Plan Overview

A Data Management Plan created using DMPonline

Title: Doxapram versus placebo in preterm newborns: a double blinded multicenter randomized controlled trial

Creator:sinno simons

Principal Investigator: sinno simons

Data Manager: sinno simons

Affiliation: Other

Funder: ZonMw (Nederlands)

Template: Datamanagement ZonMw

ORCID iD: 0000-0001-5219-5696

Project abstract:

Rationale: After preterm birth artificial ventilation is often needed because of underdeveloped lungs and breathing centre. Artificial ventilation is related to impaired outcome and therefore minimized after preterm birth. The newborns' own breathing is supported with air, oxygen and caffeine. Unfortunately, apneas and concomitant oxygen desaturations often persist and potentially affect the brain and its development. Treatment with doxapram provides a potential solution in addition to standard of care for these infants and is increasingly used off-label in European neonatal intensive care units. We hypothesize that treatment with doxapram improves the survival and long term outcome of preterm infants. Objective: The main objective of our trial is to study if doxapram is safe and effective in reducing the composite outcome death and neurodevelopmental impairment at 2 years corrected age Study design: Randomized, double blinded placebo controlled trial, stratified for center and gestational age before or after 26 weeks at birth. Block randomization will be used. Study population: 398 newborn infants admitted to the Neonatal Intensive Care unit, with a gestational age of less than 29 weeks at birth with optimal non-invasive respiratory support and caffeine treatment that still show apnea. Intervention (if applicable): Blinded continuous doxapram (infusion or gastro-enteral) or placebo (glucose 5%) infusion as long as needed. Therapy is down titrated or stopped based on the patients’ condition. If endotracheal intubation is needed study drug is stopped. After extubation study drug may be restarted. Switch to gastro-enteral administration is allowed if no iv-access is needed for other reasons. Main study parameters/endpoints: Primary outcome is death or neurodevelopmental delay at the corrected age of 2 years (15% reduction, from 50 to 35%; NNT 7 patients). Secondary outcome includes short term neonatal morbidity, as well as long term follow-up until the age of 5.5 and 8 years. Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Doxapram is already frequently used in our NICUs. Data on safety or long term effectiveness are lacking. Although doxapram seems effective to avoid endotracheal intubation, long term safety and effectiveness needs to be studied. Adverse events and side effects will be monitored. Next to the study drug infusion, there will be no other study-related interventions. All outcome variables are already collected as standard of

care. In a subset of patients doxapram plasma levels will be determined to validate the doxapram PK model (blood will only be collected during routine blood sampling, max amount 0.6 ml). The national protocol for preterm birth advices follow-up at 2, 5.5 and 8 years respectively, as in the current study. Additional questionnaires will be used to collect data on the quality of life of patients and their parents.

ID: 31885

Last modified: 27-03-2021

Grant number / URL: 80-84800-9843009

Copyright information:

Doxapram versus placebo in preterm newborns: a double blinded multicenter randomized controlled trial

1. General features of the project and data collection

1.1 Project leader contact details

Sinno Simons
Department of Neonatology, Room Sk 4113
Erasmus MC - Sophia Children's Hospital
Wytemaweg 80
3015 CB Rotterdam
the Netherlands

1.2 I have composed my DMP with the assistance of a data management expert. List his or her name, function, organisation/department, phone number and email address.

- The expert is connected to my department or institution

Drs. Annelies Ham, datamanager
Department of Neonatology
Erasmus MC - Sophia Children's Hospital
a.ham@erasmusmc.nl

1.3 In collecting data for my project, I will do the following:

- Generate new data

1.4 In my research, I will use:

- Exclusively quantitative data

1.5 I will be reusing or combining existing data, and I have the owner's permission for using or combining their data.

- No, I will not be reusing or combining existing data

1.6 In collecting new data, I will be collaborating with other parties.

- Yes, I will collect the new data in conjunction with other researchers or research groups
- Yes, we have reached agreements on the user rights of the data used in the project

1.7 I am a member of a consortium of 2 or more partners. Clear arrangements have been made regarding data management and intellectual property. (also consider the possible effect of changes within the consortium on issues of data management and intellectual property)

- Yes, clear arrangements have been made regarding data management and intellectual property through a consortium agreement

The consortium agreement is in a final draft stage. Clear arrangements within the consortium and with all sites will be made

1.8 I can give an estimate of the size of the data collection; specifically, the number of participants or subjects (“n=”) in the collection and its size in GB/TB

- Yes (please specify)

The total number of patients that will be included in the trial is 356. Most data include background and clinical characteristics and outcome data. THe included patients will be followed-up until the age of 8 years where possible.

1.9 The following end products I will make available for further research and verification (please elaborate briefly)

- Several versions of processed data
- Data documentation
- Raw data

1.10 During the project, I will have access to sufficient storage capacity and sites, and a backup of my data will be available. (please elaborate briefly)

- Yes, I will make use of my institution's standard facilities for storage and backup of my data

Data will be collected via an Openclinica e-crf and is stored on the server of the Erasmus MC

2. Legislation (including privacy)

2.1 I will be doing research involving human subjects, and I am aware of and compliant with laws and regulations concerning privacy sensitive data.

- The Wet Medisch-Wetenschappelijk Onderzoek met Mensen (WMO, or Medical Research (Human Subjects) Act) applies to my project; I will have it reviewed by a Medical Research Ethics Committee. In addition I will comply with the Kwaliteitsborging Mensgebonden Onderzoek (Quality Assurance for Research Involving Human Subjects)
- Gedragscode Goed gebruik van lichaamsmateriaal (Code of Conduct for Responsible Use of Human Tissue)
- Yes, I will involve human subjects in my research. I will comply with the Algemene Verordening Gegevensbescherming (AVG)

2.2 I will be doing research involving human subjects, and I have (a form of) informed consent from the participants for collecting their data.

