Bronchodilators for wheeze in young children presenting to primary care: a randomised, placebo-controlled, multicentre, parallel group trial.

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What is the (cost-)effectiveness of salbutamol inhalations (4x200*g for 7 days) versus placebo in children aged 6-24 months presenting to their primary care physician with wheezing?

Ethical review	Approved WMO
Status	Will not start
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON49680

Source
ToetsingOnline

Brief title
KIds WIth wheeze trial (KIWI)

Condition

- Viral infectious disorders
- Respiratory tract infections

Synonym
respiratory tract infections, wheeze

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMW/KCE

Intervention

Keyword: bronchodilators, children, infant, wheeze

Outcome measures

Primary outcome

The primary outcome is the course of the mean parent reported respiratory symptom score over 5 days.

Secondary outcome

Secondary outcomes include [a] time to recovery (recovery defined as a respiratory symptom score of 5 or lower indicating only trivial symptoms), and adverse effects over the duration to the intervention (1 week), [b] healthcare utilisation (i.e. primary care physician re-consultations, medication prescriptions (e.g. antibiotics), specialist consultations and hospital admissions), and cost-effectiveness (4 weeks), and [c] the proportion of infants with persistent wheezing on auscultation at day 5 (included as objective outcome measure).

Study description

Background summary

10% of infants are prescribed short-acting bronchodilators for wheezing per year, yet evidence to support this treatment in children younger than two years old is scarce.

Study objective

What is the (cost-)effectiveness of salbutamol inhalations (4x200*g for 7 days) versus placebo in children aged 6-24 months presenting to their primary care physician with wheezing?

Study design

A primary care based, randomized, placebo-controlled, multicentre, parallel group trial in 40 general practices and community paediatrics in Belgium and the Netherlands.

Intervention

Salbutamol inhalation 4x200ug for 7 days or inhalation of placebo.

Study burden and risks

Considering the trial includes young children with an acute illness, we have attempted to keep the burden on participants and their families to an absolute minimum while collecting essential information to assess efficacy of the active treatment. Participants will remain in the trial for 4 weeks, treatment with active treatment or placebo will last 7 days. This includes the inclusion visit with the primary care physician at day 0, a telephone call by a study nurse on day 3 and 7, a study nurse or medical student home visit on day 5, and telephone calls by the study nurse at 2 and 4 weeks. Study nurses (and medical students) will be flexible to be able to call parents at the preferred time of the day, and the home visit can be made at a time that suits parents (e.g. during the evening). Parents of participating children will be asked to record their child*s symptoms in a diary during the first 2 weeks, preferably using a diary-app. After 4 weeks, healthcare utilisation will be extracted from the child*s medical records. Data collection methods and associated burden to participants have been extensively discussed with the parents that were interviewed, and the proposed trial was judged as both feasible and acceptable by the majority of parents. Similar methods have been successfully applied in our previous trials.

Children allocated to salbutamol are exposed to side effects inherent to salbutamol (rare events include cardiovascular problems and paradoxal bronchospasm; in practice side effects of salbutamol that are reported most often are tachycardia and tremor) Since salbutamol is currently included in the national guidelines as a therapeutic option, these children may or may not have been prescribed salbutamol in usual care and are therefore not necessarily treated differently in the trial (the Dutch National Guideline states: consider a trial of salbutamol treatment and evaluate after 1-2 weeks). Children allocated to the placebo group children may experience a prolonged disease course and might need subsequent treatment with salbutamol if salbutamol indeed is effective (which is currently unknown). We however (1) do not include

patients with comorbidities or patients that are severely ill who definitely require inhalation therapy, antibiotics or referral, and (2) we do not anticipate large differences in treatment failures between the two trial arms since the few studies performed previously in primary care found small or no effects. Based on these considerations, we clinically regard the proposed study as a low risk study. Yet, since the study is performed in young children and medication is involved, we will consider the study a medium risk study to be on the safe side.

Group relatedness: The current trial needs to be performed in the group of young children 6-24 month old since, since acute wheeze in this age group is essentially different (and much more prevalent) compared to older patients. The anatomy and pathophysiology in younger children differs from older children.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

-children aged 6-24 months
- wheezing as confirmed by clinical examination (chest auscultation)
- a score of 7 or higher on a parent-reported respiratory symptom score.

Exclusion criteria

- prematurity
- major congenital malformations
- pre-existing pulmonary disease as diagnosed by a paediatrician
- continuous use of inhalation medication
- physician visit because of wheezing in previous two weeks
- or use of asthma medication in the previous two weeks
- wheezing as a result of upper airway obstruction (i.e. laryngitis subglottica/pseudocroup)
- severe illness requiring inhalation medication, prescription of antibiotics, or hospital referral; during the consultation of inclusion.

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:	Will not start
Enrollment:	150
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO Date:	14-05-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	08-07-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Not approved Date:	12-10-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-12-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-01-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	03-03-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	22-04-2021
Application type:	Amendment

Review commission: METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2020-000313-33-NL
CCMO	NL72651.041.20