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Comparing the Effectiveness of Ciprofloxacin Powder-Betamethasone topical Ointment with Ciprofloxacin and Betamethasone combination ear drops in treatment of Otitis Externa

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ABSTRACT

This clinical trial study was performed on 144 patients suspect to have otitis externa between 2017 and 2018 in the ENT clinic of Ayatollah Rouhani hospital in Babol. For the treatment on the same day, the patients were categorized into two groups randomly. In the first group, after suction clearance, ciprofloxacin powder and betamethasone ointment were used, while in the second group after suction clearance, ciprofloxacin drop and betamethasone drop were used in the ear canal. All patients reevaluated after one week. After preparation of the results of culture of the samples, 83 individuals including 44 in the first group (ciprofloxacin powder and betamethasone ointment) and 39 subjects in the second group (ciprofloxacin drop and betamethasone drop) had bacterial otitis externa. The mean intensity of pain in the first and second groups was 2.61±2.13 and 2.8.00, respectively which showed a significant difference (Pvalue<0.001). The itching was 38 (86.4%) and 6 (15.4%) cases in the first and second groups, respectively, which showed a significant difference (Pvalue<0.001). The discharge in the first and second groups was 10 (22.7%) and 1 (2.6%) respectively which again had a significant difference (Pvalue=0.007). The extent of diminished hearing in the first and second groups was 17 (38.6%) and 0 (0%), respectively, indicating a significant difference (Pvalue<0.001). Finally, inflammation in the first and second groups was 20 (45.5%) and 0 (0%), showing a significant difference (Pvalue<0.001). This study indicated use of ciprofloxacin powder and betamethasone ointment is less effective than applying ciprofloxacin drop and betamethasone drop.

1. Introduction

Otitis externa (OE) is one of the most common diseases in both children and adults groups (Roland and Stroman 2002), which categorized into different types including acute

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localized, acute diffuse, chronic, eczematous, and malignant (Carfrae and Kesser, 2008). The predisposing factors such as trauma, external objects, changes in the pH of the ear canal, constant moisture of the canal, obstruction, and skin diseases such as psoriasis and eczema play an important role in causing OE (Rosser, 2004). The most important pathogens that cause OE are bacteria, such as *Pseudomonas aeruginosa* and *Staphylococcus aureus* (Hawke, Wong et al., 1984, Rosser 2004, Osguthorpe and Nielsen 2011). Among the fungal agents, *Aspergillus* spp. (80-90%) as well as *Candida* spp. are the major causes of this disease (Narozny, Kuczkowski et al. 2006, Suliman 2015). The purulent OE is following perforation of the tympanic membrane when discharge has reached into the external ear canal and reduces sensitivity to topical ear medications (Roland 2001, Beriat, Akmansu et al. 2012). Typically, patients complain from pain and inflammation of the ear, diminished hearing, sense of pressure in the ear, itching, and purulent discharge (Carfrae and Kesser, 2008). OE is usually diagnosed through taking the history of the patients as well as physical examination and laboratory tests, and radiological investigations are rarely required (Roland and Stroman, 2002; Carfrae and Kesser, 2008). Removing the cerumen from the ear canal improves the effect of topical treatments. Clearing of the ear canal with a plastic curette or suction under direct observation is suggested. Stimulation through peroxide and warm water mixture can also be effective in removing the wastes (August, 1988). In cases of mild to moderate infections, the treatment involves prescription of topical antibiotics with or without topical steroids for 7 to 10 days (Rosser, 2004). However, for severe cases, systematic antibiotic is recommended to treat *P. aeruginosa* and *S. aureus* (Rosenfeld, Brown et al. 2006). To control pain, oral acetaminophen and no steroidal anti-inflammatory drugs are used (Osguthorpe and Nielsen 2011). In several review studies, no significant difference was found in the effectiveness of different antibiotics. (Kaushik, Malik et al. 2010, Schaefer and Baugh 2012). It has been shown that combination of oral and topical antibiotics does not increase the success rate of treatment (Roland, Belcher et al. 2008).

