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# Corticosteroids for cervical ripening and induction of labour (Review)

Kavanagh J, Kelly AJ, Thomas J

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#### [Intervention Review]

# Corticosteroids for cervical ripening and induction of labour

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# ABSTRACT

#### Background

The role of corticosteroids in the process of labour is not well understood. Animal studies have shown the importance of cortisol secretion by the fetal adrenal gland in initiating labour in sheep. Infusion of glucocorticosteroids into the fetus has also shown to induce premature labour in sheep. Given these studies it has been postulated that corticosteroids will promote the induction of labour in women. This is one of a series of reviews of methods of cervical ripening and labour induction using standardised methodology.

#### Objectives

To determine the effects of corticosteroids for third trimester cervical ripening or induction of labour in comparison with other methods of cervical priming or induction of labour.

#### Search methods

We searched the Cochrane Pregnancy and Childbirth Group Trials Register (December 2005) and bibliographies of relevant papers. We updated this search on 16 July 2009 and added the results to the awaiting classification section.

#### **Selection criteria**

Clinical trials of corticosteroids for third trimester cervical ripening or labour induction.

#### Data collection and analysis

A strategy was developed to deal with the large volume and complexity of trial data relating to labour induction. This involved a two-stage method of data extraction. We assessed trial quality. We contacted study authors for additional information. We collected adverse effects information from the trials.

#### **Main results**

Only one small trial (66 women) was included. The primary outcome vaginal birth within 24 hours was not reported. No benefit of intramuscular administration of corticosteroids with

intravenous oxytocin was found when compared with oxytocin alone. However, given the small size of this trial this result should be interpreted cautiously.



#### Authors' conclusions

The effectiveness of corticosteroids for induction of labour is uncertain. This method of induction of labour is not commonly used and so further research in this area is probably unwarranted.

[Note: The seven citations in the awaiting classification section of the review may alter the conclusions of the review once assessed.]

#### PLAIN LANGUAGE SUMMARY

#### Corticosteroids for cervical ripening and induction of labour

The role of corticosteroids in the induction of labour is uncertain.

Sometimes it is considered beneficial to bring labour on artificially. There are many different methods used and one is to give corticosteroids to ripen the cervix and induce labour. The review included only one small trial and found that there was no evidence of the effectiveness of corticosteroids on either induction of labour or cervical ripening.



# BACKGROUND

Sometimes it is considered beneficial to bring on labour artificially because of safety concerns for the mother or baby. This review is one of a series of reviews of methods of labour induction using a standardised protocol. For more detailed information on the rationale for this methodological approach, please refer to the currently published 'generic' protocol (Hofmeyr 2000). The generic protocol describes how a number of standardised reviews will be combined to compare various methods of preparing the cervix of the uterus and inducing labour.

The role of corticosteroids in the process of labour is not well understood. Animal studies have shown the importance of cortisol secretion by the fetal adrenal gland in initiating labour in sheep. Infusion of glucocorticosteroids into the fetus has been shown to induce premature labour in sheep (Liggins 1968; Mati 1973). Some assumptions have been proposed regarding the mode of action of corticosteroids, including both a paracrine and autocrine action, following the identification of glucocorticoid receptors on human amnion (Kossmann 1982). Given these studies it has been postulated that corticosteroids given intra-amniotically will promote the induction of labour in women.

#### OBJECTIVES

To determine, from the best available evidence, the effectiveness and safety of corticosteroids for third trimester cervical ripening and induction of labour in comparison with other methods of induction of labour.

#### METHODS

#### Criteria for considering studies for this review

#### **Types of studies**

Clinical trials comparing corticosteroids for cervical ripening or labour induction, with placebo/no treatment or other methods listed above it on a predefined list of methods of labour induction (see 'Methods of the review'); the trials included some form of random allocation to either group; and they reported one or more of the prestated outcomes.

#### **Types of participants**

Pregnant women due for third trimester induction of labour, carrying a viable fetus.

#### **Types of interventions**

Clinical trials comparing corticosteroids for cervical ripening or labour induction, with placebo/no treatment or other methods listed above it on a predefined list of methods of labour induction.

#### Types of outcome measures

Clinically relevant outcomes for trials of methods of cervical ripening/labour induction have been prespecified by two authors of labour induction reviews (Justus Hofmeyr and Zarko Alfirevic). Differences were settled by discussion.

Five primary outcomes were chosen as being most representative of the clinically important measures of effectiveness and complications. Subgroup analyses will be limited to the primary outcomes: (1) vaginal delivery not achieved within 24 hours (or period specified by trial authors);

(2) uterine hyperstimulation with fetal heart rate (FHR) changes;(3) caesarean section;

(4) serious neonatal morbidity or perinatal death (e.g. seizures, birth asphyxia defined by trialists, neonatal encephalopathy, disability in childhood);

(5) serious maternal morbidity or death (e.g. uterine rupture, admission to intensive care unit, septicaemia).

Perinatal and maternal morbidity and mortality are composite outcomes. This is not an ideal solution because some components are clearly less severe than others. It is possible for one intervention to cause more deaths but less severe morbidity. However, in the context of labour induction at term this is unlikely. All these events will be rare, and a modest change in their incidence will be easier to detect if composite outcomes are presented. The incidence of individual components will be explored as secondary outcomes (see below).

Secondary outcomes relate to measures of effectiveness, complications and satisfaction:

Measures of effectiveness:

(7) oxytocin augmentation.

(6) cervix unfavourable/unchanged after 12 to 24 hours;

# Complications:

- (8) uterine hyperstimulation without FHR changes;
- (9) uterine rupture;
- (10) epidural analgesia;
- (11) instrumental vaginal delivery;
- (12) meconium stained liquor;
- (13) Apgar score < 7 at 5 minutes;
- (14) neonatal intensive care unit admission;
- (15) neonatal encephalopathy;
- (16) perinatal death;
- (17) disability in childhood;
- (18) maternal side effects (all);
- (19) maternal nausea;
- (20) maternal vomiting;
- (21) maternal diarrhoea;
- (22) other maternal side-effects;
- (23) postpartum haemorrhage (as defined by the trial authors);(24) serious maternal complications (e.g. intensive care unit

admission, septicaemia but excluding uterine rupture); (25) maternal death.

Measures of satisfaction: (26) woman not satisfied; (27) caregiver not satisfied.

'Uterine rupture' includes all clinically significant ruptures of unscarred or scarred uteri. Trivial scar dehiscence noted incidentally at the time of surgery is excluded.

Additional outcomes may appear in individual primary reviews, but will not contribute to the secondary reviews.

While all the above outcomes were sought, only those with data appear in the analysis tables.

The terminology of uterine hyperstimulation is problematic (Curtis 1987). In the reviews we will use the term 'uterine hyperstimulation



without FHR changes' to include uterine tachysystole (greater than contractions per 10 minutes for at least 20 minutes) and uterine hypersystole/hypertonus (a contraction lasting at least two minutes) and 'uterine hyperstimulation with FHR changes' to denote uterine hyperstimulation syndrome (tachysystole or hypersystole with fetal heart rate changes such as persistent decelerations, tachycardia or decreased short-term variability). However, due to varied reporting there is the possibility of subjective bias in interpretation of these outcomes. Also it is not always clear from trials if these outcomes are reported in a mutually exclusive manner.

Outcomes were included in the analysis: if reasonable measures were taken to minimise observer bias; and data were available for analysis according to original allocation.

#### Search methods for identification of studies

#### **Electronic searches**

We searched the Cochrane Pregnancy and Childbirth Group Trials Register by contacting the Trials Search Co-ordinator (December 2005). We updated this search on 16 July 2009 and added the results to Studies awaiting classification.

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

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

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

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

We did not apply any language restrictions.

#### Searching other resources

We searched reference lists of trial reports and reviews by hand.

#### Data collection and analysis

A strategy has been developed to deal with the large volume and complexity of trial data relating to labour induction. Many methods have been studied, in many different groups of women undergoing labour induction. Most trials are intervention-driven, comparing two or more methods in various categories of women.

