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High Or low dose Syntocinon® for delay in labour

Submission date
11/07/2016

Recruitment status
No longer recruiting

Registration date
03/08/2016

Overall study status
Completed

Last Edited
20/09/2023

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
It is not currently known what the best care for first time mothers with delayed progress in the first stage of labour is. This topic is a research priority for the Royal College of Obstetricians and Gynaecologists. Delayed labour is relatively common, affecting between 11- 30% (equivalent to between one and three in ten) of first time mothers. The only recommended treatment is artificial oxytocin (Syntocinon®) which is given intravenously (through the vein) to stimulate contractions. A standard regimen (concentration and rate of administration) is recommended by NICE Guidelines 2014 and is widely used in the UK. Information from studies looking at different dose regimens of Syntocinon ® for delayed labour suggest that a high dose regimen may reduce the chance of Caesarean section but the available evidence is not conclusive. Syntocinon ® may cause the uterus to contract too much and the baby to become distressed so both mother and baby are carefully monitored and the dose adjusted in relation to the number of contractions and how the baby is. Research shows currently around 32% (equivalent to about three in ten) of the women who need Syntocinon® for delayed labour have an unplanned Caesarean section , which is related to a longer hospital stay, higher risk of infection, bleeding and blood clots and to increase risk of Caesarean section being required in future pregnancies. By reducing the number of Caesarean sections, these risks can also be reduced. A reduction in the Caesarean section rate of 5-8% (equivalent to nearly one in ten) in these women could save the NHS nearly £1M per year, as well as possible annual savings of £2.6M from the impact of avoiding Caesarean section in future pregnancies. The study is looking at whether treatment with a high dose of Syntocinon® reduces the need for Caesarean section in women with delayed labour.

Who can participate?
Women having their first baby and confirmed as being in delayed labour.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in group 1 are treated with the standard dose of oxytocin. Those in group 2 are treated with a high dose of oxytocin, which is double the concentration of the standard dose. All participants from both groups are followed to see, for example, whether they have to have a caesarean section, have an epidural during the labour, how long each of the three stages of labour takes and how long the birth takes altogether.

What are the possible benefits and risks of participating?
Syntocinon ® may cause the uterus to contract too much and the baby to become distressed so both mother and baby are carefully monitored and the dose adjusted in relation to the number of contractions and how the baby is.

Where is the study run from?
Birmingham Womens NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
March 2016 to May 2019

Who is funding the study?
NIHR Health Technology Assessment Programme, HTA (UK)

Who is the main contact?
Dr Sara Kenyon
HOLDS@trials.bham.ac.uk

Contact information

Type(s)
Public

Contact name
Dr Sara Kenyon

Contact details
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Additional identifiers

EudraCT/CTIS number
2015-005537-50

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
v2.0; HTA Project: 14/140/44

Study information

Scientific Title

High Or Low Dose Syntocinon® for delay in labour: the HOLDS trial

Acronym
HOLDS

Study objectives
HOLDS will provide robust evidence of clinical effectiveness of a high dose compared to the current standard dose regimen of oxytocin in reducing the need for Caesarean section (CS) for nulliparous women with confirmed delay in the first stage of labour.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West Midlands - Edgbaston Research Ethics Committee, 24/02/2016, ref: 16/WM/0014

Study design
Multicentre pragmatic randomized double-blind controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available at present

Health condition(s) or problem(s) studied
Nulliparous women with a singleton cephalic pregnancy at term (37-42 weeks gestation) with confirmed delay in labour and ruptured membranes as defined by NICE Intrapartum Care Guidelines for whom the clinical decision has been made to prescribe Syntocinon for augmentation of labour.

Interventions
HOLDS is a double- blinded randomised controlled trial which will compare the standard dose regimen of oxytocin with a high dose regimen. NICE guidance recommends a standard dose regimen of oxytocin (2mU/min increasing every 30 minutes to a maximum 32mU/min). The comparator is high dose regimen (4mU/min increasing every 30 minutes to a maximum of 64mU /min). The high dose regimen (i.e. double the concentration) has a higher starting dose, earlier attainment of conventional maximum doses (at 2 hours rather than over 4 hours) and the possible use of higher maximum doses of oxytocin compared to the standard regimen.