- Yes, and this informed consent allows for the reuse of data (note that in the Code of Conduct for Medical Research, ‘reuse’ is also referred to as ‘further use’)

The PIF was evaluated by the Medical Ethical Board in the Netherlands (Erasmus MC Rotterdam) and Belgium (University Hospital Leuven). It contains all necessary information about the trial. Parents of patients will be informed about the trial and will be provided with written information about the study. Their informed consent will be asked for participation of their child in the trial. A separate consent is asked for future use of the data.

2.3 I will be doing research involving human subjects, and I will protect my data against misuse.

- Yes, the data will be pseudonymised. (please explain how this will be done, and by which organisation) and

All included patients will retrieve a unique studynumber. The site (hospital where the patient is included) will have acces to a confidential list with the names and birth dates of the newborns.

2.4 I will stick to the privacy regulations of my organisation

- Yes

3. Making data findable

3.1 The data collection of my project will be findable for subsequent research (note: this is a key item, which you should report to ZonMw at the end of your project).

- No, I have not yet chosen an archive or catalogue/web portal

We have not yet decided on the best platform to make the data findable for subsequent research.

3.2 I will use a metadata scheme for the description of my data collection.

- No, I have not yet chosen a metadata scheme

3.3 I will be using a persistent identifier as a permanent link to my data collection (note: this is a key item, which you should report to ZonMw at the conclusion of your project).

- Yes, I will be using the DOI code

4. Making data accessible

4.1 Once the project has ended, my data will be accessible for further research and verification.

- Yes, after an embargo period (please explain)

The results of our project will be published as soon as possible. Afterwards data will be accessible.

4.2 Once the project has ended, my data collection will be publicly accessible, without any restrictions (open access).

- No, there will be access restrictions to my data collection (please explain)

Although we will make our data available to everyone who is interested (open access) we would like to be able to control / manage this process. T

4.3 I have a set of terms of use available to me, which I will use to define the requirements of access to my data collection once the project has ended (please provide a link or persistent identifier; also note that this is a key item, which you should report to ZonMw at the conclusion of your project).

- Not yet, my institution will draft a set of terms of use with the help of a legal advisor

4.4 In the terms of use restricting access to my data, I have included at least the following:

- The sharing of data for commercial purposes, taking into account the provisions of state aid law
- Collaboration in using the data set, including agreements on publication and authorship
- A steering committee, programme committee or project leader will be charged with approving data requests
- Whether or not the data set may be linked with another data set (for reasons of privacy)
- Conditions related to data security
- The reimbursement of costs, for example in obtaining the data
- The permitted period of use of the data set

As we still have to draft the terms of use we do not know the exact statements that will be included. Though, the checked statements above will at least be included. Meanwhile the infrastructure is available and data collection is started.

5. Making data interoperable

5.1 I will select a machine actionable data format, which will allow other researchers and their computers to read my data collection.

- Yes (please specify)

Castor is used as datamanagement system. All data can be extracted in a format readable by other researches.

5.2 I will select a metadata standard to allow my data collection to be linked to other collections (note: this is a key item, which you should report to ZonMw at the conclusion of your project).

- Yes, I will select a metadata standard from the list published by Biosharing (please specify)

ATC codes (medication data)
ICD-10 (disease classification)

5.3 I will be doing research involving human subjects, and I have taken into account the reuse of data and the potential combination with other data sets when taking privacy protection measurements.

- Yes, the participants have given their permission for reuse of the data, and the data have been pseudonymised

6. Making data reusable

6.1 I will ensure that the data and their documentation will be of sufficient quality to allow other researchers to interpret and reuse them (in a replication package).

- I will document the research process (please explain)
- I will perform quality checks on the data to ensure that they are complete, correct and consistent (please explain)
- In addition, I will take further quality assurance measures (please specify)
- I will document the software used in the course of the project (please specify)

A design paper will be written describing the study set up and its procedures. Furthermore, datadictionaries will be made. Within the data management system (Castor) datachecks for completeness (notifications for missing items) and correctness (crosschecks, validations, answer ranges/boundries) will be built. After data extracting datacleaning will be done according to a datacleaning SOP.

6.2 I have a number of selection criteria, which will allow me to determine which part of the data should be preserved once the project has ended. (see also question 1.9)

- No

6.3 Once the project has ended and the data has been selected, I can make an estimate of the size of the data collection (in GB/TB) to be preserved for long-term storage or archival.

- Yes (please specify)

All patient data from the NICU admittance and the outcome data will be stored and do not include large data files.

Continuous data from physiological monitoring systems, aEEG, NIRS have a larger size and will be cleaned and stored on a separate server. (size will be evaluated after extraction form the first patients)

6.4 I will select an archive or repository for (certified) long-term archiving of my data collection once the project has ended. (note: this is a key item, which you should report to ZonMw at the conclusion of your project)

- Not yet

This will be performed in line the available archive of the Erasmus MC.

6.5 Once the project has ended, I will uphold the recommended data preservation period of at least 10 years.

- Yes, in accordance with VNSU guidelines (please specify the number of years)

6.6 Data management costs during the project and preparations for archival can be included in the project budget. These costs are:

- Amount ..... (please elaborate)

The costs for the datamanager will be partly covered by the budget of the trial.

6.7 The costs of archiving the data set once the project has ended are covered.

- Yes (please elaborate)

These costs will be coverderd by the department of Pediatrics, division of neonatology.