CO-trimoxazole PRophylaxis for recurrent respiratory INfections in ChildrEn (the CO-PRINCE study)

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The aim of the CO-PRINCE study is to establish the efficacy and safety of long-term antibiotic prophylaxis with co-trimoxazolein children with recurrent upper and/or lower respiratory tract infections (including ear-nose-throat (ENT)).

Ethical review	Approved WMO
Status	Pending
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON34770

Source
ToetsingOnline

Brief title
The CO-PRINCE study.

Condition

- Respiratory tract infections

Synonym
recurrent respiratory infections; infection-prone

Research involving
Human

Sponsors and support

Primary sponsor: Jeroen Bosch Ziekenhuis
Source(s) of monetary or material Support: Subsidie bij ZonMW is aangevraagd (projectidee positief geadviseerd;definitieve aanvraag is ingediend).

Intervention

Keyword: child, co-trimoxazole, prophylaxis, recurrent respiratory infections

Outcome measures

Primary outcome

Infection frequency per person month.

Secondary outcome

Quality of life, emergence of antibiotic resistance in the commensal flora or

in a disease-causing isolated bacterium, side effects, cost-effectiveness.

Study description

Background summary

Many children suffer from recurrent respiratory infections: according to hospital registry data (DBC codes) 5000-6000 of these children per year are being followed by a pediatrician. This leads to absence from day-care or school (the children) or work (the parents). Currently, Dutch pediatricians and ENT-surgeons often use co-trimoxazole prophylaxis in these children, with considerable variability in how these children are treated (dosage, duration) and monitored (laboratory evaluation, drug levels).
This use is off-label, and may also lead to an increased carriage of microorganisms with antibiotic resistance in the population.
Data in the literature are limited, but indicate a possible effect that may wane with long-term use.

If shown beneficial, wider use of co-trimoxazole prophylaxis can diminish absence from school (the children) and work (the parents), and increase their quality of life.

Study objective

The aim of the CO-PRINCE study is to establish the efficacy and safety of long-term antibiotic prophylaxis with co-trimoxazole in children with recurrent upper and/or lower respiratory tract infections (including ear-nose-throat (ENT)).

Study design

We will compare long-term use (from the moment of inclusion until the end of April (the *cold season*) or during 3 consecutive months, whichever is longer) of 18mg/kg co-trimoxazole (3mg trimethoprim + 15mg sulfamethoxazole) bid to placebo in 170 children (>6 months and <18 years) in a multi-center randomized double blind trial. The primary outcome is infection frequency per person month. Secondary outcomes are quality of life, frequency of carriage of microorganisms with antibiotic resistance, side effects, and cost-effectiveness.

The CO-PRINCE study consortium is a unique cooperative network that brings general and university pediatric, pharmacological, and ENT-expertise together and is supported by the Medicines for Children Research Network (MCRN), ensuring quality and feasibility.

Intervention

18mg/kg co-trimoxazole (3mg trimethoprim + 15mg sulfamethoxazole) bid, until the month of April (inclusive) or during 3 months, whichever is longer (to prevent stopping the medication during the 'cold season').

Study burden and risks

Co-trimoxazole has been used for >35 years, also in children. So, no other risks than -relatively rare- known side effects are expected. The study burden comprises taking the study medication, either co-trimoxazole or placebo. Right now, children with recurrent respiratory infections are often treated with co-trimoxazole prophylaxis, resulting in either no extra burden by entering the study (co-trimoxazole would be used anyway) or taking the study medication 2 times a day. Besides that, doctors visits will take a little longer because of the study visits, and 2-4 extra venepunctures will be performed during the entire study. If separate informed consent is given, nasopharyngeal swabs and fecal samples will be collected in a subgroup every 3 months. The expected benefit on the one hand and limited burden and risks on the other hand are well balanced.

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

Children >6 months and <18 years with recurrent respiratory infections visiting pediatricians and ENT-surgeons in participating hospitals will be included if informed consent is obtained from the parents, and children (if >11 years). Definition of 'recurrent' respiratory infections: >=3 respiratory infections in the 6 months preceding study entry or start of the current therapy, or >=4 per year (documented by a doctor and treated with antibiotics).

Exclusion criteria

- known primary immunodeficiency (e.g. CVID, a/hypogammaglobulinemia);
- known secondary immunodeficiency (e.g. HIV, chemotherapy, transplantation);
- eponymous syndromes;
- chromosomal abnormalities;
- cleft palate;
- renal or hepatic insufficiency;
- known glucose-6-phosphate deficiency, cystic fibrosis, primary ciliary dyskinesia or acute porphyria;
- children using drugs known to interact with co-trimoxazole;
- children with previous allergic reaction to co-trimoxazole.

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:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2010
Enrollment:	170
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	co-trimoxazole
Generic name:	trimethoprim/sulfamethoxazole
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	08-07-2010
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

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	EUCTR2010-019170-33-NL
CCMO	NL31724.028.10