Clinical efficacy of three common treatments in acute otitis externa in primary care: randomised controlled trial

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Abstract

Objective To compare the clinical efficacy of ear drops containing acetic acid, corticosteroid and acetic acid, and steroid and antibiotic in acute otitis externa in primary care.
Design Randomised controlled trial.
Setting 79 general practices, Netherlands.
Participants 213 adults with acute otitis externa.
Main outcome measures Primary outcome: duration of symptoms (days) according to patient diaries. Secondary outcome: cure rate according to general practitioner completed questionnaires and recurrence of symptoms between days 21 and 42.
Results Symptoms lasted for a median of 8.0 days (95% confidence interval 7.0 to 9.0) in the acetic acid group, 7.0 days (5.8 to 8.3) in the steroid and acetic acid group, and 6.0 days (5.1 to 6.9) in the steroid and antibiotic group. The overall cure rates at seven, 14, and 21 days were 38%, 68%, and 75%, respectively. Compared with the acetic acid group, significantly more patients were cured in the steroid and acetic acid group and steroid and antibiotic group at day 14 (odds ratio 2.4, 1.1 to 5.3, and 3.5, 1.6 to 7.7, respectively) and day 21 (5.3, 2.0 to 13.7, and 3.9, 1.7 to 9.1, respectively). Recurrence of symptoms between days 21 and 42 occurred in 29% (50/172) of patients and was seen significantly less in the steroid and acetic acid group (0.3, 0.1 to 0.7) and steroid and antibiotic group (0.4, 0.2 to 1.0) than in the acetic acid group.
Conclusions Ear drops containing corticosteroids are more effective than acetic acid ear drops in the treatment of acute otitis externa in primary care. Steroid and acetic acid or steroid and antibiotic ear drops are equally effective.

Introduction

Acute otitis externa, an infection of the external auditory canal, is often seen in primary care. In the Netherlands the incidence is 12-14 per 1000 population per year.[1] One study from the United Kingdom reported a prevalence of more than 1% over a 12 month period.[2] During the summer the number of episodes of acute otitis externa increases, and the incidence in humid tropical areas is higher than in moderate climates.[3] Of the predisposing factors for acute otitis externa, only swimming has been shown to increase the risk.[4–6] Pathogens commonly associated with acute otitis externa are *Pseudomonas aeruginosa, Staphylococcus epidermides, Staphylococcus aureus,* and *Streptococcus pyogenes*.[7–9] Fungi and yeast are usually found in patients with chronic otitis externa or those who are immunocompromised.[10 11] Current management includes debridement followed by dressing and topical treatment with acidifying or antimicrobial agents, with or without corticosteroids.[1 2 12 13] Most general practitioners prescribe ear drops containing antibiotic with or without steroids.[2 14] Local drugs are more effective than placebo, but the evidence for superiority of any of the local agents is lacking.[15–21] Studies of otitis externa have had methodological flaws—for example, insufficient numbers of patients, invalid inclusion criteria such as otorrhoea, and using a design that was not double blind. Also relevant end points for clinical practice have not been included, such as speed of recovery and recurrence. The optimal treatment for acute otitis externa in primary care has therefore not been established. We compared the clinical efficacy of ear drops containing acetic acid, steroid and acetic acid, and steroid and antibiotics in the treatment of acute otitis externa in general practices in the Netherlands.

Methods

Acute otitis externa was defined as redness or swelling of the external auditory canal or debris within the canal, accompanied by pain, itchiness, otorrhoea, hearing loss, or a stuffy feeling, for less than three weeks. Recovery was defined according to patient's self report as no more symptoms or only one moderate symptom. Cure was the percentage of patients who had recovered according to questionnaires completed by the general practitioners. Recurrence of symptoms was defined as recurrence of symptoms after recovery between the last study visit and follow up by telephone at 42 days.

