Antibiotic prophylaxis for children with recurrent respiratory infections: towards evidence-based guidelines

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Primary: To determine whether three months of prophylactic treatment with co-trimoxazole causes a reduction in the number of days a child experiences at least two RTI symptoms in children aged 6 months to

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Infections - pathogen unspecified
Study type	Interventional

Summary

ID

NL-OMON54555

Source
ToetsingOnline

Brief title
Approach study

Condition

- Infections - pathogen unspecified

Synonym
recurrent respiratory tract infections

Research involving
Human

Sponsors and support

Primary sponsor: HagaZiekenhuis
Source(s) of monetary or material Support: Er zal gebruik worden gemaakt van lokale fondsenwerving.

Intervention

Keyword: Antibiotics, Children, profylactic, recurrent respiratory tract infections

Outcome measures

Primary outcome

To determine whether antibiotic prophylaxis is more effective than placebo in the prevention of respiratory symptoms in children with recurrent RTIs at a group-level. The difference in days with at least 2 RTI symptoms will be calculated from baseline to 3 months after inclusion.

Secondary outcome

1. To determine whether co-trimoxazole prophylactic therapy reduces:

- Time to resolution of symptoms;

- The severity of symptoms defined by the number and type of different infectious symptoms;

- Use of analgesics / antipyretics;

- Use of antibiotic treatment courses;

- Absenteeism from day care or school and/or parental absenteeism from work;

- Alterations in nutritional status.

2. To examine predictors (e.g. demographic, environmental, family history, mucosal, microbiological and immunological characteristics) for the (absence of) prophylactic treatment effect*

3. To examine whether cessation of antibiotic prophylactic treatment affects the presence of RTI symptoms and how this correlates with clinical, microbiological and immunological characteristics of the patients.

4. To record and evaluate adverse events.

5. To detect changes in microbial composition, shifts in AMR genes and

immunological changes in the group that received antibiotic prophylaxis

compared to the placebo group.

Study description

Background summary

Recurrent respiratory tract infections (RTIs) affect 15-20% of children aged 0-5 years and cause high disease burden, frequent doctor visits and are one of the main reasons for hospital admission in childhood. Despite the common use of co-trimoxazole as a prophylactic agent in children with recurrent RTIs, there are no evidence-based guidelines for its use except for children suffering from exclusively otitis media. More evidence of the effect of co-trimoxazole prophylaxis on both clinical symptoms as well as microbiome deviation and antibiotic resistance is needed.

Study objective

Primary: To determine whether three months of prophylactic treatment with co-trimoxazole causes a reduction in the number of days a child experiences at least two RTI symptoms in children aged 6 months to <=10 years with recurrent RTIs, when compared to placebo.

Secondary:
1. To determine whether co-trimoxazole prophylactic therapy reduces:
- Time to resolution of symptoms;
- The severity of symptoms defined by the number and type of different infectious symptoms;
- Use of analgesics / antipyretics;
- Use of antibiotic treatment courses;
- Absenteeism from day care or school and/or parental absenteeism from work;
- Alterations in nutritional status.

2. To examine predictors (e.g. demographic, environmental, family history, mucosal, microbiological and immunological characteristics) for the (absence of) prophylactic treatment effect

3. To examine whether cessation of antibiotic prophylactic treatment affects the presence of RTI symptoms and how this correlates with clinical, microbiological and immunological characteristics of the patients.

4. To record and evaluate adverse events:
- The occurrence of mild adverse effects as described in the Summary of Product Characteristics (SPC), such as skin rash, gastro-intestinal complaints, pruritus or mild headache;
- The occurrence of severe adverse reactions.

5. To examine short-term and long-term effects of co-trimoxazole prophylaxis on microbiota deviation, AMR and (mucosal and systemic) immunological outcomes.

Study design

Randomized double-blind placebo-controlled clinical trial comparing co-trimoxazole with placebo treatment given for 3 months in children with recurrent RTIs.

Intervention

One group receives co-trimoxazole 18mg/kg twice daily (36mg/kg/day) and the other group receives a placebo twice daily.

Study burden and risks

The study may result in minor (well known) side effects caused by the antibiotics as well as a positive effect with reduction in days with respiratory symptoms in this subgroup. The subject of the study is specifically for young children (<=10 years) since RTIs are most common among this population and antibiotic prophylaxis is prescribed frequently for this specific indication in children despite lack of evidence.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria: - Presenting to one of the participating clinics; - Age 6 months - 10 years; - Suffering from recurrent respiratory tract infections (RTIs); - Informed consent from parent(s)/caregiver(s) with legal custody. For age-specific definitions of recurrent RTIs, we took cut-offs as defined by the Dutch Society of Pediatric except for children aged 5-10 years in whom we used the same definition as younger children (2-5 years). This means yearly at least 11 and 8 parental-reported upper RTIs including, but not limited to, otitis media for children aged <2 and 2-10 years respectively. Recurrent lower RTIs (i.e. pneumonia, bronchopneumonia or acute bronchitis) are defined as at least 2 episodes per year or 3 or more episodes during the child*s life regardless of age.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Current prophylactic antibiotic use or prophylactic antibiotic use during the previous month;
- Underlying immune deficiency other than for IgA or IgG subclasses;
- Congenital abnormalities (including cleft palate, neuromuscular, cardial and syndromal disorders, hematologic disorders;
- Suffering from chronic respiratory disease, such as cystic fibrosis (CF), primary ciliary dyskinesia (PCD) or anatomical abnormalities;
- Children who only suffer from recurrent acute otitis media or chronic suppurative otitis media will be excluded since antibiotic prophylaxis has proven to be beneficial for this group;

- Known allergy to co-trimoxazole;
- Known contra-indication for co-trimoxazole, e.g. liver failure, impaired kidney function and/or hematologic disorders.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-01-2019
Enrollment:	158
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	07-05-2018
Application type:	First submission

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	17-05-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	26-03-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	28-08-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	26-10-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	12-01-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	30-03-2021
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	07-12-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	16-03-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	12-09-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	14-09-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2017-003164-13-NL
CCMO	NL63954.098.17