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Induction of labour versus expectant management for women over 35 years

Submission date
23/08/2012

Recruitment status
No longer recruiting

Registration date
23/08/2012

Overall study status
Completed

Last Edited
11/03/2016

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
British women are increasingly delaying childbirth, and if they wait till over the age of 35 they are at higher risk of many pregnancy complications. One concern is the increased risk of stillbirth (baby dying before birth) or the death of a baby within its first 28 days of life. These so called 'perinatal deaths' affect 1% of all pregnancies to women over the age of 35 years. Many doctors offer labour induction to women in this age group in the hope of forestalling the risk of the baby dying. This is popular with some parents, but many others are fearful that it will increase the need for caesarean delivery. However, recent research in other high-risk pregnancies (if the pregnancy has gone overdue, if baby is abnormally small or abnormally big, or if the mother has high blood pressure) has not shown any increase in the need for caesarean. Indeed, the effect has been rather the reverse. If induction for women over 35 did not increase caesareans, or even reduced them, it would probably save many babies lives and be very popular. We therefore plan to perform a study to test the effect of such an induction policy on caesarean section rates.

Who can participate?
Women who are pregnant with their first baby and who will be 35 years of age by the time of their expected date of delivery can take part. They must be having a single baby and the baby must be head down (cephalic presentation), which means the babys head has entered their pelvis.

What does the study involve?
We are comparing two ways of managing the pregnancies of women over 35 years of age, induction of labour at 39 weeks or no intervention. Participating women will be randomly allocated to one of these two groups. Women in the induction of labour group will have their labour induced or started artificially at 39 weeks. They will be allocated a date for induction and will come to the delivery suite that day. When they arrive the midwife will check the babys heartbeat and examine the womans cervix or neck of the womb by performing an internal examination. Depending on whether the cervix is already opening up they will start labour either with a drug called prostaglandin administered through the vagina, or by breaking the waters and giving a drug called oxytocin by intravenous infusion (a drip). Prostaglandins are inserted into the vagina in the form of a tablet, gel or a pessary by the midwife. If one dose doesnt get a woman into labour then they may need repeating. Alternatively a slow release pessary may be

used for 24 hours. Amniotomy is where the midwife artificially breaks the waters during an internal examination. This may be done right at the outset of the induction, or after the prostaglandins have had a chance to soften and open the neck of the womb. Labour induction may involve the use of a hormone called syntocinon, which causes the womb to contract; this is given through a drip or a small tube which sits in a vein that is inserted using a needle. The process of induction of labour will be exactly the same as that used in the hospital for all other women having their labour induced. Women in the no intervention group will await spontaneous labour unless a situation develops where their labour needs to be induced or they need a Caesarean section.

What are the possible benefits and risks of participating?
We believe that induction of labour at 39 weeks for women over the age of 35 is safer for babies. Complications of pregnancy and labour are more common in women over 35 years of age. Older mothers have a higher risk of stillbirth throughout pregnancy and the peak risk period is 3741 weeks. Although women over 35 are known to be a high-risk group they are currently managed the same as younger women by the majority of obstetricians. We cannot promise this study will help you but the information we get from this study will provide evidence how best to manage pregnancies in women over 35 and we hope will improve outcomes for mothers and their babies. Induction of labour is a common procedure: about 20% of pregnant women will have their labour induced for a variety of reasons. Induction of labour is not always successful and you may require a caesarean section if we fail to get you into labour. By giving drugs to stimulate the womb to contract, occasionally the womb can become over stimulated; this can result in abnormalities in the babys heart rate trace that may require action. A complication of breaking your waters artificially is that the babys umbilical cord can fall out with the first rush of amniotic fluid and this necessitates urgent delivery of your baby.

Where is the study run from?
Nottingham City Hospital (UK)

When is the study starting and how long is it expected to run for?
June 2012 to July 2014

Who is funding the study?
NIHR Research for Patient Benefit Programme (UK)

Who is the main contact?
Dr Kate Walker
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Study website
http://www.35-39trial.org

Contact information

Type(s)
Scientific

Contact name
Dr Kate Walker

Contact details

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
11891

Study information

Scientific Title
Induction of labour versus expectant management for nulliparous women over 35 years of age

Acronym
35/39 Trial

Study objectives
The primary aim of this randomised controlled trial is to test the null hypothesis that a policy of induction of labour at 39 weeks gestation for women over the age of 35 years reduces caesarean section rates. It will also enable us to collect data to test the feasibility of a larger study to test the effect of the policy of induction on perinatal death and serious neonatal morbidity. There is already evidence, albeit from non randomised studies, that such a policy would reduce adverse perinatal outcomes, in particular late stillbirth. The policy is not currently widely implemented because of fears that it would increase caesarean section rates. If induction of labour reduces the risk of intra-partum caesarean section then it would be adopted widely. This would almost certainly result in reduced late stillbirths at no maternal cost. We will also measure participants views about the two study arms to ensure that both are acceptable to women. This project provides an important opportunity to not only influence clinical practice in this important area, but to add to the increasing body of unbiased knowledge about the effects of policies of labour induction for various indications near term.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Derby 1 REC, 12/01/2012, ref: 12/EM/0003

Study design

Multi-centre randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Available under 'Useful Documents' at www.35-39trial.org

Health condition(s) or problem(s) studied
Reproductive Health & Childbirth

Interventions
Treatment group: Women over the age of 35 years with a singleton live fetus in a cephalic presentation will be assigned to induction of labour between 39 + 0/7 and 39 + 6/7 weeks.

