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Reduced antibiotic use and hospital stay in newborns with sepsis after implementation of new guidelines

Submission date
25/05/2020

Recruitment status
No longer recruiting

Registration date
28/05/2020

Overall study status
Completed

Last Edited
23/11/2020

Condition category
Neonatal Diseases

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

Plain English summary of protocol

Background and study aims
Sepsis is a life-threatening reaction to an infection, and early-onset sepsis (EOS) is a potentially life-threatening complication of birth. Clinical symptoms are often unspecific and biomarkers have low predictive values for EOS. Therefore, clinical suspicion often leads to antibiotic treatment in newborns with a negative blood test. Overuse of antibiotics may lead to increased antibiotic-resistant bacteria. Antibiotic treatment in term newborns has also been associated with increased risks of asthma, wheezing, food allergy and childhood obesity. The aim of this study is to find out whether an intervention could reduce unwarranted antibiotic use in a safe way in term newborns with culture-negative sepsis.

Who can participate?
All term newborns (week 37 + 0 to week 41 + 6) treated for EOS at Ryhov Hospital, Jönköping, Sweden before (period 1: 2016-2017) and after the intervention (period 2: 11 June 2018 to 30 September 2019). In the study, EOS was defined as onset of symptoms within 72 hours of life.

What does the study involve?
The intervention includes new treatment guidelines including C-reactive protein- and clinical symptoms-guided decision-making and shorter intravenous antibiotic treatment in term newborns meeting the criteria of the new treatment guidelines. Before the new guidelines were introduced, newborns with EOS used to be treated with at least seven days of intravenous antibiotics at the neonatal intensive care unit. According to the new treatment guidelines, the intravenous antibiotic therapy can be withdrawn after three days followed by administration of oral suspension antibiotic (amoxicillin, 20 mg/kg three times a day) for two more days in term newborns meeting the criteria of the new treatment guidelines. In the study newborns with EOS receive benzylpenicillin 50 mg/kg every 8-12 hours and amikacin 15 mg/kg every 24 hours. The new guidelines contain the following criteria: term newborn (week 37 + 0 to week 41 + 6), no need for intensive care (including invasive respiratory [breathing] support or cardiovascular [heart] support) initially when the antibiotic treatment started, the newborn appears well on day

3, the blood culture is not positive on day 3 and maximum CRP value of 80 mg/l decreasing by at least 50% during the first three days. In the study, newborns with EOS meeting the criteria of the guidelines are compared before and after the implementation of the guidelines.

What are the possible benefits and risks of participating?
Reduced antibiotic use may lead to fewer side effects of antibiotic treatment and a shorter hospital stay which is beneficial for the patient. Reduced antibiotic use may potentially increase the risk of reinfection or readmission in infected newborns.

Where is the study run from?
Ryhov Hospital (Sweden)

When is the study starting and how long is it expected to run for?
February 2018 to May 2020

Who is funding the study?
This study was financed by Ryhov County Hospital, Futurum - the academy for healthcare, Region Jönköping County, and grants from the Swedish state under an agreement between the Swedish government and the county council, the ALF agreement

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number
dnr 2018/503-31

Study information

Scientific Title
C-reactive protein- and clinical symptoms-guided strategy in term neonates with early-onset sepsis reduced antibiotic use and hospital stay

Study objectives
It is hypothesized that the implementation of the new treatment guidelines would lead to reduced antibiotic use, hospital stay and healthcare costs, with no reinfection in a cohort of term infants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/11/2018, The regional ethical committee of Linköping (Etikprövningsmyndigheten, Box 2110, 750 02 Uppsala Sweden; +46 (0)10 4750808; registrator@etikprovning.se), ref: dnr 2018/503-31

Study design
Single-centre before and after interventional study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Early-onset sepsis in term neonates

Interventions
The intervention includes new treatment guidelines introduced on 11 June 2018. The researchers decided a priori to evaluate the guidelines by comparing data from 24 months before and 15-16 months after the introduction of the guidelines after they did a sample size calculation. Period 1 was between 1 January 2016 and 31 December 2017 and period 2 was between 11 June 2018 and 30 September 2019. Infants born during period 1 were considered a control group. The guidelines include C-reactive protein- and clinical symptoms-guided decision-making and shorter intravenous antibiotic therapy. According to the new treatment guidelines, the intravenous antibiotic therapy (benzylpenicillin 50 mg/kg every 8-12 h and amikacin 15 mg /kg every 24 h) can be withdrawn after three days followed by administration of oral suspension antibiotic (amoxicillin, 20 mg/kg three times a day) for two more days in term neonates meeting the criteria of the new treatment guidelines.

The new guidelines contain the following criteria:
1. Term neonate (week 37 + 0 to week 41 + 6)
2. No need for intensive care (including invasive respiratory support or cardiovascular support) initially when the antibiotic treatment started
3. The neonate appeared well on day 3
4. The blood culture was not positive on day 3
5. Maximum CRP value of 80 mg/l decreasing by at least 50% during the first 3 days

Before the new guidelines were introduced, neonates with both culture-positive and culture-negative early-onset sepsis used to be treated with at least seven days of intravenous antibiotics at the neonatal intensive care unit.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Amoxicillin, amikacin, benzylpenicillin

Primary outcome(s)
The number of days with antibiotic treatment, collected retrospectively from medical records for Period 1 between 1 January 2016 and 31 December 2017 and period 2 between 11 June 2018 and 30 September 2019

Key secondary outcome(s))
1. Reinfection or readmission to hospital within 3 days after completed antibiotic treatment
2. Hospital stay
3. Healthcare costs calculated based on the cost per day of care
Data collected retrospectively from medical records for Period 1 between 1 January 2016 and 31 December 2017 and period 2 between 11 June 2018 and 30 September 2019

Completion date
19/05/2020

Eligibility

Key inclusion criteria
1. Term neonates in gestational week 37 + 0 to week 41 + 6
2. Clinically diagnosed as early-onset sepsis that had initiated antibiotic treatment within 72 h of life

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Neonate

Sex
All

Total final enrolment
237

Key exclusion criteria
Term neonates who received prophylactic antibiotic treatment and not because of early-onset sepsis

Date of first enrolment
01/01/2016

Date of final enrolment
30/09/2019

Locations

Countries of recruitment
Sweden

Study participating centre
Ryhov Hospital
Barn- och ungdomsmedicinska kliniken
Länssjukhuset Ryhov
Jönköping
Sweden
553 05

Sponsor information

Organisation
Ryhov County Hospital

Funder(s)

Funder type
Hospital/treatment centre

Funder Name

Ryhov County Hospital

Funder Name
The Swedish state under the agreement between the Swedish government and the county councils, the ALF agreement

Funder Name
Futurum - the academy for healthcare, Region Jönköping County

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are not publicly available due to the ethics committee specifically stating that no data which can identify a patient can be publicly available but are available from the corresponding author Johan Gyllensvärd (johan.gyllensvard@rjl.se) on reasonable request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	20/11/2020	23/11/2020	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes