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PROPranolol eye DROPs in newborns with retinopathy of prematurity (DROP-PROP)

Submission date
16/01/2014

Recruitment status
No longer recruiting

Registration date
27/03/2014

Overall study status
Completed

Last Edited
30/01/2017

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
A previous study has shown that oral propranolol is effective in preventing the progression of a disease of the eye called retinopathy of prematurity (ROP) in preterm newborns, but its safety is not sufficient. Therefore we have developed a topical delivery system and the aim of the present study is to evaluate the safety and efficacy of propranolol eye drops in preterm newborns with a precocious stage of ROP.

Who can participate?
Preterm newborns (gestational Age 23-32 weeks) with a stage 2 ROP (zone II without plus) who are admitted to the neonatal care units contributing to the study (Neonatal Intensive Care Unit, A. Meyer University Childrens Hospital of Florence and Institute of Pediatrics and Neonatology, Fondazione IRCCS Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, University of Milan) will be considered for enrolment.

What does the study involve?
All the enrolled newborns will receive propranolol. It will be applied in each eye, three times daily (every 8 hours). The treatment will continue until the complete development of retinal vascularization, but no more than 60 days.

What are the possible benefits and risks of participating?
Eye drops propranolol is considered to be effective in counteracting the progression of ROP if the treatment decreases the rate of progression from stage 2 ROP to more severe stage ROP (stage 2 or 3 with plus) from actual 38% to 19% or less. Additionally, in order to verify the treatment safety, the propranolol concentrations will be measured on dried blood spots at the steady state (10th day). The main risk of receiving eye drops propranolol is represented by the development of adverse events (i.e. bradycardia, bronchospasm, severe hypotension), similar to those occurring after oral administration. Therefore cardiovascular and respiratory parameters will be continuously monitored and blood samplings checking metabolic, renal and liver functions, as well as the evaluation of cardiac function, will be periodically performed.

Where is the study run from?
Neonatal Intensive Care Unit, A. Meyer University Childrens Hospital of Florence and Institute of

Pediatrics and Neonatology, Fondazione IRCCS Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, University of Milan (Italy)

When is the study starting and how long is it expected to run for?
The overall duration of the study will be 2 years, with the goal of enrolling 55 preterm newborns.

Who is funding the study?
A. Meyer University Children's Hospital (Italy)

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)
2013-002062-39

ClinicalTrials.gov (NCT)
NCT02014454

Protocol serial number
N/A

Study information

Scientific Title
Safety and efficacy of PROPranolol eye DROPs in newborns with retinopathy of prematurity (DROP-PROP)

Acronym
DROP-PROP

Study objectives
We have recently verified that oral propranolol is effective in preventing retinopathy of prematurity (ROP) progression in preterm newborns, but the safety of systemic administration is not adequate. In order to decrease the plasma propranolol concentrations and the adverse events, we have developed a topical delivery system. The aim of the present study is to evaluate the safety and efficacy of propranolol eye drops in preterm newborns with a precocious stage of ROP.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Pediatric Regional Ethics Committee (Comitato Etico Pediatrico Regionale) affiliated to Pediatric Ethics Committee of the Region of Tuscany (Comitato Etico Pediatrico Regionale/Regione Toscana), 24/07/2013

Study design
Interventional open-label phase 2 multicenter study

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Retinopathy of prematurity

Interventions
All the enrolled preterm newborns will receive propranolol as ophthalmic solution (0.1%): 3 microdrops of 6 µL propranolol solution (= 6 µg propranolol/microdrop) will be topically applied with a calibrated pipette, in each eye, three times daily (every 8 hours).The treatment will continue until the complete development of retinal vascularization, but no more than 60 days. The propranolol treatment will be always associated to the conventional approach adopted by the ETROP Cooperative Group.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Propranolol

Primary outcome(s)
1. Incidence rate of progression from stage 2 ROP to more severe stage ROP (stage 2 or 3 with plus, stage 4 and stage 5), evaluated by ophthalmologic examinations at baseline and at least

weekly, until the resolution of ROP
2. Plasma concentrations of propranolol at the steady state, measured on the 10th day of treatment by dried blood spots

Key secondary outcome(s))
1. Number of newborns who progress to Stage 3 without plus ROP
2. Number of newborns who progress to Stage 4 or 5 ROP with total or partial retinal detachment
3. Number of newborns who need laser treatment
4. Number of newborns who need rescue treatment with bevacizumab
5. Number of newborns who need vitrectomy
6. Collection of adverse events due to eye drop propranolol treatment

Secondary outcomes will be evaluated by ophthalmologic examinations at baseline and at least weekly, until the resolution of ROP.

Completion date
01/11/2015

Eligibility

Key inclusion criteria
1. Preterm newborns (gestational age 23-32 weeks) with stage 2 ROP, zone II without plus
2. A signed parental informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Key exclusion criteria
1. Newborns with heart failure
2. Newborns with congenital cardiovascular anomalies, except for persistent ductus arteriosus, patent foramen ovale and small ventricular septal defects
3. Newborns with recurrent bradycardia (heart rate < 90 beat per minute)
4. Newborns with second or third degree atrioventricular block
5. Newborns with hypotension
6. Newborns with renal failure
7. Newborns with actual cerebral haemorrhage
8. Newborns with other diseases which contraindicate the use of beta-adrenoreceptor blockers

Date of first enrolment
01/11/2013

Date of final enrolment
01/11/2015

Locations

Countries of recruitment
Italy

Study participating centre
A. Meyer University Childrens' Hospital
Florence
Italy
50139

Sponsor information

Organisation
A. Meyer University Children's Hospital (Italy)

ROR
https://ror.org/01n2xwm51

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
A. Meyer University Children's Hospital (Italy)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Results article	results	01/02/2017		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes