prophylactic oxygen therapy for women in labour, nor to evaluate its effectiveness for fetal distress.

Implications for research

In view of the widespread use of oxygen administration during labour and the possibility that it may be ineffective or harmful, there is an urgent need for randomized trials to assess its effects.

PLAIN LANGUAGE SUMMARY**Maternal oxygen administration for fetal distress**

Too little evidence to show whether oxygen administration to the woman during labour is beneficial to the baby.

Some babies show signs of distress, such as unusual heart rates or the passing of a bowel motion (meconium) during their mother's labour. This may be caused by a lack of oxygen passing from the woman to the baby through the placenta. Sometimes, women may be encouraged to breathe extra oxygen through a facemask (oxygen administration) to increase the oxygen available to the unborn baby. A review of two trials found too little evidence to show whether oxygen administration to the woman during the second stage of labour is beneficial to the baby. No trials of oxygen administration when the baby is showing signs of distress were found. Further research is needed.

BACKGROUND

The diagnosis of suspected fetal distress during labour, usually on the basis of fetal heart rate parameters or fetal scalp blood pH measurement, is always considered an emergency. The importance attached to it derives from the perceived association of fetal hypoxia (low oxygen levels) with perinatal morbidity/mortality and long-term disability (Marlow 1999).

Physiological studies support the notion of a relationship between maternal oxygenation and fetal wellbeing. In a randomized cross-over study, fetal habituation to vibroacoustic stimulation was normal in 17 of 18 women with normal pregnancies at term, but in only two of the 18 when breathing a 12% oxygen in nitrogen mixture (Leader 1988). Thus, among other measures, maternal oxygen therapy is commonly employed, albeit empirically, in the clinical management of suspected fetal distress. So deeply entrenched is its use in clinical practice that healthcare workers almost intuitively administer oxygen at the first suspicion of fetal distress. Oxygen administration has also been used prophylactically in the second stage of labour on the assumption that this is a time of high risk for fetal distress.

Despite this widespread use, controversy persists concerning the benefits of administered maternal oxygen for the fetus. Some studies suggest a beneficial effect (Althabe 1967; Gare 1969; McNamara 1993; Willcourt 1983). Other authors report otherwise. Saling 1963 attributed the transient rise in partial pressure of oxygen (PO₂) followed by a simultaneous drop in fetal pH and a rise in partial pressure of carbon dioxide (PCO₂) after maternal oxygen therapy to the effects of hypoxia-induced vasoconstriction of placenta vessels. Perreault 1992 found no effect on umbilical cord blood gas values following a brief period of maternal hyper-oxygenation immediately before caesarean section. Interpretation of these studies is difficult as they were conducted in diverse clinical settings, and applying differing methodologies and variable biochemical techniques for blood gas and fetal acid-base assessment. Extrapolating from animal studies, Lofaso 2007 cautions that the inhibitory effects of hyperoxia may compromise oxygenation after oxygen administration, particularly in preterm infants. However, Simpson 2005 demonstrated increased fetal oxygen saturation following maternal oxygen administration during the first stage of labour. The increase was more pronounced in fetuses with fetal oxygen saturation less than 40%, compared with those with higher oxygen content. This effect was reported to persist for more than half an hour after the oxygen was discontinued.

In support of the argument that maternal oxygen therapy has an appreciable effect on fetal oxygenation, Meschia 1999 contends that when the oxygen content is considered rather than focusing on fetal PO₂ changes alone, oxygen therapy can cause similar increments in maternal and fetal blood. Glazier 1999 describes the oxygen content of the blood perfusing the placenta from the umbilical arteries as the single most important determinant of oxygen transfer from maternal to fetal blood.

Given the current level of uncertainty about the use of oxygen during labour, it is not strange that the indications, duration, mode of administration and the optimal concentration remain contentious. Surprisingly, no randomized clinical trials have to our knowledge assessed the effectiveness of maternal oxygen therapy for fetal distress.

This review evaluated the effects of maternal oxygen therapy during labour in women with or without suspected fetal distress.

OBJECTIVES

To assess, from the best available evidence, the effects of maternal oxygen therapy for fetal distress (part 1), and prophylactic maternal oxygen therapy (part 2), on intervention rates and neonatal outcome.

