Topical ciprofloxacin versus topical gentamicin for chronic otitis media

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السيروفلوكساسين الموضعي في مقابل الجنتاميسين الموضعي في معالجة التهاب الأذن الوسطى المزمن

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خلاصة: تقدِّم هذه الدراسة مقارنة بين الفاعلية العلاجية لكل من هيدروكلوريد السيروفلوكساسين وسلفات الجنتاميسين في معالجة التهاب الأذن الوسطى المزمن. وقد شملت الدراسة 88 مريضاً تتراوح أعمارهم بين التاسعة والثانية والستين، وكانوا يعانون من التهاب صديدي مزمن بالأذن الوسطى. وقد تم توزيعهم عشوائيا على مجموعتين، وكان ذلك بين كانون الثاني/يناير 1999 وآب/أغسطس 1999. وقد عُولج أفراد المجموعة الأولى المكوَّنة من 48 مريضاً (54.5%) بهيدروكلوريد السيروفلوكساسين الموضعي، بينما أُعطي أفراد المجموعة الثانية المكوَّنة من أربعين مريضاً (45.5%) سلفات الجنتاميسين الموضعي. وقد شُفي 42 مريضاً (87.5%) من بين المرضى الثمانية والأربعين الذين تلقوا هيدروكلوريد السيروفلوكساسين، بينما فشل العلاج في ستة مرضى (12.5%). أما في مجموعة الجنتاميسين فقد شُفي 12 مريضاً فقط (30%) بينما لم يُبد 28 مريضاً أي تحسُّن سريري أو جرثومي. إن مستحضرات السيروفلوكساسين الموضعية مأمونة وأكثر نجاعة وفاعلية من الجنتاميسين الموضعي في معالجة السَّورات الحادة لالتهاب الأذن الوسطى الصديدي المزمن.

ABSTRACT We compared the therapeutic efficiency of ciprofloxacin hydrochloride and gentamicin sulfate in the treatment of chronic otitis media. A total of 88 patients aged 9–62 years with chronic suppurative otitis media were randomly placed into two groups. In the first group, 48 patients (54.5%) received topical ciprofloxacin hydrochloride, while in the second group 40 patients (45.5%) received local gentamicin sulfate. Of the 48 patients who received ciprofloxacin hydrochloride, 42 (87.5%) were cured, while in 6 patients (12.5%) the treatment failed. In the gentamicin group, 12 (30%) of the patients were cured, while 28 patients showed no clinical or bacteriological improvement. Topical ciprofloxacin is safe and more efficacious and efficient than topical gentamicin in the treatment of acute exacerbation of chronic suppurative otitis media.

La ciprofloxacine topique versus la gentamicine à action locale pour l'otite moyenne chronique
RESUME Cette étude a comparé l'efficacité thérapeutique de la ciprofloxacine hydrochloride et de la gentamicine sulfate dans le traitement de l'otite moyenne chronique. Au total, 88 patients âgés de 9 à 62 ans atteints d'une otite moyenne chronique suppurée ont été répartis au hasard en deux groupes entre janvier et août 1999. Dans le premier groupe, 48 patients (54,5 %) ont reçu de la ciprofloxacine hydrochloride à usage topique, tandis que dans le second groupe, 40 patients (45,5 %) ont reçu de la gentamicine sulfate à action locale. Sur les 48 patients qui ont reçu la ciprofloxacine hydrochloride, 42 (87,5 %) ont guéri, tandis que le traitement a échoué chez 6 patients. Dans le groupe de la gentamicine, seuls 12 (30 %) des patients ont guéri, tandis que 28 patients n'ont montré aucun signe d'amélioration clinique ou bactériologique. La préparation de ciprofloxacine topique est sans danger et plus efficace que la gentamicine à action locale dans le traitement d'une crise d'otite moyenne chronique suppurée.

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Introduction

Chronic otitis media, defined by the persistent perforation of the tympanic membrane, is often associated with suppuration. Treatment includes frequent aspiration of the otorrhoea and the use of systemic and topical antibiotics based on culture results [*1,2*]. Bacterial florae in chronic suppurative otitis media vary considerably. The predominant organisms are Gram-negative bacilli, commonly *Pseudomonas aeruginosa*. Other pathogens include *Staphylococcus aureus*, *Enterobacter* spp. and, more rarely, anaerobic bacteria. Mixed microorganisms may also be present [*3*]. Multiresistant bacteria and low concentrations of antibiotics in the middle ear are the main causes of treatment failure with conventional systemic antibiotics.

Ciprofloxacin is a fluoroquinolone that is highly active against Gram-negative bacteria, especially *Pseudomonas* spp. and methicillin-resistant *S. aureus*. The target of ciprofloxacin is DNA gyrase, a replication enzyme that plays a major role in DNA synthesis [*1*].

Gentamicin is an aminoglycoside effective against both Gram-negative and Gram-positive organisms, including *P. aeruginosa*, *Enterobacter* spp. and *S. aureus*. Its bactericidal activity against susceptible organisms is due to irreversible inhibition of protein synthesis. It has been used topically in the treatment of chronic otitis media.

We aimed to compare the therapeutic activity of ciprofloxacin and gentamicin as topical agents in the treatment of chronic suppurative otitis media, evaluating efficacy by the cessation of otorrhoea.

Methods

This study was carried out in Prince Rashid Ben Al-Hasan Hospital between January and August 1999. The study population consisted of 88 Jordanian patients with a history of chronic suppurative otitis media and intermittent mucopurulent heavy discharge for more than one year; 88% of the patients had the tubotympanic form of infection, while the remaining 12% had the atticoantral form.

All patients included in the study were examined carefully and diagnosed as having chronic suppurative otitis media before the start of treatment. There were 46 male and 42 female patients. Their ages ranged from 9 years to 62 years, with a mean of 30 years. Patients who had a history of allergy to fluoroquinolone derivatives or aminoglycosides, were under 9 years of age or had a past history of general health problems were excluded from the study. All patients gave their informed consent before entering the study and stopped taking any medication at least 10 days prior to start of treatment. Patients who failed to use the topical solution regularly or who took other medication during the study period were excluded.

The patients were divided into two groups. The first group included 48 patients who received ciprofloxacin solution prepared by dissolving ciprofloxacin hydrochloride in distilled water to obtain a final concentration of 200 μg/mL [*4*]. The second group consisted of 40 patients who received gentamicin sulfate (5 mg/mL). Five drops were administered locally three times a day for 10 days in both groups. Aerobic cultures from the deep part of the external ear canal secretion were obtained 24 hours before treatment and 24 hours after completing the treatment course. The sensitivity of the microorganisms to gentamicin and ciprofloxacin was studied *in vitro*.

Patient outcomes were evaluated by otoscopic examination. During the treatment period, follow-up examinations were performed on the second, fifth, seventh and tenth days after the start of treatment. The cessation of otorrhoea and absence of microorganisms in the post-treatment cultures were taken as indicators of clinical success. Hearing levels were assessed and audiological tests were performed before and 24 hours after treatment.

The chi-squared test was used to compare the percentages of clinical and microbiological response in the two treatment groups.

Results

Our study showed that in both groups, microorganisms could be isolated from canal swab cultures during both the pre-treatment and post-treatment periods (Tables 1 and 2). *Pseudomonas* and *Staphylococcus* species were the most common microorganisms identified.

In the group receiving ciprofloxacin, 42 of the 48 patients (87.5%) were cured, while in 6 patients (12.5%) the treatment failed. The patients who failed nevertheless showed significant clinical improvement (minimal moisture in the cavity) even though bacteria were not eradicated. The post treatment cultures of these 6 patients contained *Candida albicans*. In 30 (62.5%) of the pre-treatment cultures, the isolated microorganisms were resistant to gentamicin. No ciprofloxacin-resistant microorganisms were detected in either pre-treatment or post-treatment cultures.

Table 1 **Culture results from the pre-treatment and post-treatment periods in the group receiving ciprofloxacin**

Species	Pre-treatment (*n* = 48)	Post-treatment (*n* = 48)
Pseudomonas	30	–
Staphylococcus	6	–
Proteus	2	–
Pseudomonas and *Enterobacter*	2	–
Normal flora	8	42
Candida	–	6

– *indicates negative.*

Table 2 **Culture results from pre-treatment and post-treatment periods in the group receiving gentamicin**

Species	Pre-treatment (*n* = 40)	Post-treatment (*n* = 40)
Pseudomonas	22	22
Staphylococcus	8	4
Enterobacter	4	–
Proteus	2	2
Pneumococcus	2	–
Pseudomonas and *Enterobacter*	2	–
Normal flora	–	12

– *indicates negative.*

In the group receiving gentamicin, 12 patients (30.0%) were cured. The remaining patients showed no clinical or bacteriological improvement. Tests for antibiotic sensitivity in the pre-treatment cultures showed resistance to gentamicin in 16 out of 40 patients (40.0%). Neither group showed any significant difference in hearing levels or audiological tests before or 24 hours after treatment.

The microbiological and clinical cure rate was significantly higher in the ciprofloxacin group than in the gentamicin group ($P < 0.001$).

Discussion

Chronic suppurative otitis media is a common and potentially dangerous clinical condition that is difficult to treat because the most common infecting organisms are often resistant to antibiotics. Treatment for an acute exacerbation of chronic suppurative otitis media aims to achieve a dry, aerated ear and to prepare a subset of patients for subsequent surgery. Therapy includes frequent aspiration, protection of the ear and the use of oral or topical antibiotics.

The mode of administration of antibiotics remains controversial [*5–7*]. The most common causative agent is *P. aeruginosa*, which is often resistant to several classes of antibiotics. Therefore, the first drug of choice should be active against *Pseudomonas* species. Gentamicin, an agent that is ototoxic but highly effective against Gram-negative bacteria, was chosen for the study as it is commonly employed in the topical treatment of chronic otitis media [*8,9*]. Ciprofloxacin, a fluoroquinolone derivative, has been used clinically in oral and topical forms and numerous studies have evaluated its efficacy [*1,2,10*]. De Miguel Martinez et al. [*11*] reported that ciprofloxacin was the most effective regimen for the treatment of chronic suppurative otitis media, while Kasemsuwan and Clongsuesnek [*12*] found that topical ciprofloxacin appeared effective in curing the acute phase of chronic otitis media. Wright and Meyerhoff [*9*] observed a low percentage of remission and bacteriological eradication following a 250 mg dose of ciprofloxacin hydrochloride given orally twice a day, and good results following topical treatment with the same drug. Good results were also reported by Van de Heyning et al. [*13*] using much higher doses (750 mg twice a day) in 28 patients with suppurative otitis media. Esposito et al. [*2*] reported a high rate of clinical response in chronic suppurative otitis media to topical ciprofloxacin, and were unable to document audiometric evidence of treatment-related hearing loss. Kiris et al. [*14*] found topical ciprofloxacin to be an effective, safe and relatively inexpensive treatment for chronic otitis media, while Indudharan et al. [*15*] found that both ciprofloxacin and gentamicin were the best choices in the treatment of chronic otitis media.

Given the range of results reported by these studies, we decided to compare the clinical efficacy of topical ciprofloxacin and gentamicin.

In our study, the incidence of pre-treatment resistance to gentamicin was found to be 52.3% (46/88, 30 patients in the ciprofloxacin group and 16 patients in the gentamicin group). By contrast, none of our patients was resistant to ciprofloxacin. Furthermore, gentamicin resistance developed in 12 patients after a course of treatment, while drug resistance was not observed in any of the patient who received ciprofloxacin. Treatment failed in 6 patients in the ciprofloxacin group who developed otomycosis; otomycosis is a significant complication despite being easily managed. Otomycosis secondary to topical ciprofloxacin has also been reported by Piccirillo and Parnes [*16*].

The cure rate of ciprofloxacin treatment was 87.5% in our study, while for gentamicin the actual cure rate, taking into account the number of patients (24) who were sensitive to this agent before treatment, was 50% (12/24). The amount of ciprofloxacin in our preparation (200 μg/mL, administered as 5 drops three times a day for 10 days) is sufficient to obtain a dry ear, which is the aim of medical treatment for chronic suppurative otitis media.

Conclusion

In conclusion, topical ciprofloxacin is safe, more efficacious and more efficient than topical gentamicin in the treatment of an acute exacerbation of chronic suppurative otitis media. We suggest that this formulation be used as a first-choice therapy in these patients.

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