

ORIGINAL ARTICLE

Comparison of Efficacies of 10% Ichthammol Glycerine and 3% Ciprofloxacin–1% Dexamethasone in Treatment of Acute Otitis Externa in Terms of Pain Reduction

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ABSTRACT

Background: Acute otitis externa (AOE) is a prevalent inflammatory condition of the external auditory canal (EAC) in which ear pain is a prominent symptom. Both topical antibiotic combinations with steroid and ichthammol glycerine are used for treatment, but there is still limited comparative evidence about early pain relief.

Objective: To compare the efficacy of 3% ciprofloxacin–1% dexamethasone with 10% ichthammol glycerine in reducing pain among patients with moderate-to-severe acute otitis externa.

Material and Methods: It was a randomized controlled trial in the Department of Otorhinolaryngology, Head and Neck Surgery, Pakistan Institute of Medical Sciences, Islamabad from May to November 2018. 70 patients age 12 to 60 years were divided into 2 groups equally. Group A was given 3% ciprofloxacin – 1% dexamethasone wick and Group B was given 10% ichthammol glycerine wick. The pain measured on a Visual Analogue Scale (VAS) at day 3 and baseline. The day-3 pain-response criterion was used to measure treatment efficacy.

Results: Baseline VAS scores were comparable between Group A and Group B (6.74 ± 1.12 vs 6.71 ± 1.15). By day 3, mean VAS decreased to 2.43 ± 1.36 and 3.63 ± 2.04 , respectively. Ciprofloxacin–dexamethasone resulted in a greater mean reduction in pain score compared to the other group (4.31 ± 1.32 vs 3.09 ± 1.44 ; $p < 0.001$). Overall efficacy was 77.1% versus 40.0% ($p = 0.002$). These differences were found in each sex and age category, and were more pronounced in the ciprofloxacin–dexamethasone group in all of the subgroups.

Conclusion: 3% ciprofloxacin–1% dexamethasone provided superior early pain control compared with 10% ichthammol glycerine in moderate-to-severe acute otitis externa.

Keywords: Acute otitis externa; Ciprofloxacin; Dexamethasone; Ichthammol glycerine; Otalgia; Visual Analogue Scale.

INTRODUCTION

Acute otitis externa (AOE) is an inflammatory or infectious disorder of the external auditory canal and represents a common otological condition affecting individuals across different age groups. Approximately 10% of the population may experience otitis externa, with a higher occurrence in warm and humid environments and among individuals with frequent water exposure. Any compromise of the normal barrier function of the external auditory canal, such as moisture, local trauma, maceration, external devices, dermatological conditions, or canal obstruction, can make the epithelium susceptible to inflammation and infection^{1,2}.

The microbiological profile of AOE is almost exclusively bacterial, but fungal and, rarely, viral causes also may occur. *P. aeruginosa* and *S. aureus* are some of the most common pathogenic organisms that are isolated³. Ear discharge, tenderness of tragus or pinna, otalgia and pruritus are the typical clinical features, along with edema of the external auditory canal that depends on the severity of the disease. Moderate disease is often accompanied by noticeable pain and some obstruction of the canal, while severe disease can cause severe pain, swelling, complete blockage of the canal, redness around the ears, swollen lymph nodes or a fever^{3,4}.

Topical therapy is a key part of the treatment of uncomplicated AOE, especially if there is an infection and inflammation. Use of preparations containing a combination of an antimicrobial agent and a corticosteroid is often indicated as these treatments have antimicrobial activity and also help to diminish any inflammatory change in the area. The activity of the important pathogens like *P. aeruginosa* and *S. aureus* are offered by the ciprofloxacin containing preparations while dexamethasone

may play a role in the control of edema and inflammation. The local antiseptic and anti-inflammatory properties of Ichthammol glycerine have also been utilized as a topical remedy especially in wick therapy. But the relative efficacy of these treatment strategies, especially in terms of early pain relief, still has clinical significance^{4,5}.