METHODS

Criteria for considering studies for this review

Types of studies

All published, unpublished and ongoing randomized controlled trials comparing the effect of maternal oxygen administration for fetal distress during labour (part 1) and prophylactic oxygen administration during the second stage of labour (part 2) on clinically meaningful outcomes, with a control group (dummy or no oxygen therapy); with adequate allocation concealment; violations of allocated management and exclusions after allocation not sufficient to materially affect outcomes. We excluded quasi-randomized trials (e.g. those randomized by date of birth or hospital number) from the analysis.

Types of participants

Part 1: women with suspected fetal distress during or prior to labour.

Part 2: women without suspected fetal distress during the second stage of labour.

Types of interventions

Maternal oxygen administration versus dummy or no oxygen administration.

Types of outcome measures

The following measures of intervention and neonatal well-being were prespecified:

1. assisted vaginal delivery;
2. caesarean section;
3. maternal dissatisfaction;
4. abnormal fetal heart rate tracing;
5. cord arterial pH less than 7.2;
6. Apgar score less than seven at one minute;
7. Apgar score less than seven at five minutes;
8. neonatal resuscitation;
9. neonatal encephalopathy;
10. serious neonatal morbidity or death;
11. childhood disability.

We included the outcomes if clinically meaningful; reasonable measures were taken to minimise observer bias; missing data were insufficient to materially influence conclusions; data were available for analysis according to original allocation, irrespective of protocol violations; data were available in a format suitable for analysis.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (22 October 2012).

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

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

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

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

In the previous version of the review, we also carried out an additional search of CENTRAL (*The Cochrane Library* 2007, Issue 3). Please see [Appendix 1](#) for search terms used.

Searching other resources

We conducted a manual search of the reference lists of all identified papers.

We did not apply any language restrictions.

Data collection and analysis

For the methods used in previous updates, please see [Appendix 2](#).

For the methods to be used in future updates, please see [Appendix 3](#).

Selection of studies

Two review authors independently assessed for inclusion all the potential studies we identified as a result of the updated search. We resolved any disagreement through discussion.

No new studies were included as part of this update.

RESULTS

Description of studies

The search strategy identified six reports of studies for potential inclusion. [Sirimai 1997](#) prospectively randomized 160 women with normal labour to receive either oxygen throughout the second stage of labour or no oxygen. [Thorp 1995](#) also randomized 86

women at the onset of the second stage of labour to receive oxygen administration by face mask or no oxygen. These two studies met the inclusion criteria for this review (see table of '[Characteristics of included studies](#)').

Four studies ([Jozwik 2000](#); [Lawes 1988](#); [Simpson 2005](#); [Nesterenko 2012](#)) were excluded from the review (see table of '[Characteristics of excluded studies](#)'). [Lawes 1988](#) investigated the effect of maternal oxygen concentration (50% versus 33%) on neonatal status in women who had caesarean section under general anaesthesia. This study was excluded because the study design was not randomized and thus did not meet the inclusion criteria for this review. [Jozwik 2000](#) compared 17 women in the second stage of labour who were given oxygen by face mask with 343 controls and 24 women scheduled for elective caesarean section who had 60% oxygen at 15 litres/minute for 15 minutes compared with 116 controls. We excluded the study because it was not a randomized controlled trial. [Simpson 2005](#) prospectively evaluated three intrauterine resuscitation techniques, namely administration of intravenous fluid, maternal position and oxygen administration. Maternal fluid administration and position were evaluated using randomized design, but investigation of the effects of oxygen administration was not by a randomized design. We also excluded this trial. There were two study reports for the [Nesterenko 2012](#) trial. This was a randomized, double-blind, controlled study. [Nesterenko 2012](#) investigated the effects of maternal oxygen administration (2L/min) for at least 30 minutes before delivery on maternal and umbilical cord blood concentrations of SOD and glutathione (GSSG); 30 women were randomized to Oxygen group and 26 women into the Room Air group. This trial was excluded because maternal oxygen administration was not for fetal distress and participants were not specifically stated to be in the second stage of labour.

