ISRCTN74887957 https://doi.org/10.1186/ISRCTN74887957

Effectiveness of a sildenafil citrate suspension for pulmonary hypertension in children: a randomised pragmatic trial

Submission date	Recruitment status	[ ] Prospectively registered
30/01/2008	No longer recruiting	[ ] Protocol
Registration date	Overall study status	[ ] Statistical analysis plan
09/05/2008	Completed	[ ] Results
Last Edited	Condition category	[ ] Individual participant data
09/05/2008	Circulatory System	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Sildenafil citrate suspension versus sildenafil citrate powder paper for reduction of pulmonary hypertension in children during cardiac catheterisation: a randomised pragmatic trial

Study objectives
In Brazil, sildenafil citrate is the most accessible option for the treatment of PH and it is widely used in most hospitals. When licensing sildenafil for treatment of PH, the regulating agency kept it forbidden for people under 18 years old. In the absence of an appropriate pharmaceutical formulation for children, the staff usually crush the tablets to be added to liquid food. However, modifying a commercially available medication may lead to increased toxicity, undesirable side effects, decreased efficacy, poor patient compliance because of the medications taste and potential hazards to health care workers. Our study hypothesis is that a compounding suspension made by a pharmacist in controlled conditions will do better than the powder papers used in routine.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The project was submitted to the Ethics Committee of the Oswaldo Cruz Foundation (ref: CAAE - 0068.0.011.000-07) and will also be submitted to the Ethics Committee of every participating hospital.

Study design
Randomised pragmatic double-blind multicentre trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Pulmonary hypertension

Interventions
Power calculations:
60% of patients reduce at least 20% the mean pulmonary arterial pressure after using powder

papers of Sildenafil citrate (SC). To demonstrate that at least 80% of patients would present 20% reduction after using SC suspension with an alpha error of 5% and power of 80% it would be necessary to recruit 182 patients. The pilot intends to recruit 20 patients.

Disease information:
Pulmonary hypertension (PH) is a haemodynamic and clinic disease characterised by a progressive increase of pulmonary vascular resistance and a decrease of pulmonary vascular capacitance leading to right ventricular failure and death. It may occur in isolation (idiopathic pulmonary arterial hypertension) or it may be associated to a variety of systemic disorders (scleroderma, lupus, human immunodeficiency virus [HIV] infection) or cardiopulmonary pathologies such as congenital heart disease. PH is a rare condition and secondary pulmonary arterial hypertension prevalence is less than 0.0001% (statistics about secondary pulmonary hypertension, 2007). Although severe pulmonary arterial hypertension is uncommon, the prognosis of these patients is life threatening and treatment options are limited.

Interventions:
A sildenafil citrate suspension developed from the crushed tablets will be compared with the powder papers usually given to the children.
1. Sildenafil citrate suspension: the suspension will be prepared from both commercially available tablets and sildenafil citrate powder and the formulation must be easy to prepare at hospital pharmacies. The physical, chemical and microbiology stability of this suspension will be accessed simulating in-use conditions and the ones established by Brazilian drug laws.
2. Sildenafil citrate powder papers: the powder papers will be prepared from the crushed commercial tablets and addition of a diluent. The tablets will be sent to a private pharmacy to compound sildenafil citrate 5 mg powder papers (sachets) as its already done as a routine.

Both arms will receive sildenafil citrate 0.2 mg/kg as a single dose during cardiac catheterisation.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Sildenafil citrate (SC)

Primary outcome measure
The proportion of patients in each group that reduce pulmonary arterial hypertension in at least 20% twenty minutes after the administration of sildenafil citrate 0.2 mg/kg, during cardiac catheterisation.

Secondary outcome measures
1. At 20 minutes measured by cardiac catheterisation after administration of sildenafil citrate:
1.1. Pulmonary vascular resistance
1.2. Pulmonary vascular resistance/systemic vascular resistance
1.3. Oxygenation index or oxygen requirement
1.4. Cardiac output
1.5. Mean systemic arterial pressure and surgery indication based on the response to sildenafil
2. At 24 hours: any adverse events
3. At 2 months: cardiac surgery and death

Overall study start date
01/05/2008

Completion date
01/11/2008

Eligibility

Key inclusion criteria
1. Children from 0 to 18 years old, either sex
2. Diagnosed as having PH associated with congenital heart disease
3. Needing cardiac catheterisation with sildenafil to evaluate the response to the drug as a decision criteria to cardiac surgery

Participant type(s)
Patient

Age group
Child

Lower age limit
0 Years

Upper age limit
18 Years

Sex
Both

Target number of participants
182

Key exclusion criteria
Children will be excluded if:
1. The clinician believes that sildenafil represents an additional risk for the patient
2. The carrier refuses to sign the informed consent

Date of first enrolment
01/05/2008

Date of final enrolment
01/11/2008

Locations

Countries of recruitment
Brazil

Study participating centre
National Instutute of Quality Control in Health
Rio de Janeiro
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Sponsor information

Organisation
National Institute of Quality Control in Health - Oswaldo Cruz Foundation (Brazil)

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Sponsor type
Research organisation

Website
http://www.incqs.fiocruz.br

ROR
https://ror.org/04jhswv08

Funder(s)

Funder type
Research organisation

Funder Name
Oswaldo Cruz Foundation (Brazil)

Funder Name
National Institute of Cardiology (Brazil)

Funder Name
Pharmaceutical Industrial Technology Lab from Federal University of Rio de Janeiro (Brazil)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration