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A pilot study to understand the best way of applying antiseptic to women in labour and newborn babies to reduce the spread of bacteria

Submission date 15/02/2022	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 26/05/2022	**Overall study status** Completed	[X] Statistical analysis plan [_] Results
Last Edited 24/09/2024	**Condition category** Neonatal Diseases	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

This is a pilot study to assess the best way to apply antiseptic to mothers in labour and newborn babies. The antiseptic aims to reduce the amount of potentially harmful bacteria on the skin of newborn babies. Reducing the bacteria might be useful for preventing infections which are transmitted from mother to baby during and after labour.

This study aims to find out the best type and concentration of antiseptic to use, as well as how often it should be applied and whether it should be applied to the genital tract of women in labour or to the skin of newborn babies. In this pilot study, the researchers will investigate the amount of bacteria babies have on their skin and women have in their genital tract, and look carefully at whether, and how often, skin reactions to antiseptic occur.

The antiseptics tested in this study are called chlorhexidine and octenisept. Chlorhexidine has been used widely across the world for many decades to reduce the risk of babies dying from infection. For example, it is put on the umbilical cord of newborn babies at home in areas with high rates of deaths from infections. It is also used in labour to clean the birth canal, including before caesarean section. Octenisept is used across Europe to clean the skin of new born babies in neonatal units and also as treatment for vaginal infection in women.

However, it is not known whether applying chlorhexidine or octenisept to the birth canal of women in labour or the skin of newborn babies could reduce the risk of infection and death in newborn babies.

Who can participate?

Women presenting in labour at any gestation with or without rupture of membranes, and newborn infants born in the hospital within the last 12 hours, weighing over 1000g and not born to enrolled women.

What does the study involve?

All women and newborns will receive routine hospital care as laid out in local policies and guidelines for all procedures, except for the interventions of the study including antiseptic

application and the study's clinical and microbiological (bacterial) assessments. Labouring women and neonates will be randomly allocated into one of the seven groups. Participants, other than those allocated to the control group, will be treated with either 1% chlorhexidine (CHG), 2% CHG or 0.1% octenisept at different frequencies. For the women the antiseptic will be applied to the vagina and perineum. Participants will receive the intervention according to the frequency schedule they were assigned to (either a single application or 4 hourly during working hours, up to 6 applications), aligned with the routine vaginal examinations during labour. For the newborns the antiseptic will be applied to the whole body excluding the face and eyes. In addition, the skin of the newborns will be closely monitored for any signs of side effects to the antiseptic. Applying an antiseptic can make neonates colder and can sometimes cause skin reactions. This study will look at the balance between reducing the number of bacteria and safety.

What are the possible benefits and risks of participating?
Entering this study may not directly benefit participants. However, the information from the study will help to work out the best way to use antiseptics to prevent infections in other newborns in the future, as infections remain one of the leading causes of death in the neonatal population.

Where is the study run from?
1. St George's, University of London (UK)
2. Zomba Central Hospital (Malawi)
3. Malawi-Liverpool Wellcome Trust, Blantyre (Malawi)

When is the study starting and how long is it expected to run for?
October 2020 to August 2023

Who is funding the study?
MRC/NIHR/DfID/Wellcome Joint Global Health Trials Call 9 – Trial Development Grant & MRC Core Funding (MRC CTU at UCL) (UK)

Who is the main contact?
1. Prof. Mike Sharland, msharland@sgul.ac.uk
2. Caroline Albrecht, calbrech@sgul.ac.uk

Study website
http://cnpi-amr.org/research/neovtamr/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Strategies to reduce the vertical transmission of multi-drug resistant pathogens to neonates (NeoVT-AMR)

Acronym
NeoVTAMR

Study objectives
Topical antiseptic use leads to greater reductions in bacterial colonisation in both mothers and neonates compared to control. Reduction is greater at higher frequency of application and at higher concentration of
antiseptic.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 05/05/2021, Kamuzu University of Health Sciences (formerly College Of Medicine) Research and Ethics Committee (Mahatma Gandhi Road, Chimutu Building Room # 822, P/Bag 360 Chichiri, Blantyre 3, Malawi; +265 (0)1 871 911/01 874 377; comrec@medcol.mw), ref: P.01 /21/3248
2. Approved 05/08/2021, St George’s, University of London Research Ethics Committee (Research Ethics and Integrity Officer, Joint Research and Enterprise Services (JRES), St George's, University of London & St George's University Hospitals NHS Foundation Trust, Cranmer Terrace, Tooting, London, SW17 0RE, UK; +44 (0)208 725 6488; akristek@sgul.ac.uk), ref: 2020.0344

Study design
Factorial randomized controlled pilot trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Prevention of infection in neonates

Interventions
Randomisation is by permuted blocks to guard against bias introduced over time, such as outbreaks of pathogenic bacteria in the hospital.

