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STUDY OF EMPIRICAL THERAPY WITH COMBINED CIPROFLOXACIN EFFICACY VERSUS TOPICAL DROPS ALONE IN TUBOTYMPANIC CHRONIC SUPPURATIVE OTITIS MEDIA

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ABSTRACT

One of the prevailing otologic infections is chronic suppurative otitis media, especially the tubotympanic type for which various treatment protocols are followed. Usually, oral and topical antibiotics (mainly quinolones) are given alone or in combination. There is a lack of consensus as to whether topical drops alone are effective or a combined oral and systemic therapy should be prescribed. In our study, we have attempted to observe the efficacy of empirical therapy with combined ciprofloxacin versus topical drops only in patients with tubotympanic chronic suppurative otitis media for control of infection. **In this study, a** total of (150) patients visiting the outpatient ENT department at our Haditha general hospital/Iraq with clinically diagnosed chronic suppurative otitis media (tubotympanic type) were enrolled in our study. A detailed proforma was filled for all patients. All patients after aural toilet were subjected randomly to one of the 2 treatment methods, ie, topical ciprofloxacin ear drops plus an oral placebo or combined oral and topical ciprofloxacin, and the patients were reviewed after 1 week of treatment. It was observed that 71 of 75 (94.7%) patients responded to treatment in the group receiving topical ciprofloxacin, whereas 71 of 75 (98.7%) patients responded in the group receiving combined therapy. This difference was not significant. Moreover, age, sex and duration of discharge did not have any effect on treatment. There were minimal side effects in both groups, which were also not significant and disappeared after discontinuation of treatment. It can be concluded from this study that topical ciprofloxacin drops were as effective as combined oral and topical ciprofloxacin and that the addition of oral drug did not have any beneficial effect and added only to the cost of treatment.

KEYWORDS: Chronic suppurative otitis media (CSOM), Empirical antibiotics, Otorrhea, Pseudomonas aeruginosa.

INTRODUCTION

Experts harbor conflicting views regarding the true definition of chronic suppurative otitis media (CSOM).[1] The World Health Organization (WHO) defines CSOM as "a stage of ear disease in which there is chronic infection of the middle ear cleft, a non-intact tympanic membrane (i.e. perforated ear-drum) and discharge (otorrhea), for at least the preceding two weeks." The 2 main groups include tubotympanic or safe type with a perforation in the pars tensa without cholesteatoma and atticoantral type when the perforation is in the attic or if there is presence of cholesteatoma.[2,3]

Risk factors of chronic suppurative otitis media include young age, overcrowding, inadequate housing, poor hygiene, lack of breastfeeding, poor nutrition, eustachian tube dysfunction, and inadequate or unavailable health care. Poverty is a major risk factor in developing countries.[3] Pseudomonas aeruginosa is the most common pathogen isolated.[4] Drug sensitivity patterns show that ciprofloxacin (quinolones) is active against most of the isolates, followed by amikacin, gentamicin, and other penicillins and cephalosporins.[5,6]

Medical management aims to stop the discharge, to heal small perforations in the tympanic membrane, to improve hearing, and to prevent infections and potentially life-threatening complications. Treatment options include the following: dry mopping, topical antiseptics or antibiotics, sometimes combined with steroids and systemic antibiotics.[2] Because systemic aminoglycosides cause well-documented ototoxic and nephrotoxic side effects, systemic quinolones are often prescribed in these cases because of high incidence of gram-negative organisms such as Bacillus, Proteus, and P aeruginosa.[7] However, systemic quinolones are

contraindicated in pregnancy and in children.[8] Introduction of topical quinolones has gained interest in the medical management of CSOM because of their clinical efficacy and lack of side effects. Topical treatment with quinolones may be as effective as systemic treatment, in terms of efficacy and also safety, thereby avoiding the need for systemic therapy.[9]

A study about the drug sensitivity in 164 patients of CSOM revealed that Staphylococcus aureus showed highest sensitivity to gentamicin (82.5%), whereas P aeruginosa was 100% sensitive to ceftazidime, while the overall sensitivity to standard CSOM antibiotic is on higher side.[10] In a study on 124 people of Malawi rural areas, empirical otologic drops of ofloxacin were administered right after collection of cultures. It showed 33 failures for complete resolution of CSOM. Culture results showed that most of the persistent bacteria are either enterococci or water bacteria. Typical CSOM-causing organisms had higher sensitivity toward ofloxacin.[11] Group A was prescribed antibiotics after culture and sensitivity, whereas group B had an empirical therapy of 2 weeks without microbiology done. The results showed no significant (P = 0.2) difference between 2 groups with respect to resolution and recurrence or persistence of ear discharge.[12]

MATERIALS AND METHODS

This double-blinded, prospective, randomized trial study was conducted during a 15-month period at the ENT outpatient department of Haditha general hospital, Anbar province/Iraq on (150) randomly selected patients attending the outpatient department and diagnosed with CSOM of tubotympanic type were. They were divided into 2 groups of 75 each. Group "A" patients received only topical ciprofloxacin drops plus an oral placebo, whereas Group "B" received both oral and topical ciprofloxacin for 1 week. The patients were not informed and did not know what drug they were given, whereas the physicians were blinded and given the drugs in the form of codes, ie, codes A and B, randomly organized in sealed envelopes to maintain the randomization. There were 150 sealed non-labeled envelopes (75 for each group): half containing prescriptions for topical ciprofloxacin and oral placebo and the other half with prescription for both oral and topical ciprofloxacin. Only on opening the envelope, the treatment was started. Topical ciprofloxacin drops in both the groups were given every 8 hours with 3 to 4 drops each time for 7 days. In Group "A," oral placebo was given every 12 hours for the same duration. In Group "B," oral ciprofloxacin was given at a dose of 200 mg every 12 hours also for 7 days. Patients were reassessed in ENT OPD after 7 days, and the ear was examined with respect to discharge, perforation, and resolution/worsening of symptoms. Patients who had already received treatment within 2 weeks for the same complaint or who had taken antibiotics for other complaints, eg, upper respiratory tract infections, and patients having attic perforation or cholesteatoma/ granulations on examination or having ear pathology besides CSOM (eg, otitis externa) were excluded from the study.

Patients with anatomical abnormalities of external or middle ear on examination were also excluded from the study.

The study instrument comprised 3 sections. The first section was concerned with the demographics of the subjects and included variables such as age and sex. The second section included questions pertaining to CSOM such as duration of discharge and whether the discharge resolved after 7 days. The last section aimed to assess the adverse events arising out of the treatment regimen advised.

Statistical analysis

Data from the questionnaire were entered in SPSS (Statistical Package for the Social Sciences) version 20.0 for analysis and the results were compared.

RESULTS

In this study, (98) patients were men with the mean age of 37.2 years and (52) were women with mean age of 34.5 years, giving a male to female ratio of 1:0.54. The ages of the subjects ranged from 16 to 52 years, with a mean age of 35.1 ± 6.3 years. The mean duration of discharge was 50.4 days (SD + 41.2) with a minimum of 11 days and maximum of 85 days. The left ear was affected in 85 patients, whereas the right ear was affected in 65 patients, with none having bilateral pathology.

After a week of therapy, both the groups were compared with respect to resolution of discharge and adverse effects. Of 150 patients enrolled in this study, 145 had complete resolution of discharge, whereas 5 failed to show complete resolution. Of 75 patients, 71 (94.5%) in group "A" taking topical ciprofloxacin showed resolution of discharge, whereas 74 of 75 patients (98.7%) in group "B" had resolution of discharge. There was no statistical difference between the 2 groups with respect to effectiveness of treatment. There were minimal adverse effects in both the groups.

In group "A," only 4 failed to show any resolution of discharge. On further examination, two of the patients had fungal overgrowth which accounted for persistent otorrhea. A culture swab was taken from the other patient's ear whose discharge failed to resolve after 1 week of topical ciprofloxacin. In group "B," there was only 1 failure as shown in figure (1).

