Chemical ear peeling: a simple technique for the treatment of chronic external otitis: how we do it

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Dear Editor,

Few conditions encountered by otolaryngologists are as frustrating as chronic otitis externa and recurrent exacerbation presents a special challenge for the attending physician. The disease may be extremely therapy-resistant: a great many patients report chronic suffering from otitis externa with inadequate and inefficacious treatment attempts.[1] Current medical treatment is based on topical application of steroids, antibiotics and external auditory canal cleansing.[2] Moreover, there are no long-term outcome data on medical management.[3]

In this study we present, showing the short- and long-term clinical outcomes, a new, safe and simple therapeutic technique for the management of chronic otitis externa: chemical ear peeling (CEP).

Materials and methods

Patients

The prospective non-controlled study included 28 consecutive chronic otitis externa's acute exacerbation cases diagnosed at the 'G. Ferreri' ENT department, Policlinico Umberto I of Rome, Italy. Patients were enrolled during a 3-year period, from October 2005 to December 2008. Selection criteria were >4 episodes of acute otitis externa per year with at least two episodes in the last 8 weeks. Complete treatment documentation of follow-up visits and retrospective data of disease with a minimum duration of 1 year was available to all patients. Patients with chronic dermatologic inflammatory diseases were excluded. Study protocol is illustrated in Fig. 1. Included patients were referred to CEP at the baseline visit; culture of ear secretion with antibiotic assay was performed at diagnosis and at the test-of-cure visit. Specimens obtained with CEP were analysed by optical microscopy, scanning electron microscopy (SEM) and transmission electron microscopy (TEM). An independent institutional review board approved the study protocol and written informed consent was obtained from all the patients.

Clinical and efficacy assessment

Patients were evaluated at four scheduled visits: baseline (day 1), on-therapy (day 9), end-of-therapy (day 15), and test-of-cure (day 22). At the baseline visit the external auditory canal was cleaned for debris via suction. Primary efficacy variables were: (i) time of cessation of otorrhea, (ii) time of cessation of pain (recorded twice daily in the patient's diary), (iii) clinical cure evaluated at scheduled visits (cured; not cured), and (iv) post-CEP symptom-free interval. Patients were reassessed every 3 months or at relapse.

Chemical ear peeling

We developed this technique as we observed that ciprofloxacin/hydrocortisone drops' administration for more than 7 days (Mediflox, Bruno farmaceutici, Rome, Italy) was responsible for the formation of a subtle film in the external auditory canal. Subsequently, we observed that the precipitate is composed mainly of polyvinylic acid, excipient contained in Mediflox in a not negligible concentration. In this solution polyvinylic acid precipitates under pH 6 (peak pH 4). For this reason we tried to acidificate the external auditory canal with acetic acid 2% some hours after ciprofloxacin/hydrocortisone application. After some days we observed the formation of an easily detachable film.

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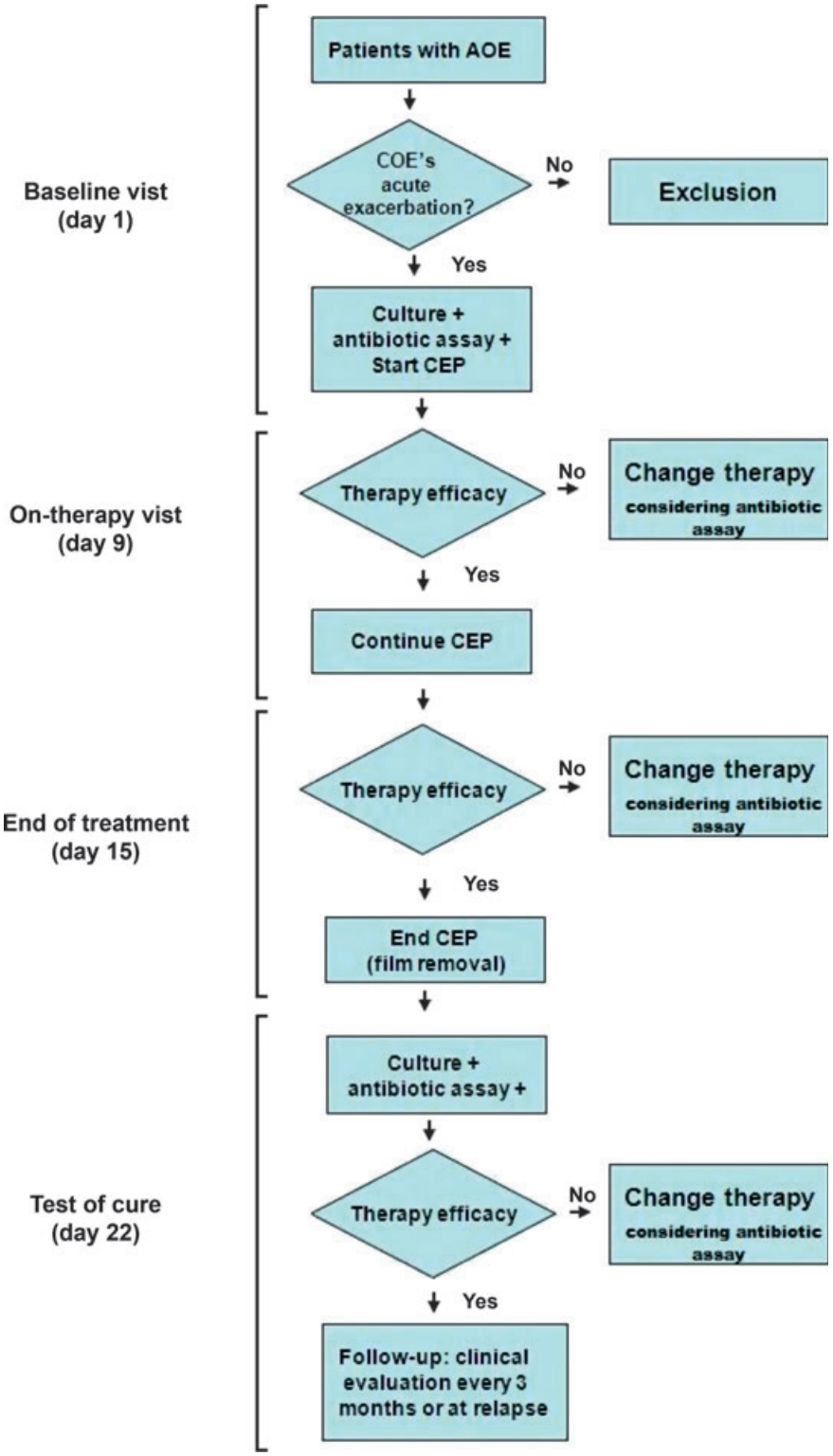

Fig. 1. Study design. At the end-of-treatment visit we observed no otoscopic improvement in two patients (7%). In these patients, with isolated ciprofloxacin-resistant pathogens, we used amoxicillin/clavulanic-acid according to the antibiotic assay results.

Chemical ear peeling consists of three phases: (i) in the first 8 days, five drops of topical ciprofloxacin-idrocortisone (2 mg/mL–10 mg/mL) are administered twice daily (8 A.M., 4 P.M) with the patient in side-lying position. (A higher dosage than the one recommended by the producer Alcon). These administrations are followed by an ear washing with acetic acid 2% (2 mL) once daily at 9 P.M. (ii) The second phase is a passive step. Due to the drying and the precipitation of the medication in acetic acid, in the following 7 days, the patient's external auditory canal is gradually completely covered by a film. (iii) After 15 days in otomicroscopy the film is removed en-bloc using a Hartman forceps. Once extracted, the specimen appears as a vacuous cylindroid constituted externally by the superficial epithelial layer detached from the external auditory canal involving a yellowish-white compact-elastic layer.

Optical and electron microscopy

Ten external auditory canal's film specimens were prepared using classic techniques. Specimens were mounted on aluminium stubs and gold coated and examined under SEM (JEOL JSM 5200, JEOL, Tokyo, Japan). TEM and optical microscopy specimens were embedded in epoxy resins and polymerised in pure resin. The resulting blocks were sectioned with a diamond knife mounted in an ultramicrotome (Reichert Ultracut, Leica Microsystems GmbH, Wetzlar, Germany). Transmission electron microscopy sections were observed using a JEOL JEM 1200 EX TEM-SCAN (JEOL, Tokyo, Japan) at an accelerating voltage of 80 kV. Semifine sections were stained with toluidine-blue and observed using an Axioskop 2 microscopy (Carl Zeiss, Oberkochen, Germany). Control samples, used to verify the microscopic appearance of the applied medication, were prepared by precipitating 10 ciprofloxacin/idrocortisone drops in boric acid 3%, and then submerging the precipitate in acetic acid 2% for 10 min.

Results

Study demographics for all 28 patients enrolled are summarised in Table S1. Twenty-three patients (82%) had only one ear enrolled. The presenting symptoms and signs were: pain in 28 patients (100%), otorrhea in 28 patients (100%), tragal tenderness in 26 patients (93%), erythema in 25 patients (89%), and fever in 2 patients (7%).

Clinical and microbiological efficacy

Main clinical outcomes are reported in Table 1. After 3 days of treatment, otorrhea and pain ceased in 20 (71%) and 22 patients (79%), respectively; at day 9 otorrhea and pain were resolved in 26 (93%) and 28 (100%) patients, respectively. At end-of-treatment and test-of-cure no patients referred pain or otorrhea but overall cure rate was 93%. In fact, we observed no otoscopic improvement in two patients (7%). At test-of-cure visit, external auditory canal appeared clinically cured in the remaining patients. Eighteen patients (64%) referred hypoacusia for 3 days before end-of-treatment; nineteen patients (68%) referred discomfort during the removal of the film. In the post-therapeutic observation period of 8–19 months (13 ± 4), new cases of otitis externa clearly reduced. To date, 16 patients (57%) have sought further medical treatment because of a recurrent external otitis event (1 new episode in 13 cases, 2 new episodes in 3 cases). Compared to the pre-CEP time, the symptom-free interval was significantly extended from 1.2 ± 0.7 to 7.9 ± 3.7 months ($P < 0.00001$) (Fig. 2).

Table 1. Clinical outcomes

Sheduled visits	Pain cessation	Otorrhea cessation	Clinical resolution
Day 3, No (%)	22 (79)	20 (71)	
Day 9, No (%)	28 (100)	26 (93)	22 (79)
EOT, No (%)	28 (100)	28 (100)	26 (93)
TOC, No (%)	28 (100)	28 (100)	26 (93)
Month 3, No (%)			25 (82)
Month 6, No (%)			17 (78)
Month 9, No (%)			14 (68)

EOT, end of treatment; TOC, test of cure.

Cultures taken from the external auditory canal on presentation showed coagulase-negative *Staphylococcus* in 11 patients (39%), *Pseudomonas aeruginosa* in 11 patients (39%) *Staphylococcus aureus* in 2 patients (7%). Others pathogens are reported in Table S2. In 26 patients (93%) pathogens were sensible to ciprofloxacin with a minimum inhibitory concentration between 0.25 and 0.5. In two cases microorganisms were resistant to ciprofloxacin (1 *Enterococcus faecalis*, 1 *Streptococcus pyogenes*). Cultures at end-of-treatment visit of the same patients were positive for the same pathogens; in these two patients we observed no otoscopic improvements at end-of-treatment and test-of-cure visits. At end-of-treatment visit others external auditory canal cultures (96%) were negative.

Optical and electron Microscopy

Optical microscopy (Fig. 3a) shows the layered structure of the film. Scanning electron microscopy and TEM

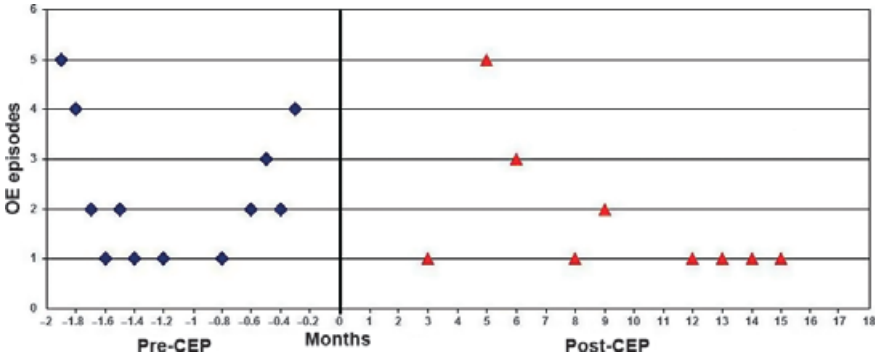

Fig. 2. Pre- and post-chemical ear peeling (CEP) free interval time. The graphic reports the pre-CEP otitis externa's last episodes and the post-CEP episodes in a follow-up period of 13 ± 4 months. After CEP, new cases of otitis externa clearly reduced. Compared to the pre-CEP time, the symptom-free interval was significantly extended from 1.2 ± 0.7 to 7.9 ± 3.7 months ($P < 0.00001$).

images showed more details (Fig. 3b): the basal layer appeared to be formed from the surface layer of external auditory canal's squamous cells (Fig. 3c); the intermediate layer was composed of bacterial aggregates immersed in an extracellular matrix, replicating the typical architecture of bacterial biofilm (Fig. 3d). These aggregates were detected in 9 of the 10 specimens. The superficial layer, compact and electron-dense, was composed of precipitated ciprofloxacin/idrocortisone in acetic acid 2% (Fig. 3e). This was confirmed by observation in TEM of the control sample (Fig. 3f).

Discussion

Current medical treatment of chronic otitis externa is based on topical application of steroids, antibiotics and external auditory canal cleansing.[1] While these standard medications are successful in the short-term therapy of acute otitis externa, it is ineffective and unsuccessful in the long-term treatment of relapsing chronic otitis externa. Moreover, side effects of long-term administration, such as local tissue atrophy (corticosteroids) and development of bacterial resistances (antibiotics), limit their use.[4]

The increasingly rough thickening and keratinisation of the meatal skin represents an avascular zone, which inhibits bi-directional penetration of both exogenous antimicrobials and endogenous protective substances.[3] As such standard topical treatment loses its effectiveness. Furthermore, the impaired epithelialisation of EAC (external auditory canal) does not allow the proper removal of the cerumen encouraging the creation of a microenvironment useful for bacterial growth and the periodic superinfection.[1]

In CEP, we observed the spontaneous detachment of the superficial epithelial layer and its removal en-bloc with the other layers of the film. This allows the complete elimination of pathogenic flora and the renewal of the external auditory canal resulting in the likely restoration of the natural defence mechanism. This is one explanation for why CEP resulted in both short- and long-term therapy successes. In fact, throughout a mean follow-up period of 13 months, no relapses were observed in 43% of the patients. Fifty-seven percent of patients had recurrent events with significantly ($P < 0.00001$) extended mean symptom-free intervals compared with pre-CEP time. In two patients with isolated ciprofloxacin-resistant pathogens, CEP was ineffective. These patients were treated with amoxicillin calvulanic-acid according to the antibiotic assay results. In this regard, antibiotic sensitivity seems to be a determinant for the success of CEP. However, ciprofloxacin was shown effective in terms of bacterial eradication in 92% of cases. The high incidence (39.28%) of coagulase-negative *Staphylococcus* probably was the result of the selection exerted by the previous antibiotic treatments. Regarding adverse events, no relevant local or systemic side effects were observed, except for a transient hypoacusia for 3 days before end-of-treatment in 18 patients (64%) (ceased after CEP film removal), and the discomfort referred by 19 patients (68%) during CEP film removal. In any case no injuries to external auditory canal were caused during the film removal.

However, present results allow us to assume that CEP produces short-term results similar to standard treatments, and with better long-term results. Moreover, electron microscopic images of CEP samples revealed bacterial clusters reproducing the ultrastructural characteristics of the biofilm.[5] This finding shows the potential that biofilm, as for others chronic ear-nose-throat diseases, may play an important pathogenetic role.[6]

