Morning versus evening induction of labour for improving outcomes

Jannet JH Bakker¹, Ben Willem J Mol², Maria Pel³, and Joris AM van der Post³

¹Department of Obstetrics and Gynaecology, Academic Medical Center, Maarssen, Netherlands

²Obstetrics and Gynaecology, Máxima Medical Center, Veldhoven, Netherlands ³Department of Obstetrics and Gynaecology, Academic Medical Center, Amsterdam, Netherlands

Abstract

This is the protocol for a review and there is no abstract. The objectives are as follows:

To assess whether induction of labour starting in the evening, coinciding with the endogenous circadian rhythm, improves the outcome of labour compared to induction of labour starting in the early morning, organised to coincide with office hours.

BACKGROUND

Description of the condition

Induction of labour is a common intervention in obstetrical practice. In the western world, labour is induced for one in every four pregnant women, mostly for reasons related to the increased risk for the mother (eg, hypertension, pre-eclampsia, diabetes, prolonged pregnancy, prelabour rupture of the membranes) or child (eg, suspected fetal growth retardation). There are many different methods used to induce labour. In clinical situations medicinal and mechanical methods are used, including the sweeping of membranes, vaginal or intracervical prostaglandins, oestrogens, amniotomy with or without intravenous oxytocin, corticosteroids, misoprostol and extra amniotic Foley catheter (Alfirevic 2006; Boulvain 2001; Boulvain 2005; Boulvain 2008; Bricker 2000; French 2001; Hofmeyr 2003; Howarth 2001; Hutton 2001; Kavanagh 2006a; Kavanagh 2006b; Kelly 2001b; Kelly 2001c; Kelly 2003; Luckas 2000; Muzonzini 2004; Neilson 2000; Thomas 2001). Traditionally, many non-medical methods are used to initiate labour like sexual intercourse, enema, breast stimulation, acupuncture, homeopathy and castor oil (Kavanagh 2005; Kelly 2001a; Smith 2003; Smith 2004).

Copyright © 2009 The Cochrane Collaboration.

Contact address: Jannet JH Bakker, Department of Obstetrics and Gynaecology, Academic Medical Center, Emmaweg 18, Maarssen, 3603 AM, Netherlands. j.j.bakker@amc.nl.

CONTRIBUTIONS OF AUTHORS

Jannet Bakker wrote the draft review protocol. Maria Pel, Ben Willem Mol and Joris van der Post worked collaboratively to advance and develop the review protocol.

Editorial group: Cochrane Pregnancy and Childbirth Group.

Publication status and date: New, published in Issue 2, 2009.

DECLARATIONS OF INTEREST

None known.

Traditionally, in most hospitals, inductions with medication start early in the morning, with the start of the working day for the day shift. The reason for the choice of this timing is probably the wish to plan the actual birth between office hours because of the availability of personnel.

Description of the intervention

The intervention is the timing of the start of the induction, in harmony with the circadian rhythm of natural birth, in the evening.

How the intervention might work

In human and animal studies spontaneous onset of labour is proven to have a circadian rhythm with a preference for start of labour in the evening (Backe 1991; Fraser, 1989; Honnebier 1991; Honnebier 1994; Lindow 2000). The biological explanation for this phenomenon is the increased sensibility of oxytocin receptors in the myometrium of the uterus to maternal oxytocin in the night compared to the daytime. Myometrial contractility is enhanced not only by increased sensitivity to oxytocin in the evening but it is also related to an increase in oxytocin receptor concentration. Many other factors might also contribute in this increase of concentration and sensibility like the variation in concentration of steroid hormones in blood where progesterone, estrone, estriol and estradiol concentration reach their lowest point in the morning Dodd 2006. So, when spontaneous contractions start in the evening, the total duration of labour and delivery shortens and less obstetrical interventions are needed (Heres 2000). Based on these observations one might assume that starting induction of labour in the evening is more beneficial for mother and child.

Why it is important to do this review

Starting induction in the evening, to coincide with the endogenous circadian rhythm, might improve the outcome of labour compared to starting induction in the early morning, organised to coincide with office hours. For hospitals staffed 24 hours a day with midwives and doctors, planning induction of labour both in the morning and the evening obviously opens possibilities for a more efficient use of hospital care resources in terms of use of labour suites.