Participants

The study was conducted between June 2000 and November 2001. We invited 143 general practitioners from 62 surgeries in the central part of the Netherlands to take part in our study; 79 general practitioners from 47 surgeries agreed to participate, and 64 refused for various reasons. The general practitioners received training in the diagnosis and treatment of acute otitis externa. Patients were considered for inclusion if they presented with signs and symptoms of acute otitis externa. Exclusion criteria were age 17 years or younger, pregnancy, chronic otitis externa (more than three weeks), a furuncle in the external auditory canal, acute otitis media, a perforated eardrum, perichondritis, fever, allergy to any of the study drugs, and having already been recruited to the study or been treated for acute otitis externa in the past month.

Treatment and randomisation

A stastistician drew up a computer generated randomisation list, with a ratio of 1:3, which was given to the hospital pharmacy. The pharmacy supplied the general practitioners with identical brown bottles containing 10 ml of ear drops, numbered according to the randomisation list.

Overall, 213 patients were randomised to three groups, each patient receiving three ear drops three times daily of either 7.2 mg acetic acid per gram of propylene glycol (acetic acid group; n=71), 0.1% triamcinolone acetonide and acetic acid (steroid and acetic acid group; n=63), or 0.66 mg dexamethasone phosphate sodium, 5 mg neomycin sulphate, and 10 000 IU polymyxin B sulphate per millilitre (steroid and antibiotic group; n=79). The ear drops were administered in a double blind fashion, according to the randomisation list. Patients collected another bottle, of the same study number, if they had not recovered after finishing the first bottle.

The patients, general practitioners, and investigators remained blinded throughout the study. To ensure double blindness and proper administration of the ear drops, a practice assistant, who was not involved in evaluating the patients, applied the first dose during the patient's initial visit for instructions.

Measurements

At the baseline visit the general practitioner recorded on a three point scale (none, moderate, severe) the signs in the external auditory canal (swelling, desquamation, redness, narrowness, otorrhoea) and auricle (traction pain, desquamation, redness, swelling). Also noted were the condition of the eardrum (normal or perforated) and its laterality. If the eardrum could not be visualised, the canal was cleaned by rinsing or by using a small suction device according to the Dutch guidelines for otitis externa.[1] A compressed dry wick (Merocel, MedTronics, Jacksonville, FL) was used if the canal walls were too swollen to allow penetration of the drug along its length. The study ear drops were applied to the visible part of the wick. After 24 hours the wick was removed and the ear inspected. This was continued until the eardrum was visible and the ear drops could penetrate the canal.

The patient was asked to give information on comorbidities (diabetes, eczema, psoriasis, or a known contact allergy), risk factors (swimming, ear cleaning or picking, and use of hearing aids, earplugs, or personal stereo more than three times a week), antibiotic use in the past month, and the number of ear infections within the past year.

During treatment, patients completed a daily diary in which they recorded the extent of pain, itchiness, otorrhoea, hearing loss, stuffy feeling (on a three point scale), side effects (burning, pain, irritation, loss of hearing, other), and compliance with treatment.

The first follow up visit was seven days after the baseline visit. If the patient had not recovered, treatment was continued, with a second follow up visit at 14 days. Patients who had not recovered continued treatment until 21 days, after which they were considered treatment failures if they had not recovered or they had been given an alternative treatment during the study period.

At each follow up, the general practitioner determined treatment compliance from the amount of drug remaining and whether the patient had recovered. After 42 days, the researchers asked the patients by telephone whether symptoms had recurred.

Outcome measures

The primary outcome measure was the duration of symptoms in days until recovery according to the diary entries. Secondary outcome measures were the cure rate at days 6-8, 13-15, and 20-22 and the recurrence of symptoms between days 21 and 42.

Statistical analyses

All analyses were carried out with SPSS version 11.0 using an intention to treat approach. Categorical differences between the three treatment groups were tested with the χ^2 test (with continuity correction). We plotted Kaplan Meier curves for duration of acute otitis externa, and we tested the differences with a log rank test. Multiple logistic regression analysis was performed to adjust for potential baseline differences in characteristics between treatment arms. The acetic acid group was the reference group. We measured the difference in severity of otoscopic signs, relapse, and side effects with Kruskal Wallis tests.

Assuming a mean duration of symptoms of 10 (SD 1.5) days, we calculated that about 60 patients would be needed per treatment arm to detect a clinically relevant difference between the treatment arms of one day at a 5% level of significance with 90% power.

Results

Overall, 213 patients were randomly assigned to one of the three treatments (fig 1). The characteristics differed slightly between

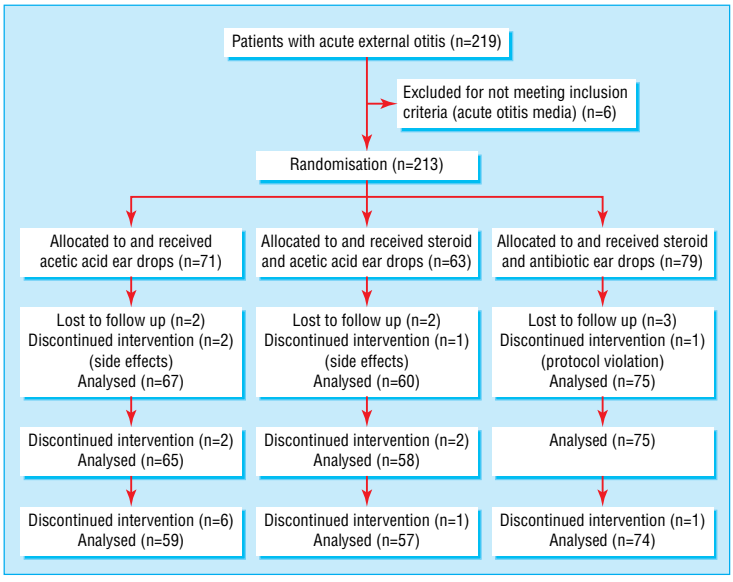

Fig 1 Flow of patients with acute otitis externa through trial of three treatments, with assessment at 7, 14, and 21 days

Table 1 Baseline characteristics of patients treated for acute otitis externa with ear drops containing acetic acid, steroid and acetic acid, or steroid and antibiotic. Values are numbers (percentages) of patients unless stated otherwise

Characteristic	Acetic acid group (n=71)	Steroid and acetic acid group (n=63)	Steroid and antibiotic group (n=79)
Male	36 (51)	31 (49)	40 (51)
Mean age (years)	40.9	48.7	41.1
Symmetrical otitis externa	18 (25)	25 (40)	26 (33)
Comorbidity:			
Diabetes	3 (4)	2 (3)	2 (3)
Eczema	7 (10)	8 (13)	6 (7)
Psoriasis	1 (1)	3 (5)	1 (1)
Contact allergy	2 (3)	3 (5)	5 (6)
Risk factors:			
Swimming	12 (17)	11 (18)	13 (17)
Ear picking	25 (35)	31 (49)	36 (46)
Hearing aid	5 (7)	3 (5)	1 (1)

the groups at baseline. We adjusted the primary and secondary outcomes to account for these differences (table 1). Overall, 160 (75%) patients complied with treatment. Ear rinsing or wick insertion occurred at baseline in 31 (48%) patients in the acetic acid group, 29 (49%) patients in the steroid and acetic acid group, and 38 (51%) patients in the steroid and antibiotic group; at the first follow up in seven (12%), five (10%), and nine (14%) patients, respectively; and at the second follow up in three (9%), two (10%), and six (21%) patients, respectively. These procedures did not significantly influence outcome. Neither procedure was necessary after the second follow up. The wick was retained for no longer than 24 hours.