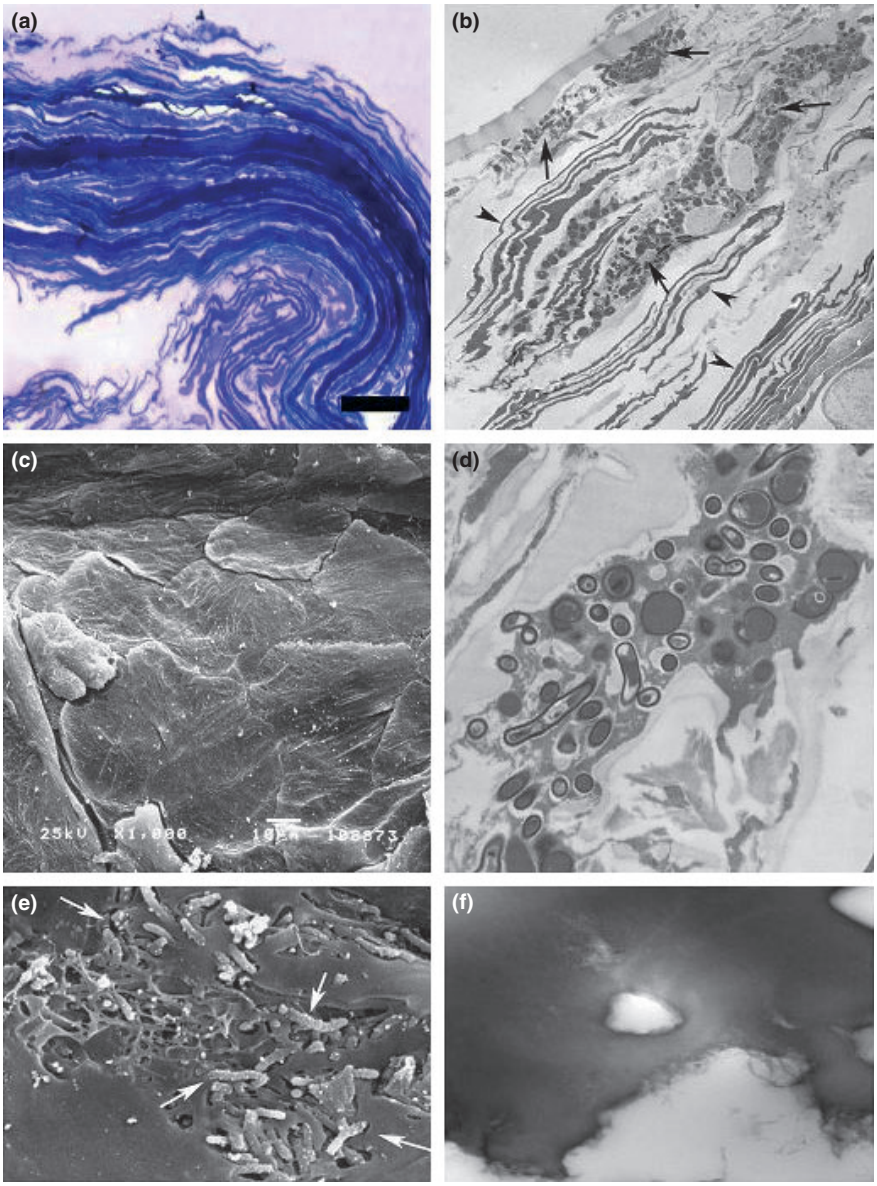

Fig. 3. Microscopic study of chemical ear peeling specimens. (a) Semithin toluidine blue stained section observed by optical microscopy shows the layered structure of the film. (b) Transmission electron microscopy evidences bacterial clusters (arrows) involved by an electron-dense material (arrowheads). (c) Scansion electron microscopy of the film's basal layer shows epithelial regularly distributed cells detached from the external auditory canal. (d) Transmission electron microscopy of the intermediate layer in a patient with positive isolation for *Enterococcus faecalis, Staphylococcus aureus* shows clusters of staphylococci and diplococci in an extracellular matrix surrounded by an electron-dense material constituted of precipited ciprofloxacin/idrocortisone in acetic acid 2%. (e) Scansion electron microscopy of the superficial layer shows electron-dense precipited material with entrapped staphylococci (arrows). (f) Transmission electron microscopy of the control sample showing its compact and electrondense structure.

Finally, a critical evaluation of this study leads to the conclusion that future trials should strive to improve the methodological quality (e.g. double-blinding) to produce more reliable estimates of treatment effects.

Conclusions

This study evaluated the feasibility and safety of CEP in the treatment of chronic otitis externa. Chemical ear peeling will be a good option for the treatment of exacerbation of

chronic otitis externa in patients without chronic dermatologic pathologies.

Keypoints

- Chronic otitis externa may be extremely therapy-resistant with inadequate and inefficacious treatment attempts.
- Current treatment is based on topical application of steroids, antibiotics and external auditory canal cleansing.
- Standard medications are successful in the short-term therapy of acute exacerbation, but could be ineffective in the long-term treatment of chronic otitis externa.
- In this study we present a new, safe and simple therapeutic technique for the management of chronic otitis externa: chemical ear peeling.
- In our series the technique produced short-term results similar to standard treatments but better long-term results.

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Conflict of interest

None to declare.

Supporting Information

Additional Supporting Information may be found in the online version of this article.

Table S1. Presenting factors.

Table S2. EAC cultures.

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Pressure-pulsed inhalation corticosteroid therapy in olfactory disorders: how we do it

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Dear Editor,

Olfactory disorder is a well-known problem and affects quality of life in patients, so further effective therapy options are needed. Pulsed-pressure inhalation (AMSA) seems to be an alternative treatment of olfactory disorder.