Risk of bias in included studies

In the study of [Thorp 1995](#), randomization was by sealed envelopes, but no further details were given. One woman randomized to the oxygenation group was excluded because of caesarean section for cord prolapse before full cervical dilation. An imbalance in the analgesia received by the oxygenation group compared with the control group is not accounted for (narcotic only: 12% versus 41% in the control group, $P < 0.05$; epidural: 71% versus 18%, respectively). No masking by means of dummy oxygen therapy was used. Compliance with oxygen therapy was reasonable.

The method of randomization in the study of [Sirimai 1997](#) was not stated. The report was available in abstract form only and contained minimal data for analysis. It was, however, included because there were not enough good quality trials addressing the question. Interpretation of the findings from the trial consequently needs to be done with circumspection.

Effects of interventions

We found no trials that assessed the effects of maternal oxygen therapy in fetal distress. Two randomized trials ([Sirimai 1997](#); [Thorp 1995](#)) assessed the use of prophylactic maternal oxygen therapy during the second stage of uncomplicated labour. Randomization was not employed in a Polish trial ([Jozwik 2000](#)) that also assessed prophylactic maternal oxygen therapy during labour. We excluded this trial.

We sought all the prespecified outcomes listed under 'Types of outcome measures'. We included two additional outcomes (cord arterial blood oxygen content (mg/dl) and cord arterial blood oxygen saturation (%)) after discussion between the review authors.

Abnormal cord blood pH values (< 7.2) were significantly more frequent in the oxygenation group than the controls (relative risk 3.51, 95% confidence interval (CI) 1.34 to 9.19). There was a tendency towards reduced cord arterial blood oxygen content and oxygen saturation in mothers treated with oxygen compared with controls: weighted mean difference (WMD) -0.80, 95% CI -2.29 to 0.69 and WMD -4.40, 95% CI -11.22 to 2.42 respectively. Other blood gas parameters also tended to favour the control group. These differences between the groups were not statistically significant.

Data on the effect of duration of oxygen administration were not presented in a uniform format suitable for combination. In the [Thorp 1995](#) trial, those receiving oxygenation for less than 10 minutes had higher umbilical artery pH values than those receiving oxygenation for longer than 10 minutes and the umbilical artery pH was also significantly higher in infants receiving oxygenation for less than 10 minutes than controls. The duration of maternal oxygen administration had no effect on cord arterial blood pH in the [Sirimai 1997](#) trial.

DISCUSSION

There were conflicting observations about the effects of the duration of maternal oxygenation on cord arterial blood pH in the two trials. Whereas [Thorp 1995](#) suggested that short-term oxygenation may be beneficial and long-term oxygenation harmful, [Sirimai 1997](#) reported that prolonged use of oxygen did not affect fetal acid-base status. However, neither trial addressed the question of the duration of oxygen therapy in a randomized format. Thus the conclusions should be regarded as speculative.

It is difficult to draw firm conclusions from some of the measures of outcome in this review as they suffered from small numbers or wide confidence intervals, or both. These included Apgar scores less than seven at one and five minutes, assisted vaginal delivery, caesarean section, and the cord arterial blood oxygen saturation.

Maternal oxygen administration did not significantly affect the cord blood arterial blood oxygen content and the need for

neonatal resuscitation. However, there were significantly more infants whose mothers received oxygen with cord arterial pH less than 7.2 compared with the infants of controls.

Remarkably, no trials on maternal oxygen administration for fetal distress were identified.

AUTHORS' CONCLUSIONS

Implications for practice

The evidence available for this review does not support the use of prophylactic maternal oxygen therapy during labour. We are not aware of randomized clinical trials to guide practice concerning the therapeutic use of maternal oxygen therapy for fetal distress.

Implications for research

In view of the widespread use of maternal oxygen therapy for fetal distress and the lack of consensus concerning its usefulness or possible harmfulness, it is most important that appropriate randomized trials be carried out in this field. Trials should specify whether the supine position, which may impair fetal oxygenation, was systematically avoided.

There are apparent gaps between basic medical science information and clinical practice. The following areas need elucidation upon which subsequent clinical research could be based.