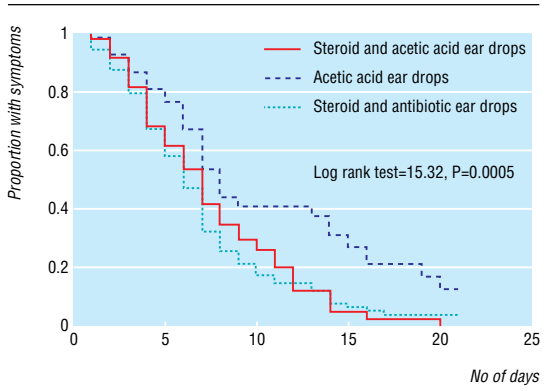

Fig 2 Kaplan Meier plot for resolution of symptoms of otitis externa in 213 patients treated with ear drops containing acetic acid, steroid and acetic acid, or steroid and antibiotic

Time to recovery

The median duration to recovery differed between the treatment arms: 8.0 days (95% confidence interval 7.0 to 9.0) in the acetic acid group, 7.0 days (5.8 to 8.3) in the steroid and acetic acid group, and 6.0 days (5.1 to 6.9) in the steroid and antibiotic group (fig 2). Adjustment for differences in baseline characteristics did not significantly change the outcome.

Cure rate

The overall cure rate for all treatment groups after 7, 14, and 21 days was 40%, 72%, and 79%, respectively. The recovery rates in the acetic acid group at days 14 and 21 were significantly less than in the other two groups (table 2). Overall, 76 (44%) of the 172 patients who were free of symptoms within 21 days showed otoscopic signs of otitis externa. A third of these patients had desquamation of the external auditory canal. Otoscopic signs were not significantly different between treatment arms.

Recurrence

Overall, 50 (29%) of the 172 patients who were symptom free within 21 days had a recurrence of symptoms between days 21 and 42. Significantly more patients in the acetic acid group had recurrence of symptoms and more severe symptoms than in the other two groups (table 3). This was not changed by adjustment for differences in characteristics at baseline. The presence of otoscopic signs at the end of the initial treatment period had no influence on recurrence of symptoms. Twelve (7%) of the 50 patients made an extra visit to their general practitioner. In nine of these the general practitioner confirmed the diagnosis of acute otitis externa.

Table 2 Cure rate according to questionnaires completed by general practitioners at 7, 14, and 21 days follow up for 199 patients with otitis externa treated with ear drops containing acetic acid, steroid and acetic acid, or steroid and antibiotic

Follow up	No of patients	Odds ratio (95% CI)	P value*	Odds ratio (95% CI)†	P value
7 days:					
Acetic acid	19/65	1		1	
Steroid and acetic acid	29/61	2.2 (1.1 to 4.6)	0.036	1.9 (0.9 to 0.04)	0.100
Steroid and antibiotic	31/73	1.8 (0.9 to 3.6)	0.108	1.8 (0.9 to 3.7)	0.089
14 days:					
Acetic acid	37/65	1		1	
Steroid and acetic acid	46/61	2.3 (1.1 to 5.0)	0.030	2.4 (1.1 to 5.3)	0.026
Steroid and antibiotic	60/73	3.5 (1.6 to 7.6)	0.002	3.5 (1.6 to 7.7)	0.001
21 days:					
Acetic acid	40/65	1		1	
Steroid and acetic acid	54/61	4.8 (1.9 to 12.3)	0.001	5.3 (2.0 to 13.7)	0.001
Steroid and antibiotic	63/73	3.9 (1.7 to 9.1)	0.001	3.9 (1.7 to 9.1)	0.001

*Logistic regression.
†Adjusted for differences at baseline.

Table 3 Recurrence of symptoms of otitis externa between days 21 and 42 in 172 patients who were symptom free within 21 days of receiving ear drops containing acetic acid, steroid and acetic acid, or steroid and antibiotic

	Symptoms			Severity	
Group	No of patients	Odds ratio (95% CI)	P value	Mean rank score	P value‡
Acetic acid	21/47	1		57.50*; 66.66†	
Steroid and acetic acid	15/57	0.3 (0.1 to 0.7)	0.007	48.38	0.069
Steroid and antibiotic	14/68	0.4 (0.2 to 1.0)	0.052	52.01	0.004

*Compared with steroid and acetic acid.
†Compared with steroid and antibiotic.
‡Mann-Whitney U test.