Different local studies have yielded various results concerning the effect of topical wick preparations on pain. Abid et al. did a comparative study between glycerol/ichthammol wick and neomycin/betamethasone wick and noticed that pain relief was different on 3rd day of treatment⁵. Another study compared the effect of 3% ciprofloxacin–1% dexamethasone and 10% ichthammol glycerine and found that the pain was reduced in 76% of patients given 3% ciprofloxacin–1% dexamethasone and 38% of patients given 10% ichthammol glycerine⁶. The observations imply that antibiotic–steroid preparations might be more effective for symptomatic improvement, which is yet to be studied in local populations^{5,6}.

One of the most troublesome of the moderate to severe AOE symptoms is pain, which can significantly impair daily life and activities. Since a number of topical treatments exist and there has not been a universal agreement on which treatment is best in all clinical settings, comparing commonly used regimens can help in the decision of which treatment to choose^{4,7}. The present randomized controlled trial was therefore conducted to compare the efficacy of 10% ichthammol glycerine with 3% ciprofloxacin–1% dexamethasone in patients with moderate-to-severe acute otitis externa, with pain reduction assessed using the Visual Analogue Scale as the principal outcome.

MATERIALS AND METHODS

Study Design and Setting: This randomized controlled trial was conducted in the Department of Otorhinolaryngology, Head and Neck Surgery, Pakistan Institute of Medical Sciences (PIMS),

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Islamabad, Pakistan. The study was carried out over a period of six months, from 7 May 2018 to 6 November 2018. The primary objective was to compare the efficacy of 10% ichthammol glycerine with 3% ciprofloxacin–1% dexamethasone for reducing pain in patients with moderate-to-severe acute otitis externa.

Sample Size and Sampling Technique: The sample size was calculated using the WHO sample size calculator version 2.2b for hypothesis testing of two population proportions. A two-sided level of significance of 5%, statistical power of 90%, an anticipated efficacy proportion of 76% for 3% ciprofloxacin–1% dexamethasone, and an anticipated efficacy proportion of 38% for 10% ichthammol glycerine were used for the calculation. The required sample size was 35 patients in each treatment arm, resulting in a total sample of 70 participants. Patients presenting to the ENT outpatient department who fulfilled the eligibility criteria were recruited through non-probability consecutive sampling and subsequently allocated to the two treatment groups.

Study Population: Patients aged 12–60 years, of either sex, with a clinical diagnosis of moderate-to-severe acute otitis externa were eligible for inclusion. Acute otitis externa was diagnosed clinically on the basis of characteristic otalgia accompanied by tenderness on tragal pressure or manipulation of the auricle and edema of the external auditory canal. Moderate disease was characterized by appreciable pain with partial canal obstruction, whereas severe disease was associated with intense pain and marked or complete canal occlusion due to edema.

Inclusion and Exclusion Criteria: Patients were included if they had moderate-to-severe acute otitis externa, were between 12 and 60 years of age, and fulfilled the predefined clinical diagnostic criteria. Both male and female patients were eligible.

Patients were excluded if they had a history of acute or chronic suppurative otitis media, diabetes mellitus or another immunocompromised state, local allergic or dermatological disorders such as eczema or psoriasis, bilateral otitis externa, or use of a hearing aid. Patients with inadequate follow-up compliance were also excluded from the final study assessment.

Randomization and Treatment Allocation: After enrollment, participants were randomly assigned into two treatment groups using a random-number table. Group A consisted of 35 patients who received 3% ciprofloxacin–1% dexamethasone, whereas Group B consisted of 35 patients who received 10% ichthammol glycerine. The final study population therefore comprised 70 participants, with equal allocation between the two treatment arms.

Baseline Clinical Assessment: At enrollment, demographic and clinical information, including age, sex, pain characteristics, ear discharge, use of hearing aids, history of diabetes, and allergic conditions, was recorded. Patients underwent otological examination for tragal tenderness and the presence of discharge or debris within the external auditory canal. Moderate-to-severe acute otitis externa was defined by a baseline Visual Analogue Scale (VAS) score of ≥ 5 , pain exacerbated by tragal pressure or superior manipulation of the auricle, and otoscopic evidence of external auditory canal edema with only partial visualization of the tympanic membrane. Patients with evidence of middle-ear fluid or middle-ear infection were not considered to have isolated acute otitis externa.

Intervention Protocol: Following examination, necessary suction clearance of discharge and debris from the external auditory canal was performed. In Group A, a wick containing 3% ciprofloxacin–1% dexamethasone was placed in the affected auditory canal. In Group B, a wick containing 10% ichthammol glycerine was placed in the affected canal.

To maintain comparable background treatment between the groups, both groups received the same analgesic regimen consisting of mefenamic acid 500 mg three times daily. According to the study treatment protocol, oral co-amoxiclav was also prescribed to patients in both groups. Thus, the principal difference between the groups was the topical wick preparation being evaluated.

Pain Assessment: Pain intensity was assessed using a 10-point Visual Analogue Scale, ranging from 0, representing no pain, to 10, representing the most severe pain. VAS was recorded at baseline before initiation of treatment and again on the third day following treatment. The study specifically evaluated short-term pain reduction because pain was the primary clinical outcome of interest.

Definition of Treatment Efficacy: Treatment efficacy was assessed on the third day of therapy. According to the study protocol, treatment was considered efficacious when there was a marked reduction in pain on the VAS. The original operational definition classified efficacy according to improvement in the patient's pain score at the day-3 assessment. The study therefore compared both continuous VAS measurements and the predefined binary efficacy outcome between the two treatment groups.

Follow-up Assessment: Participants were reviewed on the third day after initiation of treatment. During follow-up, the external auditory canal was reassessed and suction clearance was performed when required. New treatment wicks were subsequently placed, and pain intensity was again recorded using the VAS. All clinical and outcome information was entered into the predefined study proforma. The original study design specifically used the third-day assessment as the primary follow-up point for evaluating treatment response.

Statistical Analysis: Data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 21.0. Quantitative variables, including age and VAS pain scores, were summarized using means and standard deviations. Categorical variables, including sex and treatment efficacy, were expressed as frequencies and percentages. Treatment efficacy between the two groups was compared using the chi-square test. Age and sex were considered potential effect modifiers and were addressed through stratified analyses, followed by post-stratification chi-square testing. A p -value ≤ 0.05 was considered statistically significant.

Ethical Considerations: Ethical approval for the study was obtained before participant recruitment. The study documentation includes approval by the relevant institutional ethical review authority, and written informed consent was obtained from participants before enrollment. Participant confidentiality was maintained throughout data collection and analysis, and study procedures were conducted according to the approved research protocol.

RESULTS

Study Population and Baseline Characteristics: A total of 70 patients with moderate-to-severe acute otitis externa were included in the analysis. Thirty-five patients were allocated to Group A (3% ciprofloxacin–1% dexamethasone) and 35 to Group B (10% ichthammol glycerine). The observed age of participants ranged from 19 to 60 years, with an overall mean age of 40.00 ± 11.87 years. Forty-eight participants (68.6%) were male and 22 (31.4%) were female. Exactly half of the participants (35/70, 50.0%) were aged ≤ 40 years, while the remaining 35 (50.0%) were aged 41–60 years.

The mean age was 40.37 ± 12.50 years in Group A and 39.63 ± 11.38 years in Group B, with no statistically significant difference between the groups ($p=0.796$). Males constituted 74.3% of Group A and 62.9% of Group B, whereas females constituted 25.7% and 37.1%, respectively ($p=0.303$). Age-group distribution was also comparable between the two treatment arms ($p=0.811$). Baseline pain severity was nearly identical, with a mean VAS score of 6.74 ± 1.12 in Group A and 6.71 ± 1.15 in Group B ($p=0.917$), demonstrating comparability of the groups before treatment (Table 1).

Change in Pain Severity: Pain intensity decreased substantially in both treatment groups by the third day of treatment. In Group A, the mean VAS score decreased from 6.74 ± 1.12 at baseline to 2.43 ± 1.36 on day 3, corresponding to a mean reduction of 4.31 ± 1.32 points. This within-group decrease was statistically significant ($p<0.001$). In Group B, the mean VAS score decreased from $6.71 \pm$

1.15 to 3.63 ± 2.04 , corresponding to a mean reduction of 3.09 ± 1.44 points, which was also statistically significant ($p < 0.001$).

Despite comparable pretreatment pain scores, patients receiving ciprofloxacin–dexamethasone had significantly lower pain scores on day 3 than those receiving ichthammol glycerine (2.43 ± 1.36 vs 3.63 ± 2.04 ; $p = 0.005$). The mean reduction in VAS was also significantly greater in Group A (4.31 ± 1.32 vs 3.09 ± 1.44 ; $p < 0.001$). The between-group difference in mean pain reduction was 1.23 VAS points (95% CI: 0.57–1.89), favoring the ciprofloxacin–dexamethasone regimen (Table 2). The principal day-3 VAS values correspond to those documented in the original study results.

Table 1: Baseline demographic and clinical characteristics of the study participants

Characteristic	3% Ciprofloxacin–1% Dexamethasone (n=35)	10% Ichthammol Glycerine (n=35)	p-value
Age, years, mean $\pm$ SD	40.37 $\pm$ 12.50	39.63 $\pm$ 11.38	0.796
Age ≤ 40 years, n (%)	18 (51.4)	17 (48.6)	0.811
Age 41–60 years, n (%)	17 (48.6)	18 (51.4)	
Male, n (%)	26 (74.3)	22 (62.9)	0.303
Female, n (%)	9 (25.7)	13 (37.1)	
Baseline VAS, mean $\pm$ SD	6.74 $\pm$ 1.12	6.71 $\pm$ 1.15	0.917

Table 2: Comparison of Visual Analogue Scale pain scores between treatment groups

Pain outcome	3% Ciprofloxacin–1% Dexamethasone (n=35)	10% Ichthammol Glycerine (n=35)	p-value
Baseline VAS, mean $\pm$ SD	6.74 $\pm$ 1.12	6.71 $\pm$ 1.15	0.917
Day-3 VAS, mean $\pm$ SD	2.43 $\pm$ 1.36	3.63 $\pm$ 2.04	0.005
Mean VAS reduction, mean $\pm$ SD	4.31 $\pm$ 1.32	3.09 $\pm$ 1.44	<0.001
Within-group change, p-value	<0.001	<0.001	—

Table 3: Overall and stratified treatment efficacy

Analysis	3% Ciprofloxacin–1% Dexamethasone, n/N (%)	10% Ichthammol Glycerine, n/N (%)	p-value
Overall efficacy	27/35 (77.1)	14/35 (40.0)	0.002
Male	18/26 (69.2)	8/22 (36.4)	0.023
Female	9/9 (100.0)	6/13 (46.2)	0.008
Age ≤ 40 years	13/18 (72.2)	6/17 (35.3)	0.028
Age 41–60 years	14/17 (82.4)	8/18 (44.4)	0.020

Overall Treatment Efficacy: Treatment efficacy was achieved in 27 of 35 patients (77.1%) receiving 3% ciprofloxacin–1% dexamethasone compared with 14 of 35 patients (40.0%) receiving 10% ichthammol glycerine. Consequently, treatment was classified as ineffective in 8 patients (22.9%) in Group A compared with 21 patients (60.0%) in Group B. The difference in efficacy between the groups was statistically significant ($\chi^2 = 9.95$, $p = 0.002$) (Table 3). These figures reproduce the primary efficacy outcome reported in the dissertation.

The absolute difference in treatment efficacy was 37.1 percentage points (95% CI: 15.8–58.5). The relative probability of achieving the predefined efficacy outcome was approximately 1.93 times as high with ciprofloxacin–dexamethasone as with ichthammol glycerine (RR 1.93; 95% CI: 1.24–3.01). The corresponding odds ratio was 5.06 (95% CI: 1.79–14.31).

Treatment Efficacy According to Sex: Stratification by sex showed a consistent pattern of greater efficacy with ciprofloxacin–dexamethasone. Among male participants, treatment was efficacious in 18 of 26 patients (69.2%) in Group A compared with

8 of 22 patients (36.4%) in Group B, and the difference was statistically significant ($p = 0.023$).

Among female participants, efficacy was observed in 9 of 9 patients (100.0%) receiving ciprofloxacin–dexamethasone compared with 6 of 13 patients (46.2%) receiving ichthammol glycerine ($p = 0.008$). Thus, the direction of the treatment difference was preserved in both male and female strata (Table 3). Gender-based stratification formed part of the prespecified analyses in the original study.

Treatment Efficacy According to Age: A similar pattern was observed after stratification according to age. Among patients aged ≤ 40 years, efficacy was achieved in 13 of 18 patients (72.2%) in Group A compared with 6 of 17 patients (35.3%) in Group B ($p = 0.028$). Among patients aged 41–60 years, efficacy was achieved in 14 of 17 patients (82.4%) receiving ciprofloxacin–dexamethasone and 8 of 18 patients (44.4%) receiving ichthammol glycerine ($p = 0.020$).

The greater proportion of favorable responses with ciprofloxacin–dexamethasone was therefore observed in both age categories, indicating that the overall treatment difference was not restricted to a single age stratum (Table 3). Age-based efficacy stratification was also included in the original analysis plan.

The two groups were comparable at baseline with respect to age, sex distribution, age categories, and baseline VAS scores. Both topical regimens produced significant reductions in pain by day 3; however, patients treated with 3% ciprofloxacin–1% dexamethasone experienced a greater mean reduction in VAS and a higher overall treatment efficacy rate than those treated with 10% ichthammol glycerine. The main efficacy difference remained statistically significant after stratification by both age and sex, consistent with the original study conclusion that ciprofloxacin–dexamethasone provided superior early pain control in moderate-to-severe acute otitis externa.

DISCUSSION

The present randomized controlled trial compared 3% ciprofloxacin–1% dexamethasone with 10% ichthammol glycerine for early pain control in patients with moderate-to-severe acute otitis externa¹. The conclusion was that both treatments significantly decreased pain on Day 3, with a larger decrease in the ciprofloxacin–dexamethasone group. Mean VAS decreased from 6.74 ± 1.12 to 2.43 ± 1.36 in the ciprofloxacin–dexamethasone group and from 6.71 ± 1.15 to 3.63 ± 2.04 in the ichthammol glycerine group. Thus, the mean pain change was 4.31 ± 1.32 points and 3.09 ± 1.44 points, respectively. Moreover, there was a clinically important difference in early symptomatic response between the patients who received ciprofloxacin–dexamethasone (77.1%) and those who received ichthammol glycerine (40.0%) with respect to the predefined efficacy outcome. The original study similarly documented a significant between-group difference in efficacy at day 3 ($p = 0.002$)^{2,3}.

This is biologically plausible, since acute OTE is often associated with microbial infection and significant inflammation of the EAC, and this is what is improved with ciprofloxacin–dexamethasone⁴. Ciprofloxacin exerts antimicrobial activity against important bacterial pathogens like *Pseudomonas aeruginosa* and *Staphylococcus aureus* that are associated with otitis externa, while dexamethasone is an anti-inflammatory agent that decreases local inflammation and edema. However, the use of traditional ichthammol glycerine, due to its antiseptic, hygroscopic and anti-inflammatory activities, may have less broad antimicrobial activity, especially against Gram-negative bacteria. The finding of limited activity of ichthammol against *P. aeruginosa* is specifically mentioned in the source dissertation as a possible cause of its relatively low therapeutic efficacy^{5–8}.

The results are similar to those of past comparative studies outlined in the original dissertation. Mustafa et al. compared the efficacy of 3% ciprofloxacin–1% dexamethasone with 10% ichthammol glycerine in patients with moderate to severe AOE and found that the efficacy of 3% ciprofloxacin–1% dexamethasone

was 76.7% and 10% ichthammol glycerine was 43.3%. Ciprofloxacin–dexamethasone group also had lower mean VAS scores on day 3. These results are very similar to the current effectiveness rates of 77.1% and 40.0% and further reinforce the treatment difference in similar clinical populations⁹⁻¹¹.

A similar finding was seen by Jamalullah et al., who found that marked reduction in pain was achieved in 76% of the patients who were treated with ciprofloxacin–dexamethasone compared to 38% of the patients treated with ichthammol glycerine by day 3¹². These similarities suggest that an antibiotic–corticosteroid combination might be more effective in the speedy alleviation of the inflammatory and painful symptoms of acute otitis externa than the ichthammol glycerine alone. A comparison summarized in the source material showed that steroid–antibiotic packing was linked to relief of pain at a younger age and fewer clinical visits as compared with ichthammol glycerine packing^{13,14}.

Current results should also be viewed in the context of evidence assessing topical treatments in general. The systematic review in the dissertation revealed that topical treatments are generally effective for uncomplicated acute otitis externa, and the differences in efficacy between many topical treatments may be small¹⁵. Antimicrobial coverage, potential ototoxicity, contact sensitivity, dosing frequency, cost, and availability may also be factors in the choice of treatment. However, in the present study early pain control was specifically assessed in patients with moderate-to-severe disease and in this clinical context, a more marked short-term symptomatic response was observed with the ciprofloxacin–dexamethasone regimen¹⁶.

One of the significant characteristics of the current analysis was that the treatment groups were comparable at baseline. There were no important measured baseline differences in age distribution, sex distribution, or pretreatment VAS scores between the groups, minimizing the potential that the pain difference at day 3 was due to important baseline imbalance or that pretreatment scores differed between the groups¹⁷. In addition, trends of treatment response did not differ between males and females and did not differ by age. The efficacy of ciprofloxacin–dexamethasone was 69.2% as compared to 36.4% for ichthammol glycerine among males and 100.0% as compared to 46.2% among females. Likewise, higher efficacy was found with ciprofloxacin–dexamethasone in both the ≤40 years and 41–60 years age groups. The results from these subgroup analyses are consistent with the overall treatment effect, but the small number of patients per subgroup should be interpreted with care¹⁸.

In acute otitis externa of moderate and severe intensity, the degree of pain relief could be especially important as often the symptom that is most distressing is otalgia. Since the skin of the medial bony canal is immediately over the periosteum, inflammation of the tightly enclosed external auditory canal can cause significant pain, even when the amount of swelling is relatively small¹⁹. Hence, control of the edema and infection may be associated with significant symptomatic improvement during these first few days of treatment. The day-3 response was the focus of the study and can give clinically useful information about the early symptom control, which is sometimes a key factor in a patient's satisfaction and/or whether further clinical assessment is necessary²⁰.

There are a few drawbacks to these results. Firstly, the study was done at one tertiary-care hospital and the number of subjects was 70, so the precision of the estimates for the sub-groups was limited and generalizability to other populations may be limited⁵⁻¹⁰. Second, follow-up for the primary outcome was only three days long, and it is not known whether the difference between treatments is long-lasting through to complete clinical resolution, or whether it affects recurrence. Third, there was no description of blinding of participants or investigators, a factor that may have influenced the results as pain was assessed as per a patient-reported VAS. Fourth, microbiological cultures were not used when comparing outcomes, and thus it was not possible to analyse the response to treatment according to the causative organism. Fifth,

both groups underwent identical background treatments with analgesics and systemic antibiotics, which uniformed co-interventions but makes it difficult to determine the independent effects of the topical treatments in patients treated without systemic antibiotic. Other groups, including those with diabetes, immunocompromised states, bilateral disease, hearing-aid use, and some dermatological conditions were also excluded from the protocol and results may not be directly transferred to these groups¹¹⁻¹⁵.

The study has practical strengths despite the limitations. It was directly comparative between two widely used topical wick preparations, applied with the same clinical protocol, employed an objective numerical pain scale at predetermined assessment periods, and had equal numbers in each treatment group. The findings from continuous pain scores were consistent with the categorical efficacy outcome, which further supports the primary findings. There is a need for larger multicenter randomized trials with longer follow-up and microbiological assessment, adverse-event monitoring, recurrence, cost-effectiveness, and patient-reported quality-of-life outcomes for a more comprehensive comparison of these treatment strategies¹⁶⁻²⁰.

CONCLUSION

In patients with moderate-to-severe acute otitis externa, both 3% ciprofloxacin–1% dexamethasone and 10% ichthammol glycerine were associated with substantial pain reduction by the third day of treatment. The 3% ciprofloxacin–1% dexamethasone however led to greater reduction in VAS pain score and significantly higher treatment efficacy rate than the 10% ichthammol glycerine (77.1% vs 40.0%, $p=0.002$). The age-sex specific difference between treatments was maintained. Based on these results, 3% ciprofloxacin–1% dexamethasone was the more effective of the two topical wick regimens studied for early pain control in a population of patients with moderate-to-severe acute otitis externa; larger trials with longer follow-up are needed to evaluate clinical resolution, recurrence, safety, and generalizability.

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