1. The response of umbilical cord vessels to hyper-oxygenation.
2. The effect of the duration of hyper-oxygenation on umbilical cord vessels.
3. The effect of hyper-oxygenation on umbilical cord blood gas and fetal acid-base status.
4. The assessment of the most reliable indicator(s) of materno-fetal exchange and fetal well-being.

Doppler studies may be a useful way to assess the fetal response to maternal oxygen therapy.

ACKNOWLEDGEMENTS

None.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Sirimai 1997

Methods	"Prospective randomization". Method of randomization was not stated.
Participants	Inclusion criteria: women with normal labour in the second stage.
Interventions	Maternal oxygen administration throughout the second stage compared with no oxygen.
Outcomes	Umbilical cord arterial blood pH. Conclusion: oxygen administration during normal labour has no effect on fetal acid-base status, prolonged use of oxygen did not result in deterioration of fetal blood gas values.
Notes	Bangkok, Thailand. 80 women in treatment group compared with 80 controls. Abstract report only. Authors to be contacted.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment	Unclear risk	Unclear

Thorp 1995

Methods	Randomization by sealed envelopes.
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Maternal oxygen administration for fetal distress (Review)

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Thorp 1995 (Continued)

Participants	Inclusion criteria: spontaneous or induced labour at term; normal labour at the onset of second stage. Exclusion criteria: respiratory disease; diabetes; hypertension; pre-eclampsia; significant fetal heart rate abnormalities.	
Interventions	Maternal oxygen administration with face mask at flow rate of 10 L/minute, compared with no oxygen administration.	
Outcomes	Umbilical cord arterial blood gas measurement; Apgar score < 7 at 1 minute; Apgar score < 7 at 5 minutes; infants requiring resuscitation.	
Notes	<p>Kansas City, Missouri, USA.</p> <p>86 women were randomized into the study: 44 in the control group and 42 in the treatment group. One woman randomized to receive oxygen administration excluded because she was inappropriately randomized at 8 cm and required caesarean section before reaching full cervical dilation. Significantly fewer women in the oxygenation group had received narcotic analgesia alone (12% versus 41%, $P < 0.05$). Epidural analgesia had been used in 71% versus 48% respectively. Caesarean section was performed in 2% and 5% respectively, for dystocia, and vacuum delivery in 2% of each group. Of 39 women assessed for compliance, 27 had perfect compliance, 6 had 80%, 4 had 50-70% and 2 kept the mask on for 30-38% of the second stage.</p>	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Allocation concealment	Unclear risk	Unclear

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Jozwik 2000	<p>Excluded because study was not randomized.</p> <p>Methods: prospective selection (non-randomized) of patients.</p> <p>Inclusion criteria: women with normal singleton term pregnancy in labour or scheduled for elective caesarean section. Mothers should be free from disease of the respiratory system, diabetes and hypertension.</p> <p>First stage of labour should not last for more than 12 hours. Women should not be on fertility drug before pregnancy.</p> <p>For elective caesarean section, fetal lie must be longitudinal and Apgar score after 5 minutes should be matured (maximal).</p> <p>Interventions: maternal oxygen administration with face mask in second stage of labour, or women scheduled for elective caesarean section given 60% oxygen at 15 L/min for 15 minutes. Anaesthesia induced with IV Thiopental 350 mg and maintained with Isoflurane at minimum alveolar concentration (MAC) 0.8% and N₂O/O₂ ratio of 4:2 in study subjects. Induction was done with normal anaesthetic gases in controls.</p> <p>Outcome measures: umbilical cord arterial and venous blood gas measurement.</p> <p>Results: for second stage of labour, 17 women given oxygen compared with 343 controls. 24 women scheduled for elective caesarean section given oxygen were compared with 116 controls.</p>

Study	Reason for exclusion
	Conclusion: oxygen supplementation for 15 minutes during the second stage of labour or in women undergoing elective caesarean section has no meaningful influence on acid-base status and values of blood gases.
Lawes 1988	Excluded because did not meet inclusion criteria. 35 women undergoing caesarean section under general anaesthesia were allocated randomly to breathe a mixture with either 50% or 33% oxygen. Mean values for umbilical venous blood were: PO ₂ 3.9 kPa and 3.7 kPa; PCO ₂ 6.2 kPa and 6.2 kPa; pH 7.30 and 7.31 (50% and 33% groups, respectively, $P > 0.05$). No differences were found between groups for 1- or 5- minute Apgar scores.
Nesterenko 2012	Excluded because did not meet inclusion criteria. Randomized, double-blind, controlled trial determined the biological and clinical effects of oxygen administration to women in labour for at least 30 minutes before delivery. Participants were 56 women with uncomplicated term pregnancies. Study outcomes were concentrations of superoxide dismutase (SOD) and glutathione (GSSG) in maternal and umbilical cord blood. Maternal and umbilical cord blood concentrations of SOD and GSSG did not differ between the two groups at baseline and after delivery.
Simpson 2005	Excluded because evaluation of the effects of maternal oxygen administration was not by randomized design. Methods: prospective evaluation of the efficacy of intrauterine resuscitation techniques on FSpO ₂ . Inclusion criteria: healthy nulliparous women with singleton fetus in cephalic presentation undergoing induction of labour with oxytocin, having epidural anaesthesia and with reassuring fetal heart rate pattern at the time of enrollment. Mothers should be free of medical or obstetric complication or history of smoking, asthma, chronic or acute pulmonary or cardiac disease. Interventions: first phase - randomized comparison of 500 ml or 1000 ml IV fluid bolus of lactated Ringers solution over a 20-minute period for pre-epidural hydration with woman in left lateral position 15 minutes prior to IV fluid bolus, during the bolus and 15 minutes after the bolus was completed. Second phase: randomized evaluation of the effects of maternal position sequence (supine with the head of the bed elevated 30 degrees, left lateral and right lateral) on FSpO ₂ . Third phase: non-randomized evaluation of the effects of maternal oxygen administration (10 L/min). Outcome measures: FSpO ₂ , 1-minute Apgar score, 5-minute-Apgar score. Results: 42 women were randomized in the trial of the effect of IV fluid while 51 women were randomized for the evaluation of the effect of position sequences. 49 women received oxygen at 10 L/min. This was not a randomized evaluation. IV fluid bolus of 1 000 ml had a greater effect on FSpO ₂ than IV bolus of 500 ml. Fetal oxygen saturation was higher in the lateral position. Oxygen administration increased FSpO ₂ . The effect persisted for more than 30 minutes after oxygen was discontinued.

FSpO₂: fetal oxygen saturation
IV: intravenous
min: minutes

DATA AND ANALYSES

Comparison 1. Maternal oxygen for fetal distress

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Assisted vaginal delivery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Caesarean section	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Maternal dissatisfaction	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Abnormal fetal heart rate tracing	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Cord arterial pH < 7.2	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Apgar score < 7 at 1 minute	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Apgar score < 7 at 5 minutes	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Neonatal resuscitation	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Neonatal encephalopathy	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Serious neonatal morbidity or death	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Childhood disability	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 2. Prophylactic maternal oxygen

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Assisted vaginal delivery	1	85	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.07, 16.60]
2 Caesarean section	1	85	Risk Ratio (M-H, Fixed, 95% CI)	0.54 [0.05, 5.70]
3 Maternal dissatisfaction	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Abnormal fetal heart rate tracing	1	85	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.46, 3.42]
5 Cord arterial pH < 7.2	2	245	Risk Ratio (M-H, Fixed, 95% CI)	3.51 [1.34, 9.19]
6 Apgar score < 7 at 1 minute	1	85	Risk Ratio (M-H, Fixed, 95% CI)	0.15 [0.01, 2.88]
7 Apgar score < 7 at 5 minutes	1	85	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.01, 8.53]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8 Neonatal resuscitation	1	85	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.34, 2.51]
9 Neonatal encephalopathy	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Serious neonatal morbidity or death	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Childhood disability	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Cord arterial blood oxygen content (ml/dl)	1	67	Mean Difference (IV, Fixed, 95% CI)	-0.80 [-2.29, 0.69]
13 Cord arterial blood oxygen saturation (%)	1	67	Mean Difference (IV, Fixed, 95% CI)	-4.40 [-11.22, 2.42]

Analysis 2.1. Comparison 2 Prophylactic maternal oxygen, Outcome 1 Assisted vaginal delivery.