The aim of this clinical trial study to comparison of Ciprofloxacin Powder (200mg)-Betamethasone topical Ointment (1%) effectiveness with Ciprofloxacin 0.3%/ betamethasone 1% ear drops in treatment of OE patients.

2. Materials and Methods

This is a clinical trial study registered in the clinical trial registration system with the IRCT20130427013136N5. So, this project was registered in the ethical committee of Babol University of medical sciences (muBabol) with the ethical code; 9604819.

All patients referred to the ENT clinic of Ayatollah Rouhani hospital with suspected OE symptoms were included in this project. This study was performed in 2017-2018 at Babol city. The sample of the research included 144 patients suspicious to have bacterial otitis externa, who were classified randomly into two groups.

A total of 61 patients were excluded from the study, and the research was performed on 83 subjects including 44 individuals in the first group (ciprofloxacin powder 200 mg plus betamethasone ointment 1%) and 39 persons in the second group (ciprofloxacin drop 0.3% plus betamethasone drop 1%).

The inclusion criteria were as follows: negative result of the direct examination test and culture for fungal infection, and positive result for bacterial culture. The exclusion criteria included perforation of the tympanic membrane, fungal growth, or negative result in the bacterial culture.

The sampling was performed as convenient sampling. Briefly, the patients suspect to have bacterial otitis externa were placed in two groups sequentially. In the first group, a combination of ciprofloxacin powder and betamethasone ointment was used, while in the second group a combination of ciprofloxacin drop and betamethasone drop was employed.

All patients entered the study with their own approval and signed the written informed consent form for the research. The sampling was performed under microscopy guidance by an ENT subspecialist through applying sterilized tools including curette, Port cotton, ring, and under some conditions with different

suction heads, whereby ear samples including discharge and pus were drained off the ear.

After the sampling, immediately a spread of the ear pus was dragged on a slide, and after fixation, it was stained through gram staining method, whereby the existence of microorganisms was tested through the microscope.

Another part of the samples were cultured in blood agar and chocolate agar. Further, in order to rule out fungal infections, the samples were also cultured on Sabouraud dextrose agar medium with chloramphenicol and kept at 25□C.

In case of negativity of the direct and fungal culture tests with positivity of the bacterial culture test, bacterial infection diagnosis was made by biochemical tests. The disease causative bacteria were also identified through conventional methods. For the treatment, the patients suspect to have bacterial otitis externa were categorized into two groups on the same day sequentially. In the first group, after suction clearance, ciprofloxacin powder plus betamethasone ointment were used, such that they covered the external ear canal.

In the second group, after suction clearance, ciprofloxacin drop plus betamethasone drop were used. All patients were re-examined after one week in terms of disease improvement including resolution of the disease symptoms such as pain based on Visual Analogue Scale (VAS), itching according to the patient statements, discharge based on clinical examination and the patient statements, and inflammation-based on clinical examination.

2.1. Data analysis method

The data were analyzed by SPSS V16. To describe the qualitative characteristics, frequency and percentage were employed, while for describing the quantitative characteristics, mean and standard deviation were utilized. Comparison of groups was performed through the Chi-do (for qualitative variables) and paired t-test (for quantitative variables). Significance level was considered as Pvalue < 0.05 for all tests.

3. RESULTS

In this study, 5 subjects were eliminated as they did not refer for a second visit. The demographic information of the two groups is shown in Table 1.

The mean age in the first and second groups was 40.11±18.15 and 39.76± 19.24 years, respectively, showing no significant difference between the two groups (Pvalue=0.933).

According to Table 2, the most common bacteria were *P. aeruginosa*, *Diphtheroid*, Coagulase-negative *Staphylococci*, *Bacillus* spp., *S. aureus*, *E. coli*, *S. epidermidis*, *Enterobacteriaceae*, *Klebsiella pneumoniae*, and *Streptococcus* gamma hemolytic.

Based on Table 3, in the first visit, the mean pain intensity in the first and second groups was 3.75± 3.24 and 3.58± 2.90, respectively, which showed no significant difference between the two groups in terms of average pain intensity (Pvalue=0.81).