OBJECTIVES

To assess whether induction of labour starting in the evening, coinciding with the endogenous circadian rhythm, improves the outcome of labour compared to induction of labour starting in the early morning, organised to coincide with office hours.

METHODS

Criteria for considering studies for this review

Types of studies—We will include all published and unpublished randomised controlled trials. We will exclude trials that employed quasi-random methods of treatment allocation.

Types of participants—Pregnant women with the indication for induction of labour. All methods, medical, non medical or mechanical, used to induce labour will be included.

Types of interventions—The experimental group are women in which induction starts in the evening compared with a control group, women who start induction in the morning with the same method of induction.

Types of outcome measures

Primary outcomes: The primary outcome of this review will be perinatal mortality, defined as intrauterine deaths plus newborn deaths in the first week of life.

Secondary outcomes

Neonatal outcomes

1. Birth asphyxia as defined by trialist.
2. Admission to neonatal intensive care unit.
3. Neonatal convulsions.
4. Neonatal encephalopathy.
5. Use of anticonvulsants.
6. Antibiotics treatment because of signs of infection.
7. Meconium aspiration syndrome.
8. Pneumonia.
9. Neurodevelopment at childhood follow up.

Maternal outcomes

1. Mode of delivery.
2. Analgesia used.
3. Perineal trauma.
4. Need for blood transfusion.
5. Use of antibiotics because of signs of intrauterine infection.
6. Duration of birth (as defined by trialist).
7. Prolonged labour (cut off used by trialist).
8. Patient satisfaction.
9. Postnatal depression.

Health services use

1. Length of maternal admission.
2. Length of neonatal admission.

Search methods for identification of studies

Electronic searches—We will contact the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register. 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 Co-ordinator searches the register for each review using the topic list rather than keywords.

In addition, we will search MEDLINE (1966 to current) and EMBASE (1974 to current). We will report the search strategies in full in the review

We will not apply any restrictions on language or year of publication.

Data collection and analysis

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

Data extraction and management—We will design a form to extract data. For eligible studies at least two review authors will extract the data using the agreed form. We will resolve discrepancies through discussion or, if required, we will consult a third person. Data will be entered into Review Manager software (RevMan 2008) and checked 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 methodological quality of 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 2008). Any disagreement will be resolved by discussion or by involving a third assessor.

(1) 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:

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

(2) Allocation concealment (checking for possible selection bias): We will describe for each included study the method used to conceal the allocation sequence in sufficient detail and determine whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment. We will assess the methods as:

- adequate (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- inadequate (open random allocation; unsealed or nonopaque envelopes, alternation; date of birth);
- unclear.

(3) Blinding (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. Studies will be judged at low risk of bias if they were blinded, or if we judge that the lack of blinding could not have affected the results. Blinding will be assessed separately for different outcomes or classes of outcomes.

We will assess the methods as:

- adequate, inadequate or unclear for participants;
- adequate, inadequate or unclear for personnel;
- adequate, inadequate or unclear for outcome assessors.

(4) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations): 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, 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:

- adequate;

- inadequate;
- unclear.

(5) Selective 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:

- adequate (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);
- inadequate (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.

(6) Other sources of bias: 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:

- yes;
- no;
- unclear.

(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 2008). 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 relative risk 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, levels of attrition will be noted. The impact of including studies with high levels of missing data in the overall assessment of treatment effect will be explored by using sensitivity analysis.

For all outcomes analyses will be carried out, 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. 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 use the I^2 statistic to measure heterogeneity among the trials in each analysis. If we identify substantial heterogeneity (I^2 above 50%) we will explore it by prespecified subgroup analysis.

Subgroup analyses—We will conduct planned subgroup analyses classifying whole trials by interaction tests as described by Deeks 2001.

We plan to carry out subgroup analyses for the different types of interventions to induce labour and for relevant sub groups of patients like parity and prematurity.

Assessment of reporting biases—Where we suspect reporting bias (*see* selective reporting bias above), we will attempt to contact study authors asking them to provide missing outcome data. Where this is not possible, and the missing data are thought to introduce serious bias, the impact of including such studies in the overall assessment of results will be explored by a sensitivity analysis.

Data synthesis—We will carry out statistical analysis using the Review Manager software (RevMan 2008). We will use fixed-effect inverse variance meta-analysis for combining data where trials are examining the same intervention, and the trials' populations and methods are judged sufficiently similar. Where we suspect clinical or methodological heterogeneity between studies sufficient to suggest that treatment effects may differ between trials we will use random effects meta-analysis. If substantial heterogeneity, more than 50%, is identified in a fixed effect meta-analysis this will be noted and the analysis repeated using a random-effects method.

