Topical or oral antibiotics for children with acute otitis media presenting with ear discharge?*

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To establish the clinical and cost-effectiveness of antibiotic-corticosteroid eardrops as compared with oral antibiotics in children with AOMd.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Middle ear disorders (excl congenital)
Study type	Interventional

Summary

ID

NL-OMON52979

Source
ToetsingOnline

Brief title
PLOTS

Condition

- Middle ear disorders (excl congenital)
- Hepatobiliary neoplasms malignant and unspecified

Synonym
Acute Otitis Media with ear discharge, Acute Suppurative Otitis Media

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Antibiotics, Drug therapy, Otitis media, RCT, Suppurative

Outcome measures

Primary outcome

The primary outcome is the proportion of children without ear pain and fever at day 3.

Secondary outcome

Secondary outcomes are ear pain intensity/severity; fever intensity/severity; ear discharge; time to resolution of total symptoms, persistent eardrum perforation; middle ear effusion; adverse events; disease-specific quality of life; antibiotic consumption; AOM recurrences; costs and cost-effectiveness; antimicrobial resistance.

Study description

Background summary

Around 15-20% of children with AOM present with ear discharge due to a spontaneous perforation of the eardrum (AOMd). Since oral antibiotics effectively reduce ear pain and/or fever in children with AOMd, current guidance recommends general practitioners (GPs) to consider oral antibiotics for these children. However, oral antibiotics put children at risk for side effects and increase the risk of antimicrobial resistance. In children with AOMd, the perforation of the eardrum provides an opportunity to instill topical antibiotics directly into the middle ear without exposing children to systemic side effects and putting less selective resistance pressure on bacteria. Evidence on its effectiveness in children with AOMd is, however, lacking. We hypothesise that antibiotic-corticosteroid eardrops are non-inferior to oral antibiotics in resolving ear pain and fever at day 3 (72 hours after randomisation) in children aged 6 months to 12 years visiting their GP with AOMd and ear pain and/or fever.

Study objective

To establish the clinical and cost-effectiveness of antibiotic-corticosteroid eardrops as compared with oral antibiotics in children with AOMd.

Study design

A primary care based, open, randomised controlled non-inferiority trial.

Intervention

Children will be randomly allocated to either 1) hydrocortisone-bacitracin-colistin (Bacicoline-B®) eardrops, five drops, three times per day in the discharging ear(s) for 7 days or 2) amoxicillin suspension or tablets 50 mg per kilogram body weight per day, divided over three oral doses for 7 days.

Study burden and risks

Participants will be followed for a total of 3 months. This includes a baseline visit, a telephone call at day 3 and a follow-up visit at 2 weeks. Parents of participating children will be asked to record their child*s symptoms in a daily diary during the first 2 weeks and a weekly diary afterwards (up to 3 months). At the baseline and the 2 weeks home visits, otoscopy will be performed and otorrhoeal, nasopharyngeal and faecal samples will be collected. At the 2 weeks home visit tympanometry will be performed and at 3 months, a faecal sample will be collected.
Children allocated to eardrops will not be exposed to systemic side effects associated with oral antibiotics and may be at lower risk of developing antimicrobial resistance. A potential risk is that children may experience a prolonged disease course and might need subsequent treatment with oral antibiotics if antibiotic-corticosteroid eardrops appear to be inferior to oral antibiotics. We however do not anticipate large differences in treatment failures between the two active treatment groups given the difference (30%) observed between oral antibiotics and placebo in previous trials.
The main risk of eardrops is potential ototoxicity. Although the hydrocortisone-bacitracin-colistin eardrops do not contain an aminoglycoside, there still is a risk. However, based on current available literature and recent data from the Netherlands Pharmacovigilance Centre, the risk of ototoxicity associated with the use of eardrops is considered at most similar but probably lower than the risk of ototoxicity related to the middle ear infection itself. Both the Dutch College of General Practitioners and the Dutch ENT Society have balanced benefits and risks of using these eardrops in children with an active middle ear infection and concluded that the (potential) benefits outweigh the risks.
Based on these considerations, we regard the proposed study as a low risk study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Children aged 6 months to 12 years whose parents are consulting the GP with AOM and ear discharge in one or both ears (<= 7 days duration) and either parent-reported ear pain in the previous 24 hours or fever (child*s body temperature of >= 38.0°C in the previous 24 hours as reported by parents or as measured by the GP during consultation) or both.

Exclusion criteria

Children will be excluded from participation if they
1. are systemically very unwell and requires immediate oral antibiotics or immediate hospitalization (e.g. child has signs and symptoms of serious illness and/or complications such as mastoiditis/meningitis);

2. are at high risk of serious complications including children with known immunodeficiency other than partial IgA or IgG2 deficiencies, craniofacial malformation such as cleft palate, children with Down syndrome, previous ear surgery other than grommet insertion;
3. have grommets in place;
4. have a pre-existing perforation of the eardrum;
5. had an prior AOM episode (with or without ear discharge) in previous 28 days;
6. used oral antibiotics or topical antibiotics in previous 2 weeks;
7. have a known allergy or sensitivity to oral amoxicillin or hydrocortisone-bacitracin-colistin;
8. have already participated in this trial.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-12-2017
Enrollment:	350
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Amoxicillin
Generic name:	Amoxicillin
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	Bacicoline-B
Generic name:	hydrocortisone/□colistin/□bacitracin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	27-06-2017
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	23-08-2017
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-11-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-11-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-09-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-10-2022
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 23467
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2017-000332-34-NL
CCMO	NL61395.041.17
OMON	NL-OMON23467