It was observed that there was no significant difference between 2 groups in terms of sex (P = 0.61) and resolution of discharge (P = 0.36). No significant difference was found in age (P = 0.13) and duration of discharge (P = 0.18) between 2 groups. Tabular representation of categorical variables was given in table (1), whereas table (2) represents continuous variables.

Of the (20) patients who complained of adverse effects to the drugs prescribed, 7 patients were in Group "A" taking topical ciprofloxacin ear drops, whereas 13 patients were in Group "B" taking combined oral and topical ciprofloxacin as shown in figure (2). In group "A," 4 patients complained of mild ear ache, whereas only 3 patients developed fungal overgrowth. In Group "B," there were 13 patients having side effects of which 10 patients complained of transient gastrointestinal disturbance, 1 patient had mild arthralgia, and 2 patients had vertigo.

Table (1): Categorical variables and their associations.

		Group A	Group B	P value
Gender	Male	47	51	0.61
	Female	28	24	
Resolution of discharge	Yes	71	74	0.36
	No	4	1	

Table (2): Continuous variables and their associations.

	Group A	Group B	*P* value
Mean age, y	35.45±12.61	31.79±10.57	0.13
Duration of discharge, d	53.64±19.1	55.15±16.3	0.18

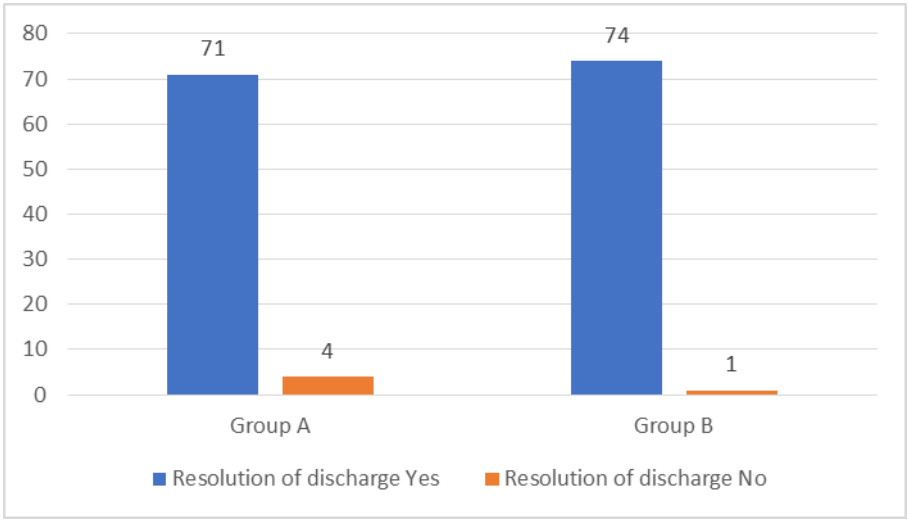

Figure (1): Group-wise resolution of discharge.

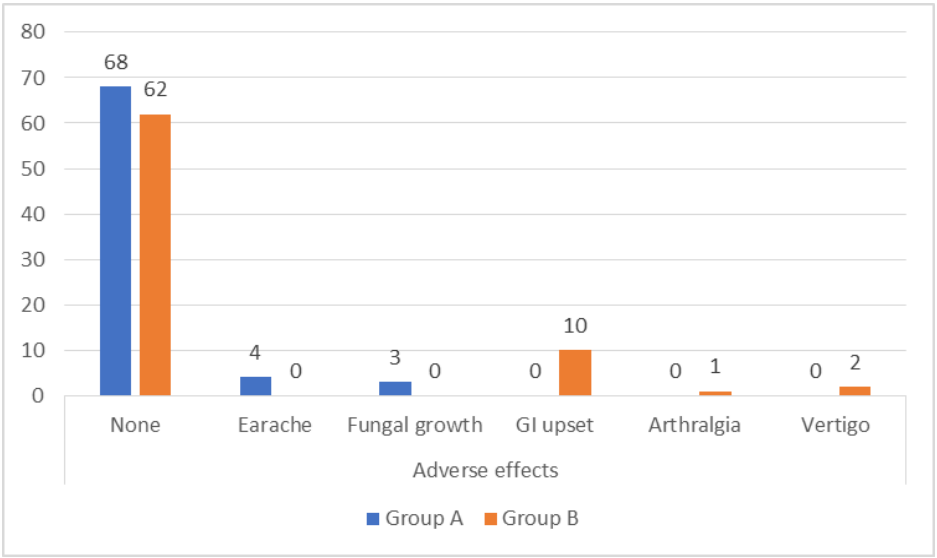

Figure (2): Comparison of adverse effects.

