Is treatment with eardrops as good as oral treatment for children with acute otitis media presenting with ear discharge?

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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 either ear pain…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON23467

Source
NTR

Brief title
PLOTS (Pijnlijk LoopOor Therapie Studie)

Condition

- Bacterial infectious disorders

Health condition

Acute Otitis media with ear discharge

Otitis media acuta met een loopoor

Sponsors and support

Primary sponsor: Sponsor: Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht
Source(s) of monetary or material Support: Subsidising party:
The Netherlands Organisation for Health Research and Development (ZonMw), Rational Pharmacotherapy 5th Open Call – grant no. 84801 5006

Intervention

Explanation

Outcome measures

Primary outcome

The proportion of children without ear pain (ear pain score 0 on the 0-6 Likert scale) and fever (body temperature below 38.0°C) at day 3.

Secondary outcome

Secondary outcomes are in short 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. Please find the more detailed secondary outcomes below (as predefined in our research protocol in 2017): Secondary outcomes are the proportion of children with at most mild ear pain (ear pain score less than 3 on the 0-6 Likert Scale) at day 3; mean ear pain score over days 0-3, number of days with ear pain (ear pain score 1 or higher on the 0-6 Likert scale); mean body temperature over days 0-3; number of days with fever (body temperature of 38.0°C or higher) during the first 2 weeks; the proportion of children with parent-reported ear discharge at day 3; number of days with parent-reported ear discharge at day 3 and during the first 2 weeks; proportion of children with otoscopically confirmed ear discharge at 2 weeks; time to resolution of total symptoms (time to all of pain, fever, discharge, being unwell, sleep disturbance, and distress/crying being rated 0 or 1 on the Likert scale); MEE and proportion of children with otoscopically confirmed eardrum perforation at 2 weeks; OM-specific quality of life at baseline, 2 weeks and 3 months; antibiotic consumption during the first 2 weeks and at 3 months; number of AOM recurrences at 3 months; number of adverse events during the first 2 weeks; costs and cost-effectiveness at 2 weeks and 3 months; the prevalence of viruses and bacteria in otorrhoea and nasopharynx samples at baseline and 2 weeks; the antimicrobial susceptibility profiling of the bacteria and the impact of the treatment regimens on antimicrobial resistance genes in the human gut ; microbiome profile of nasopharynx at baseline and 2 weeks

Study description

Background summary

Rationale: 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 adverse 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 either ear pain or fever or both.

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.

Study population: Children aged 6 months to 12 years whose parents are consulting their GP because of AOMd and either ear pain or fever or both.

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.

Main study parameters/endpoints: The primary outcome is the proportion of children without ear pain and fever at day 3. 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.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

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. At the baseline and the 2 weeks home visits, otoscopy and tympanometry (at 2 weeks only) will be performed and otorrhoeal, nasopharyngeal and faecal samples will be collected. At 3 months, a faecal sample will be collected. Data collection methods and associated burden to participants have been extensively discussed with our parent panel. The proposed methods were judged both feasible and acceptable by our parent panel and have been successfully applied in our previous trial.

Children allocated to eardrops will not be exposed to systemic adverse 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 or no treatment 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. Current status: Ongoing (restart trial september 2021).

Study objective

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 either ear pain or fever or both.

Study design

Primary outcome: day 3

Secondary outcomes: 0-3 days, 2 weeks, 3 months

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.

Contacts

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Eligibility criteria

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 hospitalisation (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 a 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

IPD sharing statement

Plan to share IPD: Undecided

Plan description
-

Ethics review

Approved WMO Date:	27-09-2017
Application type:	First submission
Review commission:	Medical Research Ethics Committees United (MEC-U) Postbus 2500 3430 EM Nieuwegein 088 320 8784 info@mec-u.nl

Study registrations

Followed up by the following (possibly more current) registration

ID: 52979
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL6535
NTR-old	NTR6723
EudraCT	2017-000332-34
CCMO	NL61395.041.17
OMON	NL-OMON52979

Study results