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The Finnish randomised controlled multicentre trial on optimal timing of labor induction in nulliparous women with post-term pregnancy

Submission date
20/07/2017

Recruitment status
No longer recruiting

Registration date
10/10/2017

Overall study status
Completed

Last Edited
28/12/2023

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Almost 10 % of all pregnancies in Finland continue beyond 41 gestational weeks, and 5 % of pregnancies continue until 42 gestational weeks. Post-term pregnancy is associated with risks for the pregnant woman and the baby, as well as high rate of caesarean sections and labour complications. However, labour induction is also associated with a high risk for prolonged labour and caesarean section, especially if the woman is having her first baby. The rates of labour induction are rising worldwide. However, the evidence on optimal timing and the optimal method of labour induction are insufficient. Labour induction by 41 gestational weeks is common in many countries. In Finland, the standard care is induction of labour between 41+5 and 42+1 gestational weeks. This study is designed to investigate if the policy of labour induction at 41 gestational weeks is better than expectant management and labour induction at 42 gestational weeks as well as study the optimal method for labour induction by comparing three different methods. The aim of this study is to find out the optimal timing and method of labour induction in post-term women having their first baby.

Who can participate?
Pregnant women aged 18 and older who are having their first baby.

What does the study involve?
Pregnant women having their first baby at 41 gestational weeks are asked to participate in the study over a three year period. Women who are interested to participate in the study are booked for an antenatal visit at 41 gestational weeks. After receiving more information and having given their consent, the participating women are randomly allocated for labour induction at 41 gestational weeks or expectant management and induction at 41+5-42+1 gestational weeks. During expectant management, another antenatal visit is booked for monitoring the well being of the baby. In both groups, the method of labour induction is also randomised. The methods of labour induction include balloon catheter, oral misoprostol tablets, and the combination of these two methods. Participants are assessed to see if induction of labour at 41

gestational weeks is better option than expectant management and induction at 41+5-42+1 gestational weeks. In addition, the induction methods are compared in order to find the most optimal method of labour induction in post-term women having their first baby.

What are the possible benefits and risks of participating?
Participants may benefit from receiving an additional antenatal visit and fetal ultrasound examination at 41 gestational weeks. There are no risks involved in participating in the study.

Where is the study run from?
The study is being run by the department of obstetrics and gynaecology of Helsinki University Hospital (Finland) and takes place in five university hospitals and in one central hospital in Finland.

When is the study starting and how long is it expected to run for?
September 2016 to September 2022

Who is the main contact?
Associate Professor Leena Rahkonen
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Study website
www.sykeinfo.fi

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HUS/1978/2016

Study information

Scientific Title
The Finnish randomised controlled multicentre trial comparing induction of labor at 41+0 gestational weeks with expectant management and labor induction at 41+5 - 42+1 gestational weeks in nulliparous women with an unfavourable cervix

Acronym
FIOTIL

Study objectives
Study aim:
The aim of this study is to investigate the optimal timing and method of labor induction in nulliparous post-term women with an unfavourable cervix.

Hypothesis:
Earlier induction of labor at 41 gestational weeks compared to expectant management and labour induction by 42 gestational weeks may reduce adverse labour outcomes without increasing the rate of caesarean deliveries.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Hospital district of Helsinki and Uusimaa Ethics committee for Women's and Children's Health and Psychiatry, 16/03/2017, ref: HUS/1978/2016

Study design
Randomised controlled multicentre trial

Primary study design

Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in English, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Nulliparity and post-term pregnancy

Interventions
Current version as of 04/04/2018:
Randomisation is performed by computer-sequenced block randomisation technique. The first randomisation (timing of labour induction) is performed at 41+0 gestational weeks. Participants are allocated to one of two groups:

Intervention group: Women randomised to this group receive early induction and are induced the same day.

Control group: Women randomised to this group have late induction and are managed expectantly, with routine fetal monitoring at 41+5 gestational weeks and induction of labour at 41+5 - 42+1 gestational weeks according to hospital policy.

The second randomisation (method of labour induction) is performed for both the intervention and control groups. The women are allocated to labour induction by Foley catheter, oral misoprostol, or combined use of Foley catheter and oral misoprostol:

Foley catheter group: A single 40-80 ml balloon catheter retained for a maximum of 24 hours. After expulsion or removal of the balloon, if cervical ripening is advanced to Bishop score >6, amniotomy is performed and intravenous oxytocin infusion is started according to the local protocol. If the cervix remains unfavourable, a new Foley catheter is placed in every 24 hours. After 72 hours of treatment, induction is considered failed.

Misoprostol group: Oral misoprostol 50 µg is administered every four hours until onset of regular contractions. After 72 hours of treatment, induction is considered failed.

Combined use of Foley catheter and misoprostol: A single 40-80 ml balloon catheter and simultaneous administration of 50 microg oral misoprostol every 4 hours until onset of regular contractions. After 72 hours of treatment, induction is considered failed.

Participation in the study ends once the participants have been discharged during the post-partum period. There is no follow up involved with participating.

Original version:
Randomisation is performed by computer-sequenced block randomisation technique. The first randomisation (timing of labour induction) is performed at 41+0 gestational weeks. Participants are allocated to one of two groups:

Intervention group: Women randomised to this group receive early induction and are induced the same day.

Control group: Women randomised to this group have late induction and are managed expectantly, with routine fetal monitoring at 41+5 gestational weeks and induction of labour at 41+5 - 42+1 gestational weeks according to hospital policy.

The second randomisation (method of labour induction) is performed for both the intervention and control groups. The women are allocated to labour induction by Foley catheter, oral misoprostol, or combined use of Foley catheter and oral misoprostol:

Foley catheter group: A single 40-60 ml balloon catheter retained for a maximum of 24 hours. After expulsion or removal of the balloon, if cervical ripening is advanced to Bishop score >6, amniotomy is performed and intravenous oxytocin infusion is started according to the local protocol. If the cervix remains unfavourable, a new Foley catheter is placed in every 24 hours. After 72 hours of treatment, induction is considered failed.

Misoprostol group: Oral misoprostol 50 µg is administered every four hours until onset of regular contractions. After 72 hours of treatment, induction is considered failed.

Combined use of Foley cathehter and misoprostol: A single 40-60 ml balloon catheter and simultaneous administration of 50 µg oral misoprostol every 4 hours until onset of regular contractions. After 48 hours of treatment, induction is considered failed.

Participation in the study ends once the participants have been discharged during the post-partum period. There is no follow up involved with participating.

Intervention Type
Mixed

Primary outcome measure
The rate of caesarean section is measured at birth using the mode of delivery.

Secondary outcome measures
Current version as of 04/04/2018:
1. Primary neonatal outcome are measured using 1 and 5 minute Apgar scores, umbilical artery blood pH and base excess values at birth, and intubation at birth
2. Neonatal intensive care episodes is measured using patient notes on admissions to neonatal intensive care unit during the first 24 hours after birth
3. Neonatal care episodes is measured using patient notes on admissions to neonatal ward during the first 24 hours after birth
4. Placental retention is measured at 1 hour from birth using the definition that surgical or pharmacological interventions are needed for placental expulsion
5. Maternal haemorrhage is measured by volume of bleeding in milliliters or weight of bleeding in grams at birth
6. Perineal tears is measured using sphincter injury at birth
7. Intrapartum and postpartum infections is measured at labour and during post-partum care

episode, using any two of the criteria: maternal fever ≥ 38ºC, fetal tachycardia, purulent discharge, uterine tenderness, and white cell count > 20
8. Maternal satisfaction is measured using Childbirth Experience questionnaire (CEQ)

Original version:
1. Primary neonatal outcome are measured using 1 and 5 minute Apgar scores, umbilical artery blood pH and base excess values at birth, and intubation at birth
2. Neonatal intensive care episodes is measured using patient notes on admissions to neonatal intensive care unit during the first 24 hours after birth
3. Neonatal care episodes is measured using patient notes on admissions to neonatal ward during the first 24 hours after birth
4. Placental retention is measured at 1 hour from birth using the definition that surgical or pharmacological interventions are needed for placental expulsion
5. Maternal haemorrhage is measured by volume of bleeding in milliliters or weight of bleeding in grams at birth
6. Perineal tears is measured using sphincter injury at birth
7. Intrapartum and postpartum infections is measured at labour and during post-partum care episode, using any two of the criteria: maternal fever ≥ 38ºC, fetal tachycardia, purulent discharge, uterine tenderness, and white cell count > 20

Overall study start date
01/09/2016

Completion date
31/12/2022

Eligibility

Key inclusion criteria
1. Pregnant women
2. Age ≥18 years
3. Nulliparous
4. Gestational age 41+0 weeks
5. Singleton pregnancy
6. Live fetus
7. Cephalic presentation
8. Intact amniotic membranes
9. Unfavourable cervix (Bishop score < 6)
10. Uncomplicated pregnancy (no pregnancy complications that require induction of labour)
11. Ability to understand oral and written information

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex

Female

Target number of participants
600

Total final enrolment
381

Key exclusion criteria
1. Multiple pregnancy
2. Breech or transverse presentation
2. Fetal malformation detected antenatally
3. Multiparous women
4. Women with a history of previous caesarean section or transfundal uterine surgery
5. Pregnancy complication that requires intervention (such as preeclampsia, intrauterine growth restriction, pregestational diabetes and insulin-dependent gestational diabetes)
6. Premature rupture of membranes
7. Clinical vaginal infection or chorionamnionitis
8. Fetal macrosomia (antenatally estimated weight ≥ 4.5 kg)
9. Maternal HIV, hepatitis B or C
10. Contraindication for vaginal delivery (such as low lying placenta or vasa previa)
11. No informed consent received

Date of first enrolment
01/03/2018

Date of final enrolment
01/03/2022

Locations

Countries of recruitment
Finland

Study participating centre
Helsinki University Hospital/Department of obstetrics and gynaecology
Haartmaninkatu 2, 00029 HUS
Helsinki
Finland
00029 HUS

Study participating centre
Tampere University Hospital/Department of obstetrics and gynaecology
Tampere
Finland
33521

Study participating centre
Turku University Hospital/Department of obstetrics and gynaecology
Turku
Finland
20521

Study participating centre
Kuopio University Hospital/Department of obstetrics and gynaecology
Kuopio
Finland
70210

Study participating centre
Oulu University Hospital/Department of obstetrics and gynaecology
Oulu
Finland
90220

Study participating centre
Keski-Suomi Central Hospital/Department of obstetrics and gynaecology
Jyväskylä
Finland
40620

Sponsor information

Organisation
Helsinki University Hospital

Sponsor details
Haartmaninkatu 2
Helsinki
Finland
00290 HUS

Sponsor type
Hospital/treatment centre

Website
http://www.hus.fi/en/Pages/default.aspx

ROR
https://ror.org/02e8hzf44

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Helsinki University Hospital

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal by 2023. Planned publication of the protocol.

Intention to publish date
31/03/2024

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication. The data sharing plans for the current study prior to results publication are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		19/12/2023	28/12/2023	Yes	No