Maternal:
Chlorhexidine gluconate (CHG) (1% or 2%) or Octenisept (OHP) vaginal and perineal application in varying frequency (once only or 4 hourly during labour), compared to control group with clean water application. Treatment will continue until 32 hours or birth. A factorial randomised design is used, with a 1:1:1:1:1:1:1 allocation into six interventions and one control arm:
1. 1% CHG once only
2. 1% CHG multiple application
3. 2% CHG once only
4. 2% CHG multiple application
5. OHP once only
6. OHP multiple application
7. Control group (clean water)

Neonatal:
Chlorhexidine gluconate (CHG) (1% or 2%) or Octenisept (OHP) whole-body application in varying frequency (once only or 24 hourly), compared to the control group with routine care. Treatment will continue until 72 hours or discharge (whichever is sooner). A factorial randomised design is used, with a 1:1:1:1:1:1:1 allocation into six interventions and one control arm:
1. 1% CHG once only
2. 1% CHG multiple application
3. 2% CHG once only
4. 2% CHG multiple application
5. OHP once only
6. OHP multiple application
7. Control group (routine care)

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Chlorhexidine 1%, chlorhexidine 2%, Octenisept (0.1% octenidine and 2% 2-phenoxyethanol)

Primary outcome measure
Individual follow up during hospital admission up to discharge in both strata and final follow 28 days after enrolment (by phone if already discharged):

Mothers:
Vaginal and perineal bacterial load: change in colony-forming units (CFUs) in the vagina (one swab) and perineum (one swab) from randomisation (before antiseptic application) to each timepoint before birth or until 32 h (0, 4, 8, 24, 28, 32 h) of microbiology data collection (efficacy)

Neonates:
Skin bacterial load: change in colony-forming units (CFUs) in the neck (one swab) and peri-rectal (one swab) from randomisation (before antiseptic application) to each timepoint before discharge or until 72 h [0, 24, 48, 72 h] of microbiology data collection (efficacy)

Secondary outcome measures
Mothers:
1. Tolerability and safety assessed using the modified maternal toxicity score (score and grade) at timepoints before birth or until 32 h (0, 4, 8, 24, 28, 32 h). This score has four domains: one symptom (vaginal/vulval irritation) and three examination signs (redness, skin break down and swelling)
2. Skin bacterial load in neonates exposed to maternal antiseptic, compared to control, measured using colony-forming units (CFUs) in the neck (one swab) and peri-rectal (one swab) at swabs taken once after birth
3. Serious adverse events collected on case report forms at each visit during the inpatient stay, by checking the medical notes and then at the day 28 follow-up visit (over the phone or in person)

Neonates:
1. Safety assessed using adapted neonatal skin condition score (absolute score and grade). This score has three domains on examination (dryness, redness, skin breakdown). Measured at 0, 24, 48, 72 h or until discharge, whichever sooner
2. Temperature (change in absolute temperature and grade [hypothermia]). Axillary temperature is measured before and after antiseptic application and once a day in all groups
3. Serious adverse events collected on case report forms at each visit during the inpatient stay, by checking the medical notes and then at the day 28 follow-up visit (over the phone or in person)

Overall study start date
01/10/2020

Completion date
31/08/2023

Eligibility

Key inclusion criteria
Mothers:
1. Presenting in labour with or without rupture of membranes

Neonates:
1. Born in Zomba central hospital
2. Postnatal age at randomisation <12 hours
3. Birth weight >1000 g

Participant type(s)
Patient

Age group
Mixed

Lower age limit
18 Years

Sex
Both

Target number of participants
294

Total final enrolment
296

Key exclusion criteria
Mothers:
1. Under the age of 18 years (minor in Malawi)
2. Any contra-indication to digital vaginal examination
3. In active labour
4. Poor perineal and vaginal skin condition as judged by a clinician
5. Planned elective caesarean-section delivery
6. Known or suspected allergy to chlorhexidine or octenidine
7. Intrauterine death confirmed or expected before randomsiation
8. Antiseptic application or enrolment in the trial determined inappropriate in the opinion of the enrolling clinician
9. Any recent or planned (within 4 hours) iodine application to the perineum or vagina
10. Unable to obtain consent

Neonates:
1. Born by planned elective caesarean section
2. Born to mothers recruited in the trial
3. Poor skin condition (skin score of 2 or more in any of three domains at the time of enrolment)
4. Known congenital or acquired skin disorder or defect at the time of enrolment
5. Antiseptic application or enrolment in the trial determined inappropriate in the opinion of the enrolling clinician
6. Any recent or planned (within 4 hours) iodine application to the body
7. Any planned or previous lumbar puncture

Date of first enrolment
01/02/2022

Date of final enrolment
31/03/2023

Locations

Countries of recruitment
Malawi

Study participating centre
Zomba Central Hospital
M3
Zomba
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University/education

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ROR
https://ror.org/040f08y74

Funder(s)

Funder type
Research organisation

Funder Name
MRC/NIHR/DfID/Wellcome Joint Global Health Trials Call 9 – Trial Development Grant & MRC Core Funding (MRC CTU at UCL)

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal. This will be published on an open-access platform. Publications include papers (including abstracts) for presentation at national and international meetings. Results of publicly-funded research should be freely available, manuscripts arising from the trial will, wherever possible, be submitted to peer-reviewed journals which enable open access via UK PubMed Central (PMC) within 6 months of the official date of final publication.

Intention to publish date
30/12/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request from Prof. Mike Sharland (neovtamr@sgul.ac.uk). Due to the potential sensitivity of the data, the data will be made available on a controlled access basis, with descriptive information on the data publicly available on clinical trial and institutional repositories along with information on how researchers will be able to access the data. This will normally be at the approval of the trial management group, in accordance with St George's, University of London policy for controlled data access. Controlled access data will be shared under standard data-sharing agreements. Prior to sharing all data will be made anonymous. Trial participants will be consented for anonymous sharing of their data at the point of recruitment.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 6.0	10/03/2023	26/06/2024	No	No
Statistical Analysis Plan	version 1.0	10/05/2023	26/06/2024	No	No