On the other hand, the mean pain intensity in the first and second groups by the second visit was 2.61± 2.13 and 0.80± 0.20, respectively, showing a significant difference between the two groups in terms of pain intensity (Pvalue<0.001). Further, 41 (93.2%) of cases in the first group and 35 (89.7%) patients in the second group had itching in the first visit, but their difference was not significant (Pvalue=0.57).

In the second visit, out of the 41 cases, only three had improved completely, while 38 (86.4%) had not improved. In the first group, at the beginning of the first visit, 35 (89.7%) had itching; after the treatment and by the second visit, 29 improved completely while 6 (15.4%) did not experience improvement, where a significant difference was observed between the two groups post treatment (Pvalue<0.001).

In the first visit, the number of subjects with discharge from the ear was 37 (84.1%) and 33 (84.6%) in the first and second groups respectively, where there was no significant difference between the two groups (Pvalue=0.94). In the first visit in

the group, 37 (84.1%) had discharge; after the treatment by the second visit, 19 improved while 10 (227%) had still discharge (Pvalue=0.007).

In the first visit, in the first group, 35 (79.5%) and in the second group 33 (84.6%) of patients had diminished hearing, and no significant difference existed between the in terms of diminished hearing (Pvalue=0.54).

In the control group, in the first visit 33 patients have discharge; after treatment and in the second visit, only one (2.6%) patient had discharge (Pvalue<0.001). The findings of clinical examinations in the first and second visits for each individual group are shown in Table 4.

Table 1. Basic information of patients participating in the study in two groups

Variable	-	Group I (ciprofloxacin powder and betamethasone ointment)	Group II (ciprofloxacin and betamethasone drops)	Total	Pvalue
Average age (years)	-	40.11 ± 18.15	39.76 ± 19.24	39.95 ± 18.56	0.93
Sex	Male	16 (36.36%)	19 (48.71%)	35 (42.16%)	0.25
	Female	28 (63.63%)	20 (51.28%)	48 (57.83%)	
Residence	Urban	29 (65.90%)	28 (71.79%)	56 (67.46%)	0.56
	Rural	15 (34.09%)	11 (28.20%)	26 (32.53%)	
History of ear disease	Positive	12 (27.27%)	11 (28.02%)	23 (27.71%)	0.92
	Negative	32 (72.72%)	28 (71.79%)	60 (72.28%)	

Table 2. The Frequency of bacteria identified in two groups

Etiologic agent of infection	Group II (ciprofloxacin and betamethasone drops)	Group I (ciprofloxacin powder and betamethasone ointment)	Total	Pvalue
Pseudomonas aeruginosa	9 (20.45%)	8 (20.51%)	17 (20.48%)	0.41
Diphtheroids	7 (15.90%)	5 (12.82%)	12 (14.45%)	
Coagulase-negative staphylococci	7 (15.90%)	5 (12.82%)	12 (14.45%)	
Bacillus	8 (18.18%)	3 (7.69%)	11 (13.25%)	
Enterobacteriaceae	1 (2.27%)	3 (7.69%)	4 (4.18%)	
Staphylococcus aureus	7 (15.90%)	3 (7.69%)	10 (12.04%)	
Klebsiella pneumoniae	1 (2.27%)	3 (7.69%)	4 (4.8%)	
Staphylococcus epidermidis	1 (2.27%)	4 (10.25%)	5 (6.02%)	
Escherichia coli	3 (6.81%)	4 (10.25%)	7 (8.43%)	
gamma haemolytic streptococcus	0 (0%)	1 (2.56%)	1 (1.20%)	

Table 3. Clinical symptoms of the patients studied at the first and second visit of the two groups