Once delay in labour is confirmed women will be randomised to the standard dose will receive a solution containing 2 x 5iu ampoules in 50mls or 500mls and those to the high dose a solution

containing 2 x 10iu in 50 mls or 500mls. Ampoules are manufactured as 5 and 10 iu and these regimens have been selected to enable the trial to be double-blinded. Intervention will last for the remainder of the first stage and until completion of the second stage of labour.

Data will be collected by the research midwife through CRFs (i.e., labour, birth and discharge and a neonatal CRFs) from clinical data routinely recorded. Data collection will start after the participant has given consent and end at discharge from hospital.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Syntocinon (Oxytocin)

Primary outcome measure
Incidence of caesarean section, data taken from medical notes

Secondary outcome measures
1. Incidence of epidural use during labour
2. Duration of first, second and third stages of labour
3. Time to birth from randomisation
4. Prevalence of mode of birth (spontaneous vaginal birth (SVB), instrumental or caesarean section)
5. Degree of perineal trauma (first, second, third and fourth)
6. Reason for caesarean section and decision to delivery interval for CS
7. Confirmed urinary retention requiring catheterisation and pulmonary oedema
8. Tachysystole (uterine contractions greater than 5 in 10 mins for 20 minutes) requiring reduction in oxytocin and/or tocolysis
9. Hyperstimulation (uterine contractions greater than 5 in 10 mins for 20 minutes resulting in non-ressurring or abnormal fetal heart rate)
10. Fetal blood sampling (FBS) during labour or significant STAN event (for those Units that use ST waveform analysis for intrapartum fetal monitoring)
11. Abnormal cardiotocogram leading to immediate birth without fetal blood sample
12. Incidence of maternal morbidity (anaphylaxis, pulmonary oedema, postpartum haemorrhage, shoulder dystocia, chorioamnioitis, uterine rupture/hysterectomy)
13. Active management of third stage of labour
14. Length of time after birth in hospital [days]
15. Admission to HDU/ITU
16. Maternal death
17. Time from randomisation to commencement of allocation
18. Total oxytocin dose
19. Time to maximum oxytocin rate
20. Maximum oxytocin dose reached
21. Gender and birthweight of neonate
22. Apgar score at 5 minutes
23. Arterial cord blood gases when collected
24. Breastfeeding rates on discharge from hospital
25. Length of time after birth in hospital [days]

26. Incidence of need to resuscitate neonate
27. Reason for neonatal review on ward (excluding routine baby check)
28. Reason for admission to neonatal unit (NNU) and level of care received (level 1,2,3) including intensive care
29. Duration of respiratory support for neonate
30. Number of days to full oral feeds
31. Incidence of seizures of neonate
32. Incidence of neonatal encephalopathy (SARNAT grade)
33. Incidence of therapeutic hypothermia (cooling) of neonate required
34. Incidence of intrapartum still birth
35. Incidence of early neonatal death (within seven days of birth)

All data taken from medical notes other than outcome 18, where the data is recorded directly onto the Clinical Records Form.

Overall study start date
01/03/2016

Completion date
31/05/2019

Eligibility

Key inclusion criteria
1. Nulliparous women with singleton cephalic pregnancy at term (37-42 weeks gestation)
2. Confirmed delay in labour and ruptured membranes for whom the clinical decision has been made to prescribe Syntocinon for augmentation of labour

According to NICE guidance [NICE 2014], labour is established when there are regular painful contractions and progressive cervical dilation from 4 cm. Delay is suspected when cervical dilation of < 2 cm in 4 hours occurs once labour is established. Delay is confirmed when progress of <1 cm in 2 hours is found on repeat vaginal examination.

