Antibiotic prophylaxis for recurrent infections (Antibiotische profylaxe voor recidiverende infecties).

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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-trimoxazole in children with recurrent upper and/or lower respiratory tract infections (including ear-nose-throat).

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON29468

Bron
NTR

Verkorte titel
CO-PRINCE study

Aandoening

Trimethoprim_Sulfamethoxazole_Combination; Respiratory_Tract_Infections; Secondary_Prevention; Infant; Child_preschool; Child; Adolescent
(trimetoprim, sulfametoxazol, co-trimoxazol, recidiverende luchtweginfecties, secundaire preventie, kind, adolescent)

Ondersteuning

Primaire sponsor: Jeroen Bosch Hospital, PO Box 90153, 5200ME 's-Hertogenbosch, the Netherlands, tel +31-73-6992000.
Overige ondersteuning: Grant application submitted and under review.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The effect on infection frequency per person month of 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 oral co-trimoxazole bid [schedule see 3 and 4.4], totaling 6mg trimethoprim and 30mg sulfamethoxazole per day in two divided doses, hereafter referred to as 36mg/kg/day(2), as compared to placebo in children with recurrent respiratory infections.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:

Many - mainly young - children suffer from recurrent respiratory infections, which hamper their quality of life and their day-care or school attendance. This is often a cause of great concern for their parents, who also suffer loss of working days. Dutch pediatricians and ENT-surgeons often prescribe co-trimoxazole prophylaxis to children with recurrent respiratory infections, but co-trimoxazole is not registered for this indication in the Netherlands, the use is off-label. Also, the dosages used and duration of prophylaxis differ, and the Dutch registration guidelines concerning the measurement of plasma concentrations and screening for side effects during long-term use are generally not followed. Data in the literature are limited.

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)), hereafter referred to as ‘recurrent respiratory infections’.

Study design:
The CO-PRINCE study is a double-blind, parallel, placebo-controlled randomized clinical trial in children >6 months and <18 years who visit a pediatrician or ENT-surgeon because of recurrent respiratory infections. After receiving informed consent, and an initial laboratory evaluation has shown no abnormalities, children will be either assigned to oral co-trimoxazole 36mg/kg/day(2) or placebo. The study medication will be started immediately after inclusion, and will be continued until the month of April (inclusive), or for 3 consecutive months, whichever is longer. This schedule is applied to enable variable continuation of the study medication to prevent stopping during the ‘cold season’, as is current common practice. Parents, children, attending physicians, nurses and researchers will be blinded. A balanced

allocation procedure within hospitals, age groups, and calendar months will be used to ensure comparability at baseline. The children will be followed up to 12 months after the end of the study medication phase, besides their regular follow-up by their own attending physician(s).

Study Population:
Inclusion criteria: Children >6 months and <18 years with recurrent respiratory infections visiting Dutch pediatricians and ENT-surgeons in participating hospitals will be included if informed consent is obtained from the parents and children (if >11 years). 'Recurrent' respiratory infections will be defined as ≥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.

Intervention:
Long-term co-trimoxazole prophylaxis (see study design).

Main study parameters/endpoints:
The primary objective of the study is the effect on infection frequency per person month of long-term use. The secondary objectives of the study are safety and long-term effects (quality of life, antibiotic resistance, side effects, cost-effectiveness.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
Co-trimoxazole is a product with marketing authorization. From the experience with the product, no risks can be expected. The safety of the patients will be assessed by monitoring for laboratory safety parameters and any adverse event. The children treated in the co-trimoxazole arm may have direct benefit by this clinical trial (fewer infections), but the children in the placebo arm will not have any direct benefit by participating in this clinical trial.

Doel van het onderzoek

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).

Onderzoeksopzet

Inclusion, study visit every 3 months during study medication use and in the 12 months thereafter. Infection frequency per person month as determined by the patient diary and daily chip-thermometer based temperature. Emergence of antibiotic resistance in nosocomial flora (culture, resistance, molecular typing), side effects (chemistry lab, blood levels), quality of life (HUI, RAND) and incremental cost-effectiveness ratios.

Onderzoeksproduct en/of interventie

After receiving informed consent, and an initial laboratory evaluation has shown no abnormalities, children will be either assigned to oral co-trimoxazole 36mg/kg/day(2) or placebo. The study medication will be started immediately after inclusion, and will be continued until the month of April (inclusive), or for 3 consecutive months, whichever is longer. This schedule is applied to enable variable continuation of the study medication to prevent stopping during the ‘cold season’, as is current common practice.

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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). 'Recurrent' respiratory infections will be defined as 3 or more respiratory infections in the 6 months preceding study entry or start of the current therapy, or 4 or more per year (documented by a doctor and treated with antibiotics).

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Known primary immunodeficiency (e.g. CVID, a/hypogammaglobulinemia);

2. Known secondary immunodeficiency (e.g. HIV, chemotherapy, transplantation);

3. Eponymous syndromes, chromosomal abnormalities, cleft palate, renal or hepatic insufficiency, known glucose-6-phosphate deficiency, cystic fibrosis, primary ciliary dyskinesia or acute porphyria;

7. Children using drugs known to interact with co-trimoxazole;

8. Children with previous allergic reaction to co-trimoxazole.

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-09-2010
Aantal proefpersonen:	170
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing
Soort: Niet van toepassing

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	NL2102
NTR-old	NTR2219
Ander register	ZonMW : 40-41500-98-9013
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A