DISCUSSION

There has been a paucity of randomized controlled trials in our setup to observe the efficacy of ciprofloxacin drops. One trial was reported in 2003, where the authors compared the effects of topical quinolones with topical aminoglycosides with encouraging results but aside from that a comparative study is lacking.[13]

Researchers have studied the effects of single and combined therapy and have come up with varying results. A study by Mittal et al concluded that topical antibiotics and aural toilets constitute the first line of treatment for CSOM. It was also observed that intravenous antibiotics show increased side effect profile and significant potential to produce antibiotic resistance.[14]

A study on the efficacy of ofloxacin showed that clinical success of oral and topical ofloxacin varies from 75% to 90%. In this evidence-based review, Manolidis et al reviewed various ear infections including otitis media which were treated with ciprofloxacin and aminoglycosides. They observed that fluoroquinolones have better efficacy as compared with aminoglycosides. It was concluded that ofloxacin 0.3% otic solution has comparable or better efficacy than most of the conventional antibacterial therapies for middle ear infections.[11]

In 1990, Esposito studied the effectiveness of oral versus topical ciprofloxacin.[15] In this randomized trial, 3 groups were assigned for oral, topical, and combined therapy with 20 patients in each group. This study favored the use of topical drops only, with a success rate of 85% and the non-necessity of oral treatment, but there was no mention about the safety profile and adverse effects of ciprofloxacin in this study.

Perhaps, the most important evidence for the use of topical ciprofloxacin comes from the Cochrane Database Reviews. In 2000, Acuin et al from Philippines published a review paper in the Cochrane Database to assess the effects of different treatments for CSOM.[16] They reviewed 24 randomized trials including 1660 people. Topical quinolones were found to be more effective than nonquinolones in 5 trials but combining topical and systemic antibiotics were not more effective than topical antibiotic drops alone. He further went on to prepare the document and guidelines for prevention of blindness and deafness for the WHO in 2004.[17] Within this document, it is also stated that topical drops alone are effective for non-complicated chronic otitis media.

It was also observed that topical quinolones have better efficacy than topical nonquinolones.[18] Acuin et al published an update of the previous reviews in 2007. This review addressed 48 different studies, discussing the management plan in the patients of CSOM with an emphasis on the usage of topical quinolones.[19]

It was observed that topical ciprofloxacin solution as a single dose is more effective and showed better tolerance rate in the patients of CSOM.[20] de Miguel in 1999 published a randomized trial of 125 patients where he selected 4 different treatment groups to study the effectiveness of ciprofloxacin in CSOM.[21] He concluded that topical ciprofloxacin remained the most effective form of treatment.

A similar study was conducted by Ramos and colleagues in 2003.[22] Five treatment groups were assigned to patients with chronically discharging ears. They concluded that topical treatment with ciprofloxacin in chronic middle ear infection revealed improved results as compared with oral administration. This study had 300 patients and compared various strengths of topical ciprofloxacin versus oral quinolone and combined forms. This study had a bias of including patients with cholesteatoma, as well, which may have led to a less favorable treatment response, although they added fluocinolone. Our study focused on patients with tubotympanic CSOM to avoid this bias.

In 2006, Carolyn et al studied 9 randomized trials including 833 participants. This review article which was published in the Cochrane Database; the authors deduced that topical quinolones can resolve aural discharge better than systemic antibiotics and they were more effective than nonquinolone topical antibiotics or antiseptics, although none of these trials reported any long-term results regarding adverse effects. There was clearly no benefit detected of adding systemic antibiotics to topical quinolones.[9]

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