STATIC IV: Efficacy of a loading dose of intravenous salbutamol in patients admitted to a PICU for severe acute asthma

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To assess the efficacy of a loading dose of intravenous salbutamol in children admitted to a PICU for severe acute wheeze or severe acute asthma. Efficacy is measured by the reduction in asthma score (Qureshi) at 1 hour after administration of the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON43695

Source
ToetsingOnline

Brief title
STATus asthmaticus on the PICU - IntraVenous salbutamol

Condition

- Bronchial disorders (excl neoplasms)

Synonym
life-threatening asthma attack, Status asthmaticus

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Stichting Astma Bestrijding;Stichting AMMODO

Intervention

Keyword: Asthma, Children, Pharmacodynamics, Salbutamol

Outcome measures

Primary outcome

The primary outcome variable is (reduction of) asthma score (Qureshi) 1 hour after administration of loading dose in the intervention group compared to the placebo group. Based on expert opinion, we consider a reduction of 2 points to represent a clinically relevant improvement.

Secondary outcome

* The (reduction of) asthma score (Qureshi) 6 hours after administration of loading dose in the intervention group compared to the placebo group.

* Cumulative dose of IV salbutamol

* Maximum infusion rate of IV salbutamol in mcg/kg/min

* Total duration of IV salbutamol treatment in hours

* Occurrence/frequency of side effects (categorical) (Tachycardia, Arrhythmia, Hypotension, Hypokalaemia, Hyperglycaemia, Lactic acidosis)

* Length of Stay on PICU in days

* Use of co-medication + dosage + timing (e.g. sodium bicarbonate, theophylline, sevoflurane)

* Use of prednisone + time/method of first administration

* Use of/duration of non-invasive/invasive mechanical ventilation in days

* Distribution of ADRB2-receptor polymorphisms (SNPs for Arginine and Glycine

on chromosomes 16 and 27) compared to normal population (non-SAA)

Study description

Background summary

In children, the standard therapy for severe acute asthma (SAA), unresponsive to continuously inhaled bronchodilators and systemic corticosteroids, is intravenous (IV) salbutamol. Although IV salbutamol is frequently used in children in a wide range, pharmacodynamic data are scarce. To date, there is an insufficient evidence base to guide initial and subsequent dosing recommendation for its IV use in children. Especially the need for a loading dose needs to be addressed. Therefore, pharmacodynamic and *kinetic data are needed to guide initial dosing strategies of IV salbutamol in children.

Study objective

To assess the efficacy of a loading dose of intravenous salbutamol in children admitted to a PICU for severe acute wheeze or severe acute asthma. Efficacy is measured by the reduction in asthma score (Qureshi) at 1 hour after administration of the loading dose, compared to placebo.

To assess the following pharmacodynamics parameters of a loading dose of intravenous salbutamol in children admitted to a PICU for severe acute wheeze or severe acute asthma.
-Maximum rate and duration of infusion of IV salbutamol
-Total (cumulative) dose of IV salbutamol
-Length of stay on PICU
-Need for other medication (e.g. sodium bicarbonate, theophyllin, sevoflurane)
-Need for non-invasive/invasive mechanical ventilation (+ duration)
-Frequency of side effects (Tachycardia, Arrhythmia, Hypotension, Hypokalaemia, Hyperglycaemia, Lactic acidosis)
-Distribution of ADBR2 receptor polymorphisms

Study design

Multi-centre, double blind randomised placebo controlled trial

Intervention

Group 1 (intervention) will receive a loading dose of IV salbutamol, in combination with standard care for SAA. Group 2 (control) will receive a placebo *loading dose* in combination with standard care for SAA.

Study burden and risks

Patients will be treated according to the standard management protocol of SAA in the PICU; in addition to standard care, the intervention group will receive an IV loading dose of salbutamol of 15 mcg/kg in 10 minutes, in accordance with current international guidelines. The effect on serum concentrations has been estimated using a PK model recently developed in our hospital using NONMEM analysis. The loading dose, added to the continuous infusion, reduces the time in which therapeutic serum concentrations are reached in the patients. Both the intervention and the control group are subject to side effects of IV salbutamol, as detailed in the SPC. Blood samples for serum concentration of salbutamol will be taken concomitantly with samples obtained for standard care; either via indwelling arterial catheter (only if already in place for treatment purposes), venipuncture or finger prick. Patients and/or guardians will be asked to fill out a short questionnaire regarding patient- and family history and disease specifics. No items of a sensitive nature are present. We will collect urine during a 6-hour of 12-hour period (depending on availability) to obtain data concerning metabolism and clearance of salbutamol. The study can only be carried out in this population, as pharmacodynamic/-kinetic results from adults cannot be extrapolated to children with SAA.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

-Between 2-18 years of age at moment of inclusion
-Admitted to PICU for Severe Acute Asthma or Severe acute (viral) wheeze
-Requiring administration of IV salbutamol

Exclusion criteria

-Patient is outside of specified age range
-Patient has already received a -loading dose- of IV salbutamol in the general hospital
-Lower airway infection with consolidation on a chest X ray
-Patient has Down*s Syndrome
-Patient has a congenital/acquired heart defect that interferes with normal asthma treatment
-Patient has a primary/secondary immunodeficiency
-Patient has a pre-existing chronic pulmonary condition, known to mimic asthma: Cystic fibrosis, Bronchopulmonary dysplasia, Bronchiolitis obliterans

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):	05-04-2017
Enrollment:	56
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ventolin
Generic name:	Salbutamol
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	27-06-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-12-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2015-003551-22-NL
Other	EudraCT - 2015-003551-22 NL
CCMO	NL55029.078.16