To avoid duplication of data in these reviews, the labour induction methods have been listed in a specific order, from 1 to 26. Each primary review includes comparisons between one of the methods (from 2 to 26) with only those methods above it on the list. Thus, the review of intravenous oxytocin (4) will include only comparisons with intracervical prostaglandins (3), vaginal prostaglandins (2) or placebo (1). Methods identified in the future will be added to the end of the list. The current list is as follows:

- 1. placebo/no treatment;
- 2. vaginal prostaglandins;
- 3. intracervical prostaglandins;
- 4. intravenous oxytocin;
- 5. amniotomy;
- 6. intravenous oxytocin with amniotomy;
- 7. vaginal misoprostol;
- 8. oral misoprostol;
- 9. mechanical methods including extra-amniotic Foley catheter;

10.membrane sweeping;

- 11.extra-amniotic prostaglandins;
- 12.intravenous prostaglandins;

13.oral prostaglandins;

14.mifepristone;

15.estrogens;

16.corticosteroids;

- 17.relaxin;
- 18.hyaluronidase;
- 19.castor oil, bath, and/or enema;
- 20.acupuncture;
- 21.breast stimulation;
- 22.sexual intercourse;
- 23.homoeopathic methods;
  - 24.nitric oxide;
  - 25.buccal or sublingual misoprostol;

26.hypnosis.

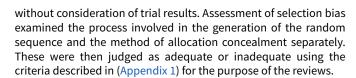
The reviews will be analysed according to the following clinical subgroups of women:

- 1. previous caesarean section or not;
- 2. nulliparity or multiparity;
- 3. membranes intact or ruptured;
- 4. cervix favourable, unfavourable or undefined.

For most reviews, the data extraction process was conducted centrally. This was co-ordinated from the Clinical Effectiveness Support Unit (CESU) at the Royal College of Obstetricians and Gynaecologists, UK, in co-operation with The Pregnancy and Childbirth Group of The Cochrane Collaboration. This process allowed the data extraction process to be standardised across all the reviews.

The trials were initially reviewed on eligibility criteria, using a standardised form and the basic selection criteria specified above. Following this, data were extracted to a standardised data extraction form, which was piloted for consistency and completeness. The pilot process involved the researchers at the CESU and previous authors in the area of induction of labour.

Information was extracted regarding the methodological quality of trials on a number of levels. This process was completed



Performance bias was examined with regards to whom was blinded in the trials, i.e. patient, caregiver, outcome assessor or analyst. In many trials the caregiver, assessor and analyst were the same party. Details of the feasibility and appropriateness of blinding at all levels were sought.

We included individual outcome data in the analysis if data met the prestated criteria in 'Types of outcome measures'. We processed trial data using the methodology described in the Cochrane Collaboration Handbook (Clarke 2000). We analysed data extracted from the trials on an intention-to-treat basis (when this was not done in the original report, re-analysis was performed wherever possible). If data were missing, clarification was sought from the original authors. If the attrition was such that it might significantly affect the results, these data were excluded from the analysis. This decision rested with the authors of primary reviews and is clearly documented. If missing data become available, they will be included in the analyses.

We extracted data from all eligible trials to examine how issues of quality influence affect size in a sensitivity analysis. In trials where reporting was poor, methodological issues were reported as unclear or clarification sought.

Due to the large number of trials, double data extraction was not feasible and agreement between the three data extractors was therefore assessed on a random sample of trials.

Once the data had been extracted, they were distributed to the individual authors, who entered them into the Review Manager software (RevMan 2000), checked them for accuracy, and analysed them using the RevMan software. For dichotomous data, we calculated relative risks and 95% confidence intervals and, in the absence of heterogeneity, we pooled results using a fixed-effect model.

The predefined criteria for sensitivity analysis included all aspects of quality assessment as mentioned above, including aspects of selection, performance and attrition bias.

Primary analysis was limited to the prespecified outcomes and subgroup analyses. In the event of differences in unspecified outcomes or subgroups being found, these were analysed post hoc, but clearly identified as such to avoid drawing unjustified conclusions.

For this update, the one trial identified was independently assessed by two authors (J Kavanagh and A Kelly).

#### RESULTS

#### **Description of studies**

Eight trials were identified by the search strategy and considered for inclusion in this review (Barkai 1997; Craft 1976; Grudev 1988; Grudev 1990; Jenssen 1977; Mati 1973; Penev 1985; Ziaei 2003). (Seven reports are awaiting assessment.) Three studies were excluded from this review because they were not randomised controlled trials, two were controlled clinical trials (Craft 1976; Grudev 1990) and one was a one group pre-test posttest evaluation(Penev 1985).

One identified study (Barkai 1997) was excluded because it involved a complex intervention of extra-amniotic dexamethasone or saline in combination with a Foley catheter inflated to 30 ml. This paper will be included in the review on 'other methods used for induction of labour'.

Two studies were eligible for inclusion in the review. One study of 11 women (Mati 1973) involved an intra-amniotic injection of 20 mg of dexamethasone or a similar volume of saline. It was felt by the authors that this form of intervention for induction of labour would not be performed now and hence results were not presented.

The second study (Jenssen 1977) examined the effect of a course of oral dexamethasone on rates of spontaneous labour compared with no treatment on 120 women. The subsequent method of induction is not specified and no definable prespecified outcomes were reported. Allocation in this study was by alternation.

One study, a randomised controlled trial comparing intramuscular injections of aprophen with prednisolone in 32 women with prolonged pregnancy is awaiting assessment (Grudev 1988). The full report of the trial is in Bulgarian and requires translation.

#### **Included studies**

One study was eligible for inclusion (Ziaei 2003), this was a randomised controlled trial comparing intramuscular injections of dexamethasone phosphate with intravenous oxytocin in a group of 66 pregnant women at term with a favourable cervix. The intervention group received two intramuscular injections of dexamethasone phosphate, the first on enrolment to the trial, the second 12 hours later. Twenty-four hours after enrolment both the intervention group and the control group received intravenous oxytocin.

#### **Risk of bias in included studies**

One study was identified which met the inclusion criteria for this review (Ziaei 2003). This was a double-blind randomised controlled trial of 66 women. Randomisation was by random number table, though concealment of allocation was unclear.

#### **Effects of interventions**

One trial, involving 66 women, is included. No benefit of intramuscular administration of corticosteroids with intravenous oxytocin was found when compared with oxytocin alone. The primary outcome vaginal birth within 24 hours was not reported. There was a non-significant trend towards fewer caesarean sections in the intervention group, (6% versus 15%, relative risk 0.40, 95% confidence interval 0.08 to 1.92). There were no instances of uterine hyperstimulation with or without fetal heart rate changes. No babies in either group had an Apgar score less than seven at five minutes, nor were there any incidences of maternal fever.



#### DISCUSSION

The effectiveness of corticosteroids for induction of labour is uncertain. This method of induction of labour is not commonly used and further research in this area is probably unwarranted.

#### AUTHORS' CONCLUSIONS

#### Implications for practice

The effectiveness of corticosteroids for induction of labour is uncertain. Corticosteroids cannot be recommended for induction of labour in clinical practice on the basis of this trial evidence. [Note: The seven citations in the awaiting classification section of the review may alter the conclusions of the review once assessed.]

#### **Implications for research**

Given that corticosteroids are not now in common use for induction of labour, the authors consider that further research in this area is probably unwarranted.

#### ACKNOWLEDGEMENTS

Thanks to Sonja Henderson, Lynn Hampson and Claire Winterbottom for their support in the production of this review. Also thanks to Zarko Alfirevic, Justus Hofmeyr and Jim Neilson.



# REFERENCES

#### References to studies included in this review

#### Ziaei 2003 {published data only}

Ziaei S, Rosebehani N, Kazeminejad A, Zafarghandi S. The effects of intramuscular administration of corticosteroids on the induction of parturition. *Journal of Perinatal Medicine* 2003;**31**:134-9.

#### References to studies excluded from this review

#### Barkai 1997 {published data only}

Barkai G, Cohen S, Kees S, Lusky A, Margalit V, Mashiach S, et al. Induction of labor with use of a Foley catheter and extraamniotic corticosteroids. *American Journal of Obstetrics and Gynecology* 1997;**177**:1145-8.

#### Craft 1976 {published data only}

Craft I, Brummer V, Horwell D, Morgan H. Betamethazone induction of labour. *Proceedings of the Royal Society of Medicine* 1976;**69**:827-8. [MEDLINE: 1005467]

#### Grudev 1990 {published data only}

Grudev D. Delivery in prolonged pregnancy following preparation and induction with aprofen and prednisolone [Razhdane pri prenosena bremennost sled podgotovka i induktsiia s aprofen i prednizolon]. *Akusherstvo i Ginekologiia* 1990;**29**:14-8. [MEDLINE: 2252139]

#### Jenssen 1977 {published data only}

Jenssen H, Wright PB. The effect of dexamethasone therapy in prolonged pregnancy. *Acta Obstetricia et Gynecologia Scandinavica* 1977;**56**:467-73.

#### Mati 1973 {published data only}

Mati JKG, Horrobin DF, Bramley PS. Induction of labour in sheep and in humans by single doses of corticosteroids. *BMJ* 1973;**2**:149-51.

#### Penev 1985 {published data only}

Penev I. Dexamethasone induction and preparation for labor in prolonged pregnancy [Induktsiia i podgotovka na razhdaneto pri prenosena bremennost s dekametazon]. *Akushertsvo i Ginekologiia* 1985;**24**(1):27-35.

#### **References to studies awaiting assessment**

#### Cohen 1997 {published data only}

Cohen SB, Schiff E, Kees S, Lusky A, Mashiach S. Induction of labor using a foley catheter and extra-amniotic corticosteroids. *American Journal of Obstetrics and Gynecology* 1997;**176**(1 Pt 2):S191.

#### Grudev 1988 {published data only}

Grudev D, Novachkov L, Geshev G, Krushkov I. Use of aprophen in the preparation for and induction of labor. [Prilozhenie na aprophen za podgotovka i induktsiia na razhdaneto]. *Akusherstvo i Ginekologiia* 1988;**27**(4):39-43.

#### Kashanian 2007 {published data only}

Kashanian M, Zarrin DR. Evaluation of the effect of extraamniotic normal saline infusion (EASI) alone or in combination with dexamethazone for the induction of labor [abstract]. 31st British International Congress of Obstetrics and Gynaecology; 2007 July 4-6; London, UK. 2007:210.

#### Kashanian 2008 {published data only}

Kashanian M, Dadkhah F, Mokhta F. Effect of intramuscular administration of dexamethasone on the duration of labor. *International Journal of Gynecology & Obstetrics* 2008;**102**(3):259-62.

#### Kashanian 2008a {published data only}

Kashanian M, Fekrat M, Naghghash S, Ansari NS. Evaluation of the effect of extra-amniotic normal saline infusion alone or in combination with dexamethasone for the induction of labor. *Journal of Obstetrics and Gynaecology Research* 2008;**34**(1):47-50.

#### Mansouri 2003 {published data only}

Mansouri M, Pour Javad A, Panahi G. Induction of labor with use of a Foley catheter and extra-amniotic corticosteroids. *Medical Journal of the Islamic Republic of Iran* 2003;**17**(2):97-100.

#### Zafarghandi 2004 {published data only}

Zafarghandi A, Zafarghandi N, Baghaii N. Foley catheter cervical ripening with extra-amniotic infusion of saline or corticosteroids: a double-blind randomized controlled study. *Acta Medica Iranica* 2004;**42**(5):338-42.

#### **Additional references**

#### Clarke 2000

Clarke M, Oxman AD, editors. Cochrane Reviewers' Handbook 4.1 [updated June 2000]. In: Review Manager (RevMan) [Computer program]. Version 4.1. Oxford, England: The Cochrane Collaboration, 2000.

#### Curtis 1987

Curtis P, Evans S, Resnick J. Uterine hyperstimulation. The need for standard terminology. *Journal of Reproductive Medicine* 1987;**32**:91-5.

#### Hofmeyr 2000

Hofmeyr GJ, Alfirevic Z, Kelly AJ, Kavanagh J, Thomas J, Neilson JP, et al. Methods for cervical ripening and labour induction in late pregnancy: generic protocol. *Cochrane Database of Systematic Reviews* 2009, Issue 3. [DOI: 10.1002/14651858.CD002074.pub2]

#### Kossmann 1982

Kossmann JC, Bard H, Gibb W. Characterization of specific steroid binding in human amnion at term. *Biology of Reproduction* 1982;**27**:320-6.



