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Comparison between two antibiotic schemes to improve the results in patients with premature rupture of membranes

Submission date
16/08/2023

Recruitment status
No longer recruiting

Registration date
29/08/2023

Overall study status
Completed

Last Edited
29/08/2023

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Premature rupture of membranes (PROM) is a pregnancy complication when your water breaks before labor starts. The treatment scheme of choice in patients with PROM before 34 weeks, who do not present an infection within their amniotic cavity (intraamniotic infection), is not entirely clear. The national standards of Chile indicate that two antibiotics should be used together. There may be a better rate of absence of intraamniotic infection after treatment with three antibiotics together, reaching a broad spectrum of coverage against germs. Keeping the amniotic cavity free of infection is a determining factor in the management of this type of patient since it improves perinatal health. The aim of this study is to evaluate which antibiotic scheme (a regimen of two antibiotics, ampicillin and erythromycin, versus a regimen of three antibiotics, ceftriaxone, metronidazole and clarithromycin) has better results in maintaining the intraamniotic cavity without infection.

Who can participate?
Women over 18 years of age who are pregnant between 24+0 and 32+6 weeks of single live gestation, with PROM and without intraamniotic infection

What does the study involve?
Patients will be randomly divided into two groups (a regimen of two antibiotics, ampicillin and erythromycin, versus a regimen of three antibiotics, ceftriaxone, metronidazole and clarithromycin). Antibiotics will be administered for 10 days and after 48 to 72 days of finishing the antibiotics, a new test of intrauterine infection will be carried out. The latency of both antibiotic schemes (the days that elapse between starting the antibiotics and the birth), the perinatal results of the newborn and eventual maternal compromises are also measured.

What are the possible benefits and risks of participating?
As both antibiotic schemes are approved for use in pregnant women, patients will not be exposed to risks. However, by agreeing to participate in the study, they must undergo a study of amniotic fluid after the use of antibiotics, which adds an associated risk since this analysis is performed with a sample of amniotic fluid obtained by amniocentesis (puncture of the uterus

until reaching the amniotic cavity and obtaining amniotic fluid). Among the risks associated with this procedure is the possibility of triggering labor or producing bleeding within the amniotic cavity or causing injuries to the umbilical cord or directly to the fetus, but all these possible complications occur in less than 1% of cases. On the other hand, by agreeing to participate, they will be able to help determine with a better basis and scientific evidence whether using a new antibiotic therapy scheme that has greater coverage against germs improves the results both for them and for their fetuses.

Where is the study run from?
Padre Hurtado Hospital (Chile)

When is the study starting and how long is it expected to run for?
May 2021 to December 2024

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Rodrigo Benitez Penroz, rodrigo.benitezpenroz@gmail.com

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil Known

Secondary identifying numbers
16943243

Study information

Scientific Title
Comparison between triassociated and biassociated antibiotic scheme in patients with premature rupture of membranes between 24+0 and 32+6 weeks, with negative amniocentesis for intra-amniotic infection: a multicenter randomized prospective study (TRIBIAN)

Acronym
TRIBIAN

Study objectives
The triassociated antibiotic scheme has better results in patients with PROM under 33 weeks with negative amniocentesis for intraamniotic infection (IAI), in terms of persistence of the absence of IAI and increased latency period compared to the biassociated scheme

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 20/05/2022, Cómite De Etica Servicio De Salud Metropolitano Sur Oriente (Camino Las Lavandulas 7984, Santiago, 8340267, Chile; +56 (0)225762401, +56 (0)225765163; comiteeticocientifico@ssmso.cl), ref: 78283446

Study design
Multicenter interventional randomized trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)

Hospital

Study type(s)
Treatment

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
Antibiotic treatment in patients with preterm premature rupture of membranes, less than 33 weeks