Side effects

Side effects were mentioned by 158 (74%) patients at least once. Only two patients in the acetic acid group and one patient in the steroid and acetic acid group discontinued treatment because of side effects. Although the acetic acid group did have more severe burning, pain, or irritation than the other two groups, we found no significant differences between treatment groups.

Discussion

Ear drops containing corticosteroid are more effective in the treatment of acute otitis externa than those containing acetic acid. In patients treated with acetic acid ear drops symptoms lasted longer, the cure rate was poorer, and there was more recurrence of symptoms than in patients treated with ear drops containing steroid with either acetic acid or antibiotic. Patients treated with acetic acid ear drops also showed more recurrence of symptoms than those treated with steroid ear drops. Steroid and antibiotic ear drops were equally as effective as steroid and acetic acid ear drops. It would seem that the effectiveness of acetic acid ear drops is improved by the local anti-inflammatory effect of a corticosteroid. The antibacterial agents (neomycin and polymyxin B) used in our study are effective against most of the pathogens common to acute otitis externa. However, our results also suggest that the aspecific effect of pH lowering by acetic acid is as effective as the theoretically more specific antibacterial effect of antibiotics if both treatments are combined with a local corticosteroid.

The duration of symptoms in our study is less than that of another study with symptom duration as an end point.[15] This study compared the efficacy of otosporin ear drops with aluminium acetate ear drops in 129 service men in Cyprus and found that symptoms lasted for a mean duration of 9-11 days. The warmer climate in Cyprus may explain the difference. Our cure rate of 68% after 14 days agrees with other studies. Another study found a cure rate of 68% after 11-13 days when ofloxacin was compared with corticosporin.[22] Cure rates between 68% and 100% after 14 to 21 days have also been reported, but these studies were mostly conducted in hospital settings and only reported the results from on-treatment analysis.[16 18 23] We could find no large studies reporting cure rates at 7 days or studies reporting on recurrence or otoscopic signs after resolution of symptoms.

The characteristics of the patients in our study differed slightly at baseline. Adjustment for these differences did not significantly change the outcome. Our study drugs are commonly used for the local treatment of acute otitis externa in primary care.[1 2 15–20] We did not include a placebo group as other studies have already shown that local treatment with placebo is less effective than acetic acid, antibiotic, corticosteroids, or combinations of these.[23 24] Our study protocol was designed to closely resemble daily practice, in which the causal agent is unknown and treatment started on an empirical basis. We included important end points for daily practice, such as speed of recovery and recurrence of symptoms.

What is already known on this topic

Acute otitis externa is a common disease in primary care

Most general practitioners prescribe local treatment with corticosteroid and antibiotic ear drops

What this study adds

Local treatment of acute otitis externa is more effective with steroid ear drops than with acetic acid ear drops

Steroid and acetic acid ear drops are as effective as steroid and antibiotic ear drops

We recommend that acetic acid ear drops should no longer be used to treat adults patients with acute otitis externa in primary care. Since no clear advantage was found in using ear drops containing neomycin and polymyxin B, treatment choice should be based on the risks of allergy and antibiotic resistance.

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Contributors: FAMvB was responsible for the study design, data collection, statistical analysis, and writing the paper; he will act as guarantor for the paper. WMS was responsible for data collection and assisted in the statistical analysis and writing the paper. NPAZ was responsible for the statistical analysis. TJMV was responsible for the study design, data collection, and writing the paper.

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Competing interests: None declared.

Ethical approval: The ethical committee of the University Medical Centre Utrecht approved the study protocol, and all participants gave written informed consent before enrolment.

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