Type of visit	Variable	Positive/negative	Group I (ciprofloxacin powder and betamethasone ointment)	Group II (ciprofloxacin and betamethasone drops)	Total	P value
First visit	Mean pain intensity	-	3.75 ±3.24	3.75 ± 2.90	3.67 ±3.07	0.81
	Itching	Positive	41 (93.2%)	35 (89.7%)	76 (91.6%)	0.57
		negative	3 (6.8%)	4 (10.3%)	7 (8.4%)	
	Discharge	Positive	37 (84.1%)	33 (84.6%)	70 (84.3%)	0.94
		negative	7 (15.9%)	6 (15.4%)	13 (15.7%)	
	Hearing loss	Positive	35 (79.5%)	33 (84.6%)	68 (81.9%)	0.54
		negative	9 (20.5%)	6 (15.4%)	15 (18.1%)	
Second visit	Mean pain intensity	-	2.13 ± 2.61	0.20 ± 0.80	1.22 ± 2.19	< 0.001
	Itching	Positive	38 (86.4%)	6 (15.4%)	44 (53%)	< 0.001
		negative	6 (13.6%)	33 (84.6%)	39 (47%)	
	Discharge	Positive	10 (22.7%)	1 (2.6%)	11 (13.3%)	0.007
		negative	34 (77.3%)	38 (97.4%)	72 (86.7%)	
	Hearing loss	Positive	17 (38.6%)	0 (0%)	17 (79.5%)	< 0.001
		negative	27 (61.4%)	39 (100%)	66 (20.5%)	

Table 4. Clinical examination findings at first and second visits in two groups

Type of visit	Variable	Positive/negative	Group I (ciprofloxacin powder and betamethasone ointment)	Group II (ciprofloxacin and betamethasone drops)	Total	P value
First visit	Swelling	Positive	26 (59.1%)	27 (69.2%)	53 (63.9%)	0.33
		negative	18 (40.9%)	12 (30.8%)	30 (36.1%)	
	Discharge	Positive	37 (84.1%)	33 (84.6%)	70 (84.3%)	0.94
		negative	7 (15.9%)	6 (15.4%)	13 (15.7%)	
Second visit	Swelling	Positive	20 (45.5%)	0 (0%)	20 (24.1%)	< 0.001
		negative	24 (54.5%)	39 (100%)	63 (75.9%)	
	Discharge	Positive	10 (22.7%)	1 (2.6%)	72 (86.7%)	0.007
		negative	34 (77.3%)	38 (97.4%)	13 (13.3%)	

4. Discussion

The present study was performed with the aim of comparing the effectiveness of ciprofloxacin powder plus betamethasone ointment and that of ciprofloxacin drop plus betamethasone drop in treating bacterial otitis externa. It was found that use of ciprofloxacin powder plus betamethasone drop was less effective than the treatment with ciprofloxacin drop plus betamethasone drop. Mosges et al. reported that the effectiveness of ciprofloxacin drop 0.2% is not less than that of polymyxin

B/neomycin/hydrocortisone mixture (Drehobl, Guerrero et al., 2008).

In this study, the effectiveness of the drop form of ciprofloxacin and betamethasone drop was greater than that of ciprofloxacin powder plus betamethasone ointment, where this relationship was significant for the drop form.

In the study by Pino et al., the success of treatment with the ciprofloxacin 0.2% ear solution without topical corticosteroids was reported as 86.6%. It was concluded that ciprofloxacin 0.2% ear solution is a suitable option for treating acute otitis externa (Pino Rivero V, Pantoja et al. 2007).

In this study, the treatment success rate through ciprofloxacin drop plus betamethasone drop was 87.2%, which is in line with the above-mentioned study. In the study by Pistorius et al in treating acute otitis externa, the success rate of the treatment with ciprofloxacin 0.2% drop was 93%, while with ciprofloxacin ear drop and hydrocortisone drop, was 90% (Pistorius, Westberry et al. 1999), which is different with the success percentage of treatment with ciprofloxacin drop and betamethasone drop in our study.

This discrepancy can be attributed to different type of causative microorganisms, ear anatomy, immune system, and the duration of disease onset. Russell et al. examined 100 patients with otitis externa, and found microbial agents for this condition only in 40% of cases (Russell, Donnelly et al., 1993).

