Clinical trial results:
Antibiotic Prophylaxis and Intervention for Postpartum Infections following Caesarean Section

Summary

EudraCT number	2012-002068-29
Trial protocol	DK
Global end of trial date	30 April 2015

Results information

Result version number	v1 (current)
This version publication date	09 October 2021
First version publication date	09 October 2021
Summary attachment (see zip file)	Unpublished data (UnpublishedData_220819.pdf)

Trial information

Trial identification

Sponsor protocol code	1-09-09-2012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02072798
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Southern Denmark
Sponsor organisation address	Kloevervaenget 10, 10. floor, Odense, Denmark, 5000
Public contact	Nana Hyldig, Odense University Hospital, 0045 64415156, nana.hyldig@ouh.regionsyddanmark.dk
Scientific contact	Nana Hyldig, Odense University Hospital, 0045 64415156, nana.hyldig@ouh.regionsyddanmark.dk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2015
Global end of trial reached?	Yes
Global end of trial date	30 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main large-scale trial was altered into a smaller pilot study with the object to investigate the timing of prophylactic antibiotics in women undergoing CS, with particular focus on maternal and neonatal outcomes

Protection of trial subjects:

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Background therapy:

Participants in both groups received a single dose of intravenous cefuroxime 1.5 g dissolved in 100 ml NaCl. Cefuroxime, a second-generation cephalosporin, is the standard prophylaxis recommended in the Danish National Guidelines and has been selected because it is active against streptococci, staphylococci, and most enterobacteria.

Evidence for comparator:

The effect of prophylactic antibiotics is optimal if the dose is administrated in the hour before the surgical incision, and the risk can be reduced further if the antibiotic is administrated in the 30 minutes prior to incision. Administration more than two hours before or after the incision increases the risk of SSI due to insufficient concentration of antibiotics in the surgical field. However, previously the recommendation was a single dose of antibiotic administered immediately after umbilical cord clamping, rather than preoperatively, to avoid placental transfer. Subsequently, individual studies and systematic reviews have demonstrated that pre-incision antibiotic prophylaxis compared to that after cord clamping is advantageous for the mother with no apparent disadvantage to the neonate. As a result, countries such as the United States, England and Canada have changed their national guidelines recommending that the timing should be 15 to 60 minutes prior to skin incision. The neonatal outcomes most frequently studied are neonatal sepsis, neonatal septic work-up and admission to the special care baby unit. No studies report on placental transfer of antibiotics, the possible effects on the neonatal gut micobiome, or long-term follow-up.

Actual start date of recruitment	28 January 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research, Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	42
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All women giving brith by elective CS at Odense University Hospital were informed the day before her planned elective CS by a project nurse, who handed out written together with oral information. Women declining participation received iv. Cefuroxim 1,5g post umbilical cord clamping, as standard practice at the time of the project.

Pre-assignment

Screening details:

Inclusion criteria: Age ≥ 18 year, able to read and understand Danish, gestation age ≥ 28 weeks, BMI < 30 kg/m2.
Exclusion criteria: Hypersensitivity to cephalosporin antibiotics, previous severe reaction to penicillin, systemic exposure to any antibiotic agent within 1 week before CS, very sick newborn infants treated with antibiotic.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

The pilot study is a non-blinded RCT because we only want to collect blood samples from infants delivered by mothers in the intervention group. Thus, to avoid taking blood sample from infants in the control group, the study was unblinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention arm

Arm description:

Participants in the intervention arm was given 1500 mg iv Cefuroxim administrated 15 to 60 minuts before the caesarean section incision was made.

Arm type	Experimental
Investigational medicinal product name	Cefuroxime
Investigational medicinal product code	
Other name	cephalosporin
Pharmaceutical forms	Concentrate and solvent for intravesical solution
Routes of administration	Intravenous use

Dosage and administration details:

Cefuroxime is a second-generation cephalosporin. The summery product characteristics (SPC) of cefuroxime is described at the Danish Health and Medicines Authority’s webpage www.produktresume.dk

The woman in the intervention group was given 1500 mg iv Cefuroxime dissolved in 100 ml NaCl administrated 15 to 60 minutes before the surgical incision.

Arm title	Control arm

Arm description:

Participants in the control arm was given 1500 mg iv Cefuroxime after after umbilical cord clamping as current practice at the time of the study.

Arm type	Active comparator

Investigational medicinal product name	Cefuroxime
Investigational medicinal product code	
Other name	cephalosporin
Pharmaceutical forms	Concentrate and solvent for intravesical solution
Routes of administration	Intravenous use

Dosage and administration details:

Cefuroxime is a second-generation cephalosporin. The summery product characteristics (SPC) of cefuroxime is described at the Danish Health and Medicines Authority's webpage www.produktresume.dk

The woman in the control group was given 1500 mg iv Cefuroxime dissolved in 100 ml NaCl administrated after umbilical cord clamping.

Number of subjects in period 1	Intervention arm	Control arm
Started	22	20
Completed	22	20

Baseline characteristics

Reporting groups	
Reporting group title	Intervention arm
Reporting group description:	
Participants in the intervention arm was given 1500 mg iv Cefuroxim administrated 15 to 60 minuts before the caesarean section incision was made.	
Reporting group title	Control arm
Reporting group description:	
Participants in the control arm was given 1500 mg iv Cefuroxime after after umbilical cord clamping as current practice at the time of the study.	

Reporting group values	Intervention arm	Control arm	Total
Number of subjects	22	20	42
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	31.5	31.6	
standard deviation	± 5.0	± 4.8	-
Gender categorical			
All participants were women			
Units: Subjects			
Female	22	20	42
Male	0	0	0

End points

End points reporting groups

Reporting group title	Intervention arm
Reporting group description:	
Participants in the intervention arm was given 1500 mg iv Cefuroxim administrated 15 to 60 minuts before the caesarean section incision was made.	
Reporting group title	Control arm
Reporting group description:	
Participants in the control arm was given 1500 mg iv Cefuroxime after after umbilical cord clamping as current practice at the time of the study.	

Primary: maternal infectious morbidity

End point title	maternal infectious morbidity
End point description:	
End point type	Primary
End point timeframe:	
from time of caesarean section undtil 30 days after surgery	

End point values	Intervention arm	Control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	20		
Units: number	2	7		

Statistical analyses

Statistical analysis title	logistic regression
Comparison groups	Intervention arm v Control arm
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Regression, Logistic
Parameter estimate	Risk ratio (RR)
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	1.12

Adverse events

Adverse events information	
Timeframe for reporting adverse events: The day of caesarean section until 30 days after surgery	
Assessment type	Systematic

Dictionary used	
Dictionary name	non
Dictionary version	0

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Serious adverse events	overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 42 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 42 (9.52%)		
Pregnancy, puerperium and perinatal conditions			
Bleeding time abnormal	Additional description: Bleeding from the vagina the first few days after caesarean section.		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2013	The trial was original designed to investigate "Antibiotic prophylaxis and Intervention for postpartum infections following caesarean section" with focus on mothers giving birth by caesarean section. Due to lack of funding the trial was redesigned to be a a feasibility study with focus on the newborn infants: "Antibiotics and gut microbiota among newborn infants".

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31053348

http://www.ncbi.nlm.nih.gov/pubmed/27240549