#### Liggins 1968

Liggins GC. Premature parturition after infusion of corticosteroids or cortisol into foetal lambs. *Journal of Endocrinology* 1968;**42**:323-9.

#### RevMan 2000 [Computer program]

The Cochrane Collaboration. Review Manager (RevMan). Version 4.1 for Windows. Oxford, England: The Cochrane Collaboration, 2000.

# CHARACTERISTICS OF STUDIES

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

#### Ziaei 2003

#### References to other published versions of this review

#### Kavanagh 2001

Kavanagh J, Kelly AJ, Thomas J. Corticosteroids for induction of labour. *Cochrane Database of Systematic Reviews* 2001, Issue 2. [DOI: 10.1002/14651858.CD003100.pub2]

Methods	Randomisation by random number tables. Concealment of allocation unclear. Double blind.
Participants	66 post-term (41 weeks or over) women with a favourable cervix.
Interventions	Experimental group: 2 x 10 mg intramuscular dexamethasone phosphate q 12 hours with iv oxytocin at 24 hours. Control group: iv oxytocin at 24 hours.
Outcomes	<ol> <li>Uterine hyperstimulation with FHR changes.</li> <li>Caesarean section.</li> <li>Uterine hyperstimulation without FHR changes.</li> <li>Apgar score &lt; 7 at 5 minutes.</li> <li>Maternal fever.</li> </ol>
Notes	
Risk of bias	

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

FHR: fetal heart rate IV: intravenous

# Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Barkai 1997	Complex intervention of extra-amniotic dexamethasone or saline in combination with a foley catheter inflated to 30 ml. This paper will be included in the review on 'other methods used for induction of labour'.
Craft 1976	Not an RCT and no primary outcomes reported.
Grudev 1990	Controlled clinical trial non-random.
Jenssen 1977	Comparison of a course of oral dexamethasone with no treatment. The subsequent method of in- duction is not specified and no definable primary outcomes are reported.

Study	Reason for exclusion
Mati 1973	Comparison of 20 mg intra-amniotic betamethasone with sterile saline. Limited outcome report- ing. Not included as not viewed as acceptable current clinical practice by the authors.
Penev 1985	One group pre-test post-test design.

RCT: randomised controlled trial

# DATA AND ANALYSES

# Comparison 1. Corticosteroids versus control (all women)

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
2 Uterine hyperstimulation without fetal heart rate changes	1	66	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Caesarean section	1	66	Risk Ratio (M-H, Fixed, 95% CI)	0.4 [0.08, 1.92]
8 Uterine hyperstimulation without fetal heart rate changes	1	66	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Apgar score < 7 at 5 minutes	1	66	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Maternal fever	1	66	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

# Analysis 1.2. Comparison 1 Corticosteroids versus control (all women), Outcome 2 Uterine hyperstimulation without fetal heart rate changes.

Study or subgroup	Treatment	Control		Risk Ratio			Weight	<b>Risk Ratio</b>
	n/N	n/N		M-H, Fixe	d, 95% CI			M-H, Fixed, 95% CI
Ziaei 2003	0/33	0/33						Not estimable
Total (95% CI)	33	33						Not estimable
Total events: 0 (Treatment), 0 (Control)	1							
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
	E.	wours trootmont	01 02	0.5	2	5 10 r	-	

Favours treatment 0.1 0.2 5 10 Favours control

# Analysis 1.3. Comparison 1 Corticosteroids versus control (all women), Outcome 3 Caesarean section.

Study or subgroup	Treatment	Control			Risk Ratio			Weight	<b>Risk Ratio</b>
	n/N	n/N		M-H	<mark>ا, Fixed, 95</mark> ۹	% CI			M-H, Fixed, 95% CI
Ziaei 2003	2/33	5/33	1				100%	0.4[0.08,1.92]	
	Fa	vours treatment	0.01	0.1	1	10	100	Favours control	

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Study or subgroup	Treatment	Control			Risk Ratio	)		Weight	<b>Risk Ratio</b>
	n/N	n/N		М-Н,	Fixed, 95	5% CI			M-H, Fixed, 95% CI
Total (95% CI)	33	33						100%	0.4[0.08,1.92]
Total events: 2 (Treatment), 5 (Control)	)								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.15(P=0.25)									
	Fa	avours treatment	0.01	0.1	1	10	100	Favours control	

# Analysis 1.8. Comparison 1 Corticosteroids versus control (all women), Outcome 8 Uterine hyperstimulation without fetal heart rate changes.

Study or subgroup	Treatment	Control			Ri	sk Rat	tio			Weight	<b>Risk Ratio</b>
	n/N	n/N			M-H, F	ixed,	95% CI				M-H, Fixed, 95% Cl
Ziaei 2003	0/33	0/33									Not estimable
Total (95% CI)	33	33									Not estimable
Total events: 0 (Treatment), 0 (Control)											
Heterogeneity: Not applicable											
Test for overall effect: Not applicable											
	Fa	avours treatment	0.1	0.2	0.5	1	2	5	10	Favours control	

# Analysis 1.13. Comparison 1 Corticosteroids versus control (all women), Outcome 13 Apgar score < 7 at 5 minutes.

Study or subgroup	Treatment	Control			Ri	sk Rat	io			Weight	Risk Ratio
	n/N	n/N			M-H, F	ixed, 9	5% CI				M-H, Fixed, 95% CI
Ziaei 2003	0/33	0/33									Not estimable
Total (95% CI)	33	33									Not estimable
Total events: 0 (Treatment), 0 (Control	)										
Heterogeneity: Not applicable											
Test for overall effect: Not applicable											
	Fa	avours treatment	0.1	0.2	0.5	1	2	5	10	Favours control	

# Analysis 1.22. Comparison 1 Corticosteroids versus control (all women), Outcome 22 Maternal fever.

Study or subgroup	Treatment	Control		Risk Ratio						Weight	<b>Risk Ratio</b>
	n/N	n/N			M-H, F	ixed, 9	95% CI				M-H, Fixed, 95% CI
Ziaei 2003	0/33	0/33									Not estimable
Total (95% CI)	33	33									Not estimable
Total events: 0 (Treatment), 0 (Control)											
Heterogeneity: Not applicable											
Test for overall effect: Not applicable											
	Fa	avours treatment	0.1	0.2	0.5	1	2	5	10	Favours control	



# APPENDICES

# Appendix 1. Methodological quality of trials

Methodological item	Adequate	Inadequate
Generation of random sequence	Computer generated sequence, random number tables, lot drawing, coin tossing, shuffling cards, throwing dice.	Case number, date of birth, date of ad- mission, alternation.
Concealment of alloca- tion	Central randomisation, coded drug boxes, sequentially sealed opaque envelopes.	Open allocation sequence, any procedure based on inadequate generation.

# WHAT'S NEW

Date	Event	Description
17 July 2009	Amended	Search updated. Six reports added to Studies awaiting classifica- tion (Cohen 1997; Kashanian 2007; Kashanian 2008; Kashanian 2008a; Mansouri 2003; Zafarghandi 2004.)

# HISTORY

Protocol first published: Issue 2, 2000 Review first published: Issue 2, 2001

Date	Event	Description
24 April 2008	Amended	Converted to new review format.
9 February 2006	New citation required and conclusions have changed	We updated the search in December 2005. The original review in- cluded no trials. With this update, we included one randomised controlled trial (Ziaei 2003), which provided little evidence of ef- fect; excluded five further studies; and added one study, which requires translation, to the Studies awaiting classification.

# CONTRIBUTIONS OF AUTHORS

J Kavanagh and AJ Kelly: data extraction and analysis. J Kavanagh J, AJ Kelly and J Thomas drafted the review.

# DECLARATIONS OF INTEREST

None known.

# SOURCES OF SUPPORT

#### Internal sources

• EPPI-Centre, Social Science Research Unit, Institute of Education, University of London, UK.



#### **External sources**

• No sources of support supplied

# INDEX TERMS

# Medical Subject Headings (MeSH)

\*Anti-Inflammatory Agents; \*Cervical Ripening; \*Dexamethasone; \*Glucocorticoids; Administration, Topical; Labor, Induced [\*methods]; Pregnancy Trimester, Third

#### **MeSH check words**

Female; Humans; Pregnancy