In this study, in 98.54% of cases, microbial cause was found, which is not in line with the above finding. In the study by Kiakojuri et al. (2018) in northern Iran on 72 patients with concurrent otitis, the patients were categorized into case and control groups. The case group received treatment with ceftazidime powder and miconazole ointment, while the control group received only miconazole. The patients were re-examined after two weeks off the treatment initiation (Kiakojuri, Omran et al. 2018).

Diagnosis was concurrent otitis based on the clinical signs and symptoms as well as bacterial and fungal manifestations in the direct test and culture. Inflammation, itching, and discharge were found in 67.7%, 64.7%, and 90.3% of patients in the case group, and in 47.1%, 26.3%, and 93.1% of patients in the control group, respectively. Complete improvement of clinical signs and symptoms was observed in 23 (67.6%) of patients in the case group and in 11 (28.9%) of patients in the control group.

The most common bacteria reported were *S. epidermidis* and *P. aeruginosa* (Kiakojuri, Omran et al. 2016). Elsewhere, Lorent et al. (2014) in Barcelona compared the effectiveness of ciprofloxacin ear drop plus fluocinolone acetonide with ciprofloxacin ear drop alone. In their study, 590 patients seven years old and older were chosen. It was found that the speed of clinical improvement was higher when using ciprofloxacin drop and fluocinolone in comparison with ciprofloxacin drop alone. Eight cases of mild side effects were reported; 3 in concurrent use of ciprofloxacin and fluocinolone and 5 cases when using ciprofloxacin alone (Mösges, Nematian-Samani et al. 2011).

In another research by Roland in May 2007 in Texas, the patients received combined treatment of ciprofloxacin 0.3% plus dexamethasone twice per day along with the combination of polymyxin B/neomycin/hydrocortisone three times a day. The pain of those who were treated by ciprofloxacin/dexamethasone decreased within a shorter time (12 h), compared to the case of applying polymyxin B/neomycin/hydrocortisone combination (Roland, Younis et al. 2007).

In the study by Pistorius in Albania conducted in November 1999, the effectiveness of using ciprofloxacin 0.2% ear drop with or without hydrocortisone was compared with that of polymyxin B/neomycin/ hydrocortisone suspension in patients with diffuse acute otitis externa. Out of the 703 patients studied, 239 received ciprofloxacin alone, 236 took ciprofloxacin plus hydrocortisone, and 228 were prescribed the polymyxin b/neomycin/hydrocortisone suspension (Pistorius, Westberry et al. 1999).

The treatment was administered for seven days. All of treatments were well

tolerated, and the percentage of drug-dependent side effects was the same in all of the three treatments. It was reported that the ciprofloxacin ear drop with or without hydrocortisone had a better effectiveness in comparison with polymyxin B/neomycin/hydrocortisone suspension. In addition, the use of hydrocortisone to ciprofloxacin accelerates improvement of pain in patients in comparison to the case when ciprofloxacin is used alone (Russell, Donnelly et al. 1993).

Generally, it is observed that most of the studies on the bacterial otitis externa have focused on comparing the effectiveness of use of topical antibiotics plus topical corticosteroids and use of topical antibiotics alone. On the other hand, no study similar to the subject of this research has been performed so far.

Further, considering the study on comparing the effectiveness of ceftazidime powder and miconazole ointment and that of miconazole ointment alone in the concurrent otitis treatment and the effectiveness of ceftazidime powder was observed, and since this powder is not FDA-approved, thus this study has been performed on comparing the effectiveness of ciprofloxacin powder plus betamethasone ointment and that of ciprofloxacin drop and betamethasone drop, which are FDA approved. In this way, a more effective and convenient treatment could be suggested to patients with bacterial otitis externa.

Conclusion

The results of this study indicated that use of ciprofloxacin powder plus betamethasone ointment was far less effective than employing ciprofloxacin drop plus betamethasone drop. Further, betamethasone drop plus ciprofloxacin powder cannot be an effective treatment for bacterial otitis externa. Accordingly, this treatment is not recommended for such patients.

Refereces

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