Analysis 2.2. Comparison 2 Prophylactic maternal oxygen, Outcome 2 Caesarean section.

Analysis 2.4. Comparison 2 Prophylactic maternal oxygen, Outcome 4 Abnormal fetal heart rate tracing.

Analysis 2.5. Comparison 2 Prophylactic maternal oxygen, Outcome 5 Cord arterial pH < 7.2.

Analysis 2.6. Comparison 2 Prophylactic maternal oxygen, Outcome 6 Apgar score < 7 at 1 minute.

Analysis 2.7. Comparison 2 Prophylactic maternal oxygen, Outcome 7 Apgar score < 7 at 5 minutes.

Analysis 2.8. Comparison 2 Prophylactic maternal oxygen, Outcome 8 Neonatal resuscitation.

Analysis 2.12. Comparison 2 Prophylactic maternal oxygen, Outcome 12 Cord arterial blood oxygen content (ml/dl).

Analysis 2.13. Comparison 2 Prophylactic maternal oxygen, Outcome 13 Cord arterial blood oxygen saturation (%).

APPENDICES

Appendix 1. CENTRAL search terms

Authors searched CENTRAL (*The Cochrane Library* 2007, Issue 3) using the terms 'oxygen*' and 'maternal*' and 'fetal or foetal' and 'distress'.

Appendix 2. Methods of data collection and analysis used in previous versions

Data collection and analysis

Selection of studies

We independently assessed for inclusion all potential trials we identified as a result of the search strategy, without consideration of the results. We resolved any disagreement through discussion.

Data extraction and management

We designed a form to extract data. Both authors independently extracted data using the agreed form. We resolved discrepancies through discussion. We used the Review Manager software ([RevMan 2003](#)) to double enter all the data. When information regarding any of the above was unclear, we contacted the authors of the original reports to provide further details.

Assessment of risk of bias in included studies

We assessed the validity of each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions ([Higgins 2005](#)). Methods used for the generation of the randomization sequence was described for each trial.

(1) Selection bias (randomization and allocation concealment)

We assigned a quality score for each trial, using the following criteria:

- (A) adequate concealment of allocation: such as telephone randomization, consecutively-numbered sealed opaque envelopes;
- (B) unclear whether adequate concealment of allocation: such as list or table used, sealed envelopes, or study does not report any concealment approach;
- (C) inadequate concealment of allocation: such as open list of random-number tables, use of case record numbers, dates of birth or days of the week.

(2) Attrition bias (loss of participant e.g. withdrawals, dropouts, protocol deviations)

We assessed completeness to follow up using the following criteria:

- (A) less than 5% of loss of participants;
- (B) 5% to 9.9% of loss to follow up;
- (C) 10% to 19.9% loss of participants;
- (D) more than 20% loss of participants.

(3) Performance bias (blinding of participants, researchers and outcome assessment)

We assessed blinding using the following criteria:

- (1) blinding of participants (yes/no/unclear);
- (2) blinding of caregiver (yes/no/unclear);
- (3) blinding of outcome assessment (yes/no/unclear).

Measures of treatment effect

We carried out statistical analysis using the Review Manager software ([RevMan 2003](#)). We used fixed-effect meta-analysis for combining data in the absence of significant heterogeneity if trials were sufficiently similar. If we found heterogeneity, we explored this by sensitivity analysis followed by random-effects if required.

Dichotomous data

For dichotomous data, we presented results as summary relative risk with 95% confidence intervals (CI).

Continuous data

For continuous data, we used the weighted mean difference (WMD) when outcomes were measured in the same way between trials. We intended to utilize standardized mean difference to combine trials that measured the same outcome, but used different methods.

Dealing with missing data

We analyzed data on all participants with available data in the group to which they were allocated, regardless of whether or not they received the allocated intervention. If in the original reports participants were not analyzed in the group to which they were randomized, and there was sufficient information in the trial report, we restored them to the correct group.

Assessment of heterogeneity

We applied test of heterogeneity between trials using the I^2 statistic. We considered I^2 values greater than 50% as indicating substantial heterogeneity ([Higgins 2005](#)).

Appendix 3. Methods of data collection and analysis to be used in future updates of this review

Data collection and analysis

Selection of studies

Two review authors will independently assess for inclusion all the potential studies we identify as a result of the search strategy. We will resolve any disagreement through discussion or, if required, we will consult a third review author.

Data extraction and management

We will design a form to extract data. For eligible studies, two review authors will extract the data using the agreed form. We will resolve discrepancies through discussion or, if required, we will consult the third review author. We will enter data into Review Manager software ([RevMan 2011](#)) and check for accuracy.

When information regarding any of the above is unclear, we will attempt to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

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

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

We will describe for each 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 will assess 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); or
- unclear risk of bias.

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

We will describe for each included study the method used to conceal allocation to interventions prior to assignment and will assess whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We will assess 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 will describe for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We will consider that studies are at low risk of bias if they were blinded, or if we judge that the lack of blinding would be unlikely to affect results. We will assess blinding separately for different outcomes or classes of outcomes.

We will assess 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 will describe for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We will assess blinding separately for different outcomes or classes of outcomes.

We will assess 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 will describe for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We will state 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 is reported, or can be supplied by the trial authors, we will re-include missing data in the analyses which we undertake.

We will assess methods as:

- low risk of bias (e.g. no 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 will describe for each included study how we investigated the possibility of selective outcome reporting bias and what we found.

We will assess 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 will describe for each included study any important concerns we have about other possible sources of bias.

We will assess whether each 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 will make explicit judgements about whether studies are at high risk of bias, according to the criteria given in the *Handbook* (Higgins 2011). With reference to (1) to (6) above, we will assess the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. We will explore the impact of the level of bias through undertaking sensitivity analyses - see Sensitivity analysis.

Measures of treatment effect

Dichotomous data

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

Continuous data

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

Dealing with missing data

For included studies, we will note levels of attrition. 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 will carry out analyses, as far as possible, on an intention-to-treat basis, i.e. we will attempt to include all participants randomised to each group in the analyses, and all participants will be 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 will be the number randomised minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

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 I^2 is greater than 30% and either 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

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

Data synthesis

We will carry out statistical analysis using the Review Manager software ([RevMan 2011](#)). 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 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

If we identify substantial heterogeneity, we will investigate it using subgroup analyses and sensitivity analyses. We will consider whether an overall summary is meaningful, and if it is, use random-effects analysis to produce it.

Sensitivity analysis

We will carry out sensitivity analysis to explore the effects of trial quality assessed by allocation concealment and other risk of bias components, by omitting studies rated as inadequate for these components. We will restrict this to the primary outcomes.

WHAT'S NEW

Date	Event	Description
12 November 2012	New citation required but conclusions have not changed	One new trial identified and excluded.
22 October 2012	New search has been performed	Search updated.

HISTORY

Protocol first published: Issue 2, 1996

Review first published: Issue 2, 1996

Date	Event	Description
11 February 2008	Amended	Converted to new review format.
30 June 2007	New search has been performed	We identified one new trial when we reran the search in June 2007. The trial (Simpson 2005) was excluded in this update.
25 June 2003	New citation required and conclusions have changed	Substantive amendment
23 June 2003	New search has been performed	We identified two new trials when we reran the search in March 2003. One has been included (Sirimai 1997) and one excluded (Jozwik 2000) in this update.

CONTRIBUTIONS OF AUTHORS

GJ Hofmeyr prepared the original version of the review. B Fawole updated the review in June 2003 and 2012, and has primary responsibility for maintaining the review.

DECLARATIONS OF INTEREST

None known.

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Internal sources

- University of the Witwatersrand (GJ Hofmeyr), South Africa.
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- HRP-UNDP/UNFPA/WHO/World Bank Special Programme in Human Reproduction, Geneva (B Fawole), Switzerland.

INDEX TERMS

Medical Subject Headings (MeSH)

*Labor Stage, Second; Fetal Distress [*therapy]; Oxygen Inhalation Therapy [*methods]

MeSH check words

Female; Humans; Pregnancy