Pediatric Ards Neuromuscular blockade (PAN) study: Life-threatening acute respiratory failure in children: to breathe or not to breathe spontaneously, that's the question. A multicentre, randomised, double-blind, placebo controlled study.

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To test the hypothesis that early use of neuromuscular blocking agents for 48 hours in paediatric patients younger than 5 years of age with moderate-to-severe paediatric acute respiratory distress syndrome will lead to at least a 20% reduction in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON46725

Source
ToetsingOnline

Brief title
PAN study

Condition

- Respiratory disorders NEC

Synonym
Paediatric acute respiratory distress syndrome

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,ZonMW

Intervention

Keyword: - Mechanical ventilation, - Neuromuscular blockade, - Paediatric acute respiratory distress syndrome, - Respiratory morbidity

Outcome measures

Primary outcome

The main study parameter is the cumulative respiratory morbidity score 12

months after PICU discharge, adjusted for confounding by age, gestational age,

family history of asthma and/or allergy, season in which questionnaire was

filled out and parental smoking.

Secondary outcome

1. Effects of NMBAs on pulmonary and systemic inflammation

2. Effects of NMBAs on oxygenation and ventilation

3. Effects of NMBAs respiratory system mechanics

4. Incidence of adverse drug reactions related to rocuronium

a. Occurrence of hypotension or tachycardia with the need for intervention by

means of medication or fluid challenge

b. Number of re-intubations

5. Concomitant use of sedatives and/or analgesics

6. Prevalence of critical illness polyneuropathy and myopathy

7. Prevalence of ventilator-associated pneumonia

8. Prevalence of organ dysfunction

9. Prevalence of withdrawal syndrome and delirium

10. The number of ventilator-free days at day 28

11. The length of PICU and hospital stay

Study description

Background summary

Paediatric acute respiratory distress syndrome (ARDS) is a manifestation of severe, life-threatening lung injury. Care for paediatric patients is mainly supportive and based on what works in adults and personal experiences, including the use of mechanical ventilation. However, differences in lung physiology and immunology between (young) children and adults suggests that adaptation of adult practices into paediatrics may not be justified. A study in adults with severe ARDS showed that early use of neuromuscular blocking agents (NMBA) improved 90-day survival and increased time off the ventilator without increasing muscle weakness. It is unknown if this is also true for paediatric ARDS. Thus, the next step is to determine the effects of NMBAs on patient outcome in children with moderate-to-severe ARDS. We hypothesize that NMBAs in mechanically ventilated children younger than 5 years of age with moderate-to-severe paediatric ARDS (i.e. oxygenation index > 12 and PEEP > 5 cmH2O despite adequate sedation) reduce respiratory morbidity during follow-up because they reduce lung and systemic inflammation, improve oxygenation and improve lung mechanics during the acute phase of illness.

Study objective

To test the hypothesis that early use of neuromuscular blocking agents for 48 hours in paediatric patients younger than 5 years of age with moderate-to-severe paediatric acute respiratory distress syndrome will lead to at least a 20% reduction in respiratory morbidity 12 months after discharge from the paediatric intensive care unit (PICU).

Study design

Prospective multicentre randomised double blind placebo controlled trial.

Intervention

Patients will be randomised to receive either a bolus plus a continuous infusion of rocuronium bromide 10 mg/ml at a rate of 0.1 ml/kg/hr (compatible with the recommended dosage of 1 mg/kg/hr (investigational product) or a bolus

plus 0.1 ml/kg/hr isotonic saline (NaCl 0.9%) (control).

Study burden and risks

The risks associated with this study are minimal based on the following arguments:
a) patients in the intensive care unit are under constant tight observation, so any change in vital parameters is noted immediately. Furthermore, patients with severe lung injury are commonly deeply sedated;
b) blood samples are only taken from an indwelling arterial catheter or central venous catheter, which are already in place for clinical purposes. Blood samples for this study will combined as much as possible with routine blood sampling part of daily clinical care;
c) endotracheal suctioning is routinely performed in mechanically ventilated patients by nurses taking care of the patients; for this study suctioning specimens are collected to measure the pulmonary inflammatory response so no extra suctioning procedures will be performed; and
d) the investigational drug is commonly used in (paediatric) critical care; hence, there is a good understanding of this drug.

It is important to study the effects of neuromuscular blocking agents on patient outcome in the paediatric context. There are numerous differences in lung physiology and immunology between (young) children and adults indicating that adaptation of adult practices into paediatrics may not be justified.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

- Informed consent
- Age younger than 5 years
- Need for invasive mechanical ventilation with PEEP 5 cmH2O
- Early moderate - to - severe paediatric acute respiratory distress syndrome originating from any cause:
* Acute onset of disease, and
* Oxygenation index > 12, and
* One or more (bilateral) infiltrates on chest radiograph, and
* No evidence of left ventricular failure or fluid overload, and
* Within the first 96 hours of PICU admission
- Arterial line or central venous line present

Exclusion criteria

- No informed consent
- Known allergy or intolerance to rocuronium
- Continuous administration of neuromuscular blockade prior at the time of meeting the criteria for paediatric acute respiratory distress syndrome
- Bolus administration of neuromuscular blockade within 1hr before meeting the criteria for paediatric acute respiratory distress syndrome
- Chronic respiratory failure on home ventilation
- Intracranial hypertension
- Bone marrow transplantation
- Pre-existing pulmonary hypertension
- Congenital heart disease with left - to - right shunting
- Cyanotic congenital heart disease
- (Suspected) underlying neuromuscular or metabolic disorder
- Expected duration of mechanical ventilation less than 48 hours
- Withdrawal of life-sustaining treatment or other treatment limitations

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-12-2019
Enrollment:	178
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Esmeron
Generic name:	Rocuronium bromide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Sodium Chloride 0,9%
Generic name:	Sodium Chloride 0,9%
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	06-12-2017
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-04-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-02-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-04-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-09-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-05-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-003670-40-NL
ClinicalTrials.gov	NCT02902055
CCMO	NL63608.042.17