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
1500

Key exclusion criteria
1. Multiparous women
2. Nulliparous women who:
2.1. Are undergoing induction of labour
2.2. Have a BMI >40 at booking

2.3. Have a multiple pregnancy
2.4. Have existing cardiac disease, bleeding disorders, diabetes (either pre-existing or gestational), previous uterine surgery
2.5. Have had significant antepartum haemorrhage
2.6. Are under 16 years of age
2.7. Have a known contra-indication to oxytocin therapy as listed in the Summary of marketing Product Characteristics

Date of first enrolment
01/03/2017

Date of final enrolment
31/08/2018

Locations

Countries of recruitment
England

United Kingdom

Wales

Study participating centre
Birmingham Womens NHS Foundation Trust
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2TG

Study participating centre
Birmingham Women and Children`s Hospital
Steelhouse Lane
Birmingham
United Kingdom
B4 6NH

Study participating centre
Royal Victoria Infirmary Newcastle
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
St Mary's Hospital
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
University Hospital of Wales
Heath Park Way
Cardiff
United Kingdom
CF14 4XW

Study participating centre
St Thomas' Hospital London
Westminster Bridge Road
Lambeth
London
United Kingdom
SE1 7EH

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

Study participating centre
Burnley General Hospital
Casterton Avenue

Burnley
United Kingdom
BB10 2PQ

Study participating centre
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Sunderland Royal Hospital
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
Liverpool Women's Hospital
Crown Street
Liverpool
United Kingdom
L8 7SS

Study participating centre
West Middlesex University hospital
Twickenham Road
Isleworth
United Kingdom
TW7 6AF

Study participating centre
Norfolk and Norwich Hospital
Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre
Royal Preston
Sharoe Green Lane North
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre
Princess Anne Hospital
Coxford Road
Southampton
Southampton
United Kingdom
SO16 5YA

Study participating centre
The Princess Royal Hospital, Telford
Apley Castle
Apley
Telford
United Kingdom
TF1 6TF

Study participating centre
St James's University Hospital Leeds
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Leeds General Hospital
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
Royal Cornwall Hospital
Treliske

Truro
United Kingdom
TR1 3LQ

Sponsor information

Organisation
Birmingham Womens NHS Foundation Trust

Sponsor details
Mindelsohn Way
Edgbaston
Birmingham
England
United Kingdom
B15 2TG

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/056ajev02

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

Analysis and write up should be completed by June 2019 and will be disseminated accordingly:
1. Guidelines: The information is expected to be rapidly incorporated into guidelines by the RCOG, and NICE, and disseminated to maternity units for implementation.
2. Lay information resources: Production of lay information with links to appropriate maternity organisations, particularly the National Childbirth Trust (NCT) and the NHS Choices. Lay information will describe the circumstances for intervention, and the advantages of the higher oxytocin rate, if found beneficial. Results will be posted on the website and disseminated widely using social media.
3. Conferences: The findings will be presented and disseminated via the British Maternal Fetal Medicine Society(BMFMS), RCOG and other national and international conferences.
Peer reviewed publications: The results of the trial will be published in a high impact peer reviewed Journal as an Open Access publication. We will disseminate the completed paper to the Department of Health, the Scientific Advisory Committees of the RCOG and the RCM.
NIHR Journals Library: If funded, the NIHR Journals Library will help with dissemination of findings and will provide an important, permanent and comprehensive record of the study.
4. Media: In consultation with the investigators and appropriate journal, a press release will be issued to the media upon publication of the results. The pilot study has already been the subject of an interview on BBC Radio 4 'Woman's Hour'.
5. Education: via RCM CPD courses, and the Obstetrician and Gynaecologist (TOG) midwives and doctors will be updated.

Results of the study will be shared with staff members at research sites and other related trials in the area and we will provide a generic results presentation. A formal notification to the ethics committee, MHRA, the manufacturing authorisation holder and sponsors will be made. Outreach to other key stakeholders (trial networks, health advocates) involved in related trials is planned.

The trial team has key individuals to optimise the dissemination of results. The Chair of Intrapartum Care CSG (Sara Kenyon), the Honorary Secretary of the BMFMS (Tracey Johnston) and the Editor in Chief of The Obstetrician and Gynaecologist (TOG) (Jason Waugh), Associate Editor of Archives of Diseases in Childhood (Andy Ewer) and a NCT volunteer (Ruth Hewston) are all co-applicants.

Intention to publish date

31/05/2020

Individual participant data (IPD) sharing plan

The data sharing plans for the current study 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?
HRA research summary			20/09/2023	No	No