Interventions
Participants are randomized using the Excel program and their national identification document into two groups. Group A is managed with biassociated antibiotics: (first 48 hours) ampicillin 1 g every 6 hours intravenously + erythromycin 500 mg every 6 hours po, after 48 hours of treatment ampicillin is changed to amoxicillin 500 mg every 8 hours until completing 10 days of treatment. Group B will be managed with a triassociated antibiotic regimen (ceftriaxone 2 g intravenously every 24 hours, metronidazole 500 mg intravenously every 8 hours, clarithromycin 500 mg every 12 hours orally. After 10 days of treatment, 72 hours will be waited to perform a control amniocentesis and thus compare what percentage of each group remained without intraamniotic infection

Intervention Type
Other

Primary outcome measure
Control amniocentesis after antibiotic treatment and comparison of infection parameters, such as glucose, cell count, GRAM test and cell culture, at 14 days after the start of antibiotic treatment (10 days of antibiotics and 72 hours after the end, the new amniotic fluid analysis will be performed).

Secondary outcome measures
1. The latency period (the period that elapses from diagnosis to delivery): comparison between the date of initiation of antibiotic therapy and the date of birth on the birth certificate
2. The need for respiratory support in the newborn (NB) recorded in clinical records in the first 30 days of life
3. The prevalence of premature abruption of the placenta with normal insertion: clinical diagnosis recorded in the clinical record by the obstetrician or midwife who attends the delivery or caesarean section in the first 6 hours postpartum
4. The prevalence of neonatal necrotizing enterocolitis during the first 30 days of life, through clinical-radiological diagnosis
5. The prevalence of neonatal sepsis during the first 30 days of life, by clinical diagnosis made by a neonatologist using the Kaiser Permanente research classification"Neonatal Early-Onset Sepsis Calculator
6. The hospital stay in the neonatal intensive care unit during the first 30 days of life, through clinical records
7. The prevalence of clinical choriamyonitis diagnosed using Gibbs criteria from the start of antibiotic treatment until delivery
8. Maternal mortality from the moment of diagnosis until 42 days postpartum, evaluated by

death certificate
9. Neonatal mortality from the moment of diagnosis until 28 days of life, evaluated by death certificate
10. The prevalence of puerperal endometritis using clinical diagnosis for the first 30 days after delivery
11. The reason for terminating the pregnancy (scheduled interruption of pregnancy vs emergency due to an added diagnosis, determined by evaluating clinical records)

Overall study start date
01/05/2021

Completion date
20/12/2024

Eligibility

Key inclusion criteria
1. Pregnant women between 24+0 and 32+6 weeks
2. Diagnosis of premature rupture of membranes
3. Negative admission amniocentesis for intra-amniotic infection

Participant type(s)
Patient

Age group
All

Lower age limit
18 Years

Upper age limit
50 Years

Sex
Female

Target number of participants
60 patients, 30 in each group

Key exclusion criteria
1. Patients outside the gestational age range
2. Positive admission amniocentesis for intra-amniotic infection
3. Concomitant infectious process that requires antibiotics (e.g. COVID-19; pyelonephritis, bacterial pneumonia, tonsillitis or another that requires antibiotic use)
4. Patient with a history of recent use of antibiotics in the last 10 days
5. Patient allergic to any of the antibiotics proposed in the different schemes
6. Patient undergoing multiple pregnancy
7. Patients who do not wish to participate and therefore do not sign the informed consent

Date of first enrolment

20/05/2022

Date of final enrolment
20/11/2024

Locations

Countries of recruitment
Chile

Study participating centre
Hospital Padre Hurtado
Esperanza 2150
San Ramon
Santiago
Chile
8880465

Study participating centre
Hospital La Florida
Froilán Roa 6542
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Sponsor information

Organisation
Hospital Padre Hurtado

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Sponsor type
Hospital/treatment centre

Website

http://www.hph.cl/

ROR
https://ror.org/03b3qq257

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
28/02/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Dr Rodrigo Benitez Penroz (rodrigo.benitezpenroz@gmail.com)

The type of data that will be shared: The tabulation of the data will be able to be shared.
Dates of availability: After the publication of the study.
Whether consent from participants was required and obtained: Informed consent is required and the patient enters the study only if she has previously accepted and signed it.
Any ethical or legal restrictions: The study is approved by the ethics committee and has no particular ethical restrictions.

IPD sharing plan summary
Available on request