High Or low dose Syntocinon® for delay in labour

Submission date	Recruitment status No longer recruiting	[X] Prospectively registered		
11/07/2016		☐ Protocol		
Registration date 03/08/2016	Overall study status Completed Condition category Pregnancy and Childbirth	Statistical analysis plan		
		Results		
Last Edited		Individual participant data		
20/09/2023		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

University of Birmingham Edgbaston Birmingham United Kingdom B15 2TT 0121 415 8298 HOLDS@trials.bham.ac.uk

Additional identifiers

EudraCT/CTIS number 2015-005537-50

IRAS number

ClinicalTrials.gov number

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

V2.0,111A110JCCC. 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 \times 5iu ampoules in 50mls or 500mls and those to the high dose a solution

containing 2 \times 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

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
- 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