Control group: Women over the age of 35 years with a singleton live fetus in a cephalic presentation will be assigned to expectant management i.e. awaiting spontaneous onset of labour. Those without any medical indication for induction will be offered induction of labour anywhere between T+7 and T+14, the exact time to be determined by consultants usual practice.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Caesarean section

Secondary outcome measures
Maternal outcomes
1. Mode of delivery
1.1 Vaginal delivery
1.2 Assisted vaginal delivery (forceps or ventouse)
1.3 Caesarean section
2. Onset of labour
2.1 Spontaneous
2.2 Induction
2.3 Planned caesarean section
3. Indication for induction of labour
3.1 Randomised to treatment
3.2 Gestational age > 41 weeks

3.3 Preterm (< 37 weeks) prelabour rupture of membranes
3.4 Term (> 37 weeks) prelabour rupture of membranes > 24 hours
3.5 Fetal growth restriction
3.6 Reduced fetal movements
3.7 Intrauterine fetal death
3.8 Pregnancy induced hypertension
3.9 Pre-eclampsia
3.10 Eclampsia
3.11 Obstetric cholestasis
3.12 Gestational diabetes
3.13 Suspected fetal distress
3.14 Maternal request
3.15 Other
4. Method of induction of labour (as many as apply)
4.1 Prostaglandin tablet regime
4.2 Prostaglandin gel regime
4.3 Prostaglandin slow-release pessary
4.4 Artificial rupture of amniotic membranes
4.5 Oxytocin
5. Indication for Caesarean section
5.1 Arrest of first stage of labour
5.2 Arrest of second stage of labour
5.3 Failed instrumental delivery
5.4 Fetal distress
5.5 Failure to progress and fetal distress
5.6 Maternal complication
5.7 Elective
5.9 Other
6. Intrapartum complications
6.1 Placental abruption
6.2 Cord prolapse
6.3 Postpartum haemorrhage
6.4 Shoulder dystocia
7. Postpartum morbidity
7.1Requiring blood transfusion
7.2Systemic infection temp > 38C

Neonatal outcomes
1. Live birth
2. Stillbirth (a baby delivered with no signs of life after 24 completed weeks of pregnancy)
3. Birth weight
4. Sex
5. Death before discharge from hospital
6. Apgar at 1 min
7. Apgar at 5 min
8. Apgar at 10 minutes allow missing data
9. Cord blood artery pH and BD allow missing data
10. Cord blood vein pH and BD allow missing data
11. NICU admission duration (days)
12. If no cord blood and NICU admission required first fetal pH obtained
13. Birth trauma
13.1 Subdural haematoma

13.2 Intracerebral or intraventricular haemorrhage
13.3 Spinal-cord injury
13.4 Basal skull fracture
13.5 Peripheral-nerve injury present at discharge from hospital
13.6 Long bone fracture
13.7 Seizures (occurring at less than 24 hr of age or requiring two or more drugs to control them)
13.8 Hypotonia (for at least 2 hrs)
13.9 Abnormal level of consciousness (hyperalert, drowsy or lethargic; stupor/decreased response to pain; coma)
13.10Tube feeding for > 4 days
13.11 Intubation and ventilation for > 24 hrs
13.12 Cooling required
13.13 Oxygen required
13.14 CPAP required

Outcomes for pilot study
1. The recruitment rate per hospital.
2. The age distribution of participating women.
3. Compliance with the treatment arms of the trial.
4. The overall gestational age distribution of the two groups.
5. Completeness of outcome data

Maternal delivery expectation/experience measured by the Childbirth Experience Questionnaire (Dencker et al, BMC Pregnancy and Childbirth 2010). We will invite a sample of participants to join focus groups to explore in-depth their views.

Overall study start date
11/06/2012

Completion date
02/07/2014

Eligibility

Key inclusion criteria
Nulliparous women who will be over 35 years at the expected date of delivery, with:
1. A singleton live fetus
2. A cephalic presentation
3. Gestational age between 36 weeks + 0 days and 39 weeks + 6 days
4. No medical contra-indication to induction of labour
5. No medical contra-indication to pregnancy being allowed to proceed to term plus 10 days
6. Willingness to participate in the trial
7. Written informed consent
8. Female participants

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
UK Sample Size: 630

Key exclusion criteria
1. Women with a known lethal fetal congenital abnormality.
2. Women with a contra-indication to labour or vaginal delivery (e.g. evidence of fetal compromise such that labour would be contra-indicated; fetal congenital anomaly or condition that might cause a mechanical problem at delivery such as hydrocephalus or cystic hygroma; placenta praevia)
3. Women with a contra-indication to expectant management (e.g. gestational diabetes, proteinuric hypertension (>250mg/l or BP > 140/90 on more than two occasions, two hrs apart)
4. Women with a previous myomectomy.
5. Women who book late for antenatal care and have no dating scan performed between before 22 weeks to provide an accurate EDD.
6. Women who have undergone IVF using donor eggs in the current pregnancy

Date of first enrolment
11/06/2012

Date of final enrolment
02/07/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Nottingham City Hospital
Nottingham
United Kingdom
NG5 1PB

Sponsor information

Organisation
Nottingham University Hospitals NHS Trust (UK)

Sponsor details

Queens Medical Centre
Derby Road
Nottingham
England
United Kingdom
NG7 2UH

Sponsor type
Hospital/treatment centre

Website
http://www.nuh.nhs.uk/

ROR
https://ror.org/05y3qh794

Funder(s)

Funder type
Government

Funder Name
NIHR Research for Patient Benefit Programme (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	11/12/2012		Yes	No
Results article	results	03/03/2016		Yes	No