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

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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-...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22966

Bron
NTR

Verkorte titel
APPROACH study

Aandoening

recurrent respiratory tract infections in children; recidiverende luchtweginfecties bij kinderen

Ondersteuning

Primaire sponsor: Juliana Children's Hospital (Haga Teaching Hospital) / UMC Utrecht
Overige ondersteuning: Juliana Children's Hospital (Haga Teaching Hospital) / UMC Utrecht

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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. We will use a negative binomial regression analysis with outcome the number of days with at least two respiratory symptoms and use the number of days monitored as offset.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: 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.

Objective: Primary: To determine whether antibiotic prophylaxis is more effective than placebo in prevention of respiratory symptoms in children with recurrent RTIs. Secondary: 1. To determine whether co-trimoxazole prophylactic therapy reduces time to resolution of symptoms, severity of symptoms, use of antipyretics/antibiotics, absenteeism from day-care or school and 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 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. Study population: A total of 158 children (aged 6 months – 10 years) presenting to one of the participating hospitals with recurrent RTIs and fulfilling inclusion criteria.

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

Main study parameters/endpoints: Primary: The number of days with respiratory symptoms from baseline to 3 months after inclusion. Secondary: The number of days with respiratory symptoms from baseline to 6 months after inclusion, microbiome deviation and antibiotic resistance of nasopharyngeal and gut bacteria.

Doel van het onderzoek

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.

Onderzoeksopzet

T=0: Screening for inclusion, start trial medication, collection of samples, questionnaire and start daily diary

T=1 month: sample collection, monthly questtionaire (repeats every month)

T=3 months: stop trial medication, lab tests, sample collection

T=6 months: sample collection, stop diary, last questionnaire.

Onderzoeksproduct en/of interventie

Children will be randomized to one of 2 oral regimens for 3 months: co-trimoxazole 36 mg/kg/day (2 x 18 mg/kg) (n=79) or placebo twice daily (n=79).

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Recurrent upper RTIs: for children aged <2 years yearly at least 11 and for children aged 2-10 years yearly at least 8 parental-reported upper RTIs including, but not limited to, otitis media. 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- 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 but not limited to cleft palate, neuromuscular or cardiac disorders and syndromes);
- Suffering from chronic respiratory disease, such as cystic fibrosis (CF), primary ciliary dyskinesia (PCD) or anatomical abnormalities;
- Only experiencing recurrent AOM or chronic suppurative otitis media without other recurrent RTIs;
- Known allergy to co-trimoxazole;
- Known contra-indication for co-trimoxazole, e.g. liver failure or impaired kidney function and/or haematologic disorders.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-07-2018
Aantal proefpersonen:	158
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	31-05-2018
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7044
NTR-old	NTR7249
Ander register	MEC-nr : 18-008

Resultaten

Samenvatting resultaten
None