Subgroup analysis and investigation of heterogeneity—We plan to carry out the following subgroup analyses:

1. primiparae;
2. multiparae;
3. for each method used to induce labour.

The following outcomes will be used in subgroup analysis:

- perinatal mortality;
- mode of delivery;
- duration of labour.

For fixed effect meta-analyses we will conduct planned subgroup analyses classifying whole trials by interaction tests as described by Deeks 2001. For random-effects meta-analyses we will assess differences between subgroups by inspection of the subgroups' confidence intervals; non-overlapping confidence intervals indicate a statistically significant difference in treatment effect between the subgroups.

Sensitivity analyses—We will carry out sensitivity analyses to explore the effect of trial quality for important outcomes in the review. Where there is risk of bias associated with a particular aspect of study quality (e.g. inadequate allocation concealment), this will be explored by sensitivity analyses in order to assess for any substantive difference to the overall result.

Acknowledgments

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

HISTORY

Protocol first published: Issue 2, 2009

Additional references

- Alfirevic 2006 . Alfirevic Z, Weeks A. Oral misoprostol for induction of labour. Cochrane Database of Systematic Reviews. 2006; (2) DOI: DOI: 10.1002/14651858.CD001338.pub2.
- Backe 1991 . Backe B. A circadian variation in the observed duration of labor. Possible causes and implications. Acta Obstetrica et Gynecologica Scandinavica. 1991; 70:465–68. [PubMed: 1763611]
- Boulvain 2001 . Boulvain M, Kelly A, Lohse C, Stan C, Irion O. Mechanical methods for induction of labour. Cochrane Database of Systematic Reviews. 2001; (4) DOI: DOI: 10.1002/14651858.CD001233.
- Boulvain 2005 . Boulvain M, Stan C, Irion O. Membrane sweeping of induction of labour. Cochrane Database of Systematic Reviews. 2005; (1) DOI: DOI: 10.1002/14651858.CD000451.pub2.
- Boulvain 2008 . Boulvain M, Kelly A, Irion O. Intracervical prostaglandins for induction of labour. Cochrane Database of Systematic Reviews. 2008; (1) DOI: DOI: 10.1002/14651858.CD006971.
- Bricker 2000 . Bricker L, Luckas M. Amniotomy alone for induction of labour. Cochrane Database of Systematic Reviews. 2000; (4) DOI: DOI: 10.1002/14651858.CD002862.
- Deeks 2001 . Deeks, JJ.; Altman, DG.; Bradburn, MJ. Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger, M.; Davey Smith, G.; Altman, DG., editors. Systematic reviews in health care: meta-analysis in context. BMJ Books; London: 2001.
- Dodd 2006 . Dodd, Jodie; Crowther, Caroline A.; Robinson, Jeffrey S. Morning Compared With Evening Induction of Labor: A Nested Randomized Controlled Trial. Obstetrics and Gynecology. Aug; 2006 108(2):350–360. M. PhD, FRANZCOG. MD, FRANZCOG. FRANZCOG. [PubMed: 16880306]
- Fraser, 1989 . Fraser WD, McLean FH, Usher RH. Diurnal variation in admission to hospital of women in labour. Canadian Journal of Surgery. 1989; 32:33–5.
- French 2001 . French L. Oral prostaglandins E2 for induction of labour. Cochrane Database of Systematic Reviews. 2001; (2) DOI: DOI: 10.1002/14651858.CD003098.
- Heres 2000 . Heres MH, Pel M, Borkent-Polet M, Treffers PE, Mirmiran M. The hour of birth: comparisons of circadian pattern between women cared for by midwives and obstetricians. Midwifery. 2000; 16:173–6. [PubMed: 10970750]
- Higgins 2008 . Higgins, JPT.; Green, S., editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.0 [updated February 2008]. The Cochrane Collaboration; 2008. Available from www.cochrane-handbook.org
- Hofmeyr 2003 . Hofmeyr GJ, Gülmezoglu AM. Vaginal misoprostol for cervical ripening and induction of labour. Cochrane Database of Systematic Reviews. 2003; (1) DOI: 10.1002/14651858.CD000941.

- Honnebier 1991 . Honnebier MB, Jenkins SL, Wentworth RA, Figueroa JP, Nathanielsz PW. Temporal structuring of delivery in the absence of a photoperiod: preparturient myometrial activity of the rhesusmonkey is related to maternal body temperature and depends on the maternal circadian system. *Biology of Reproduction*. 1991; 45:617–25. [PubMed: 1751637]
- Honnebier 1994 . Honnebier MB, Nathanielsz PW. Primate parturition and the role of the maternal circadian system. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 1994; 55:193–203. [PubMed: 7958165]
- Howarth 2001 . Howarth GR, Botha DJ. Amniotomy plus intravenous oxytocin for induction of labour. *Cochrane Database of Systematic Reviews*. 2001; (3) DOI: DOI: 10.1002/14651858.CD003250.
- Hutton 2001 . Hutton E, Mozurkewich E. Extra-amniotic prostaglandins for induction of labour. *Cochrane Database of Systematic Reviews*. 2001; (2) DOI: DOI: 10.1002/14651858.CD003092.
- Kavanagh 2005 . Kavanagh J, Kelly AJ, Thomas J. Breast stimulation for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews*. 2005; (3) DOI: DOI: 10.1002/14651858.CD003392.
- Kavanagh 2006a . Kavanagh J, Kelly AJ, Thomas J. Corticosteroids for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews*. 2006; (2) DOI: DOI: 10.1002/14651858.CD003100.pub2.
- Kavanagh 2006b . Kavanagh J, Kelly AJ, Thomas J. Hyaluronidase for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews*. 2006; (2) DOI: DOI: 10.1002/14651858.CD003097.pub2.
- Kelly 2001a . Kelly AJ, Kavanagh J, Thomas J. Castor oil, bath and/or enema for cervical priming and induction of labour. *Cochrane Database of Systematic Reviews*. 2001; (2) DOI: DOI: 10.1002/14651858.CD003099.
- Kelly 2001b . Kelly AJ, Kavanagh J, Thomas J. Relaxin for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews*. 2001; (2) DOI: DOI: 10.1002/14651858.CD003103.
- Kelly 2001c . Kelly AJ, Tan B. Intravenous oxytocin alone for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews*. 2001; (3) DOI: DOI: 10.1002/14651858.CD003246.
- Kelly 2003 . Kelly AJ, Kavanagh J, Thomas J. Vaginal prostaglandins (PGE2 and PGF2a) for induction of labour at term. *Cochrane Database of Systematic Reviews*. 2003; (4) DOI: DOI: 10.1002/14651858.CD003101.
- Lindow 2000 . Lindow SW, Jha RR, Thompson JW. 24 hour rhythm to the onset of preterm labour. *BJOG: an international journal of obstetrics and gynaecology*. 2000; 107:1145–8. [PubMed: 11002959]
- Luckas 2000 . Luckas M, Bricker L. Intravenous prostaglandins for induction of labour. *Cochrane Database of Systematic Reviews*. 2000; (4) DOI: DOI: 10.1002/14651858.CD002864.
- Muzonzini 2004 . Muzonzini G, Hofmeyr GJ. Buccal or sublingual misoprostol for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews*. 2004; (4) DOI: DOI: 10.1002/14651858.CD004221.pub2.
- Neilson 2000 . Neilson JP. Mifepristone for induction of labour. *Cochrane Database of Systematic Reviews*. 2000; (4) DOI: DOI: 10.1002/14651858.CD002865.
- RevMan 2008 . The Cochrane Collaboration. Review Manager (RevMan). 5.0. The Nordic Cochrane Centre: The Cochrane Collaboration; Copenhagen: 2008.
- Smith 2003 . Smith CA. Homeopathy for induction of labour. *Cochrane Database of Systematic Reviews*. 2003; (4) DOI: DOI: 10.1002/14651858.CD003399.
- Smith 2004 . Smith CA, Crowther CA. Acupuncture for induction of labour. *Cochrane Database of Systematic Reviews*. 2004; (1) DOI: DOI: 10.1002/14651858.CD002962.pub2.
- Thomas 2001 . Thomas J, Kelly AJ, Kavanagh J. Oestrogens alone or with amniotomy for cervical ripening or induction of labour. *Cochrane Database of Systematic Reviews*. 2001; (4) DOI: DOI: 10.1002/14651858.CD003393.

* Indicates the major publication for the study