

# Comparison of Boric Acid and Combination Drug of Polymyxin, Neomycin and Hydrocortisone (polymyxin NH) in the Treatment of Acute Otitis Externa

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## ABSTRACT

**Introduction:** Acute otitis externa is an inflammation of the external auditory canal known as "swimmer's ear". Direct costs including medical treatment, painkillers, antibiotics, steroids or both and indirect costs are also remarkable.

**Aim:** The aim of this study was to compare the effect of boric acid and polymyxin, neomycin and hydrocortisone composition in the treatment of acute otitis externa.

**Materials and Methods:** This randomized clinical trial was carried out on 80 patients aged more than 17-year-old who were referred to Kashani hospital clinic with a diagnosis of acute otitis externa by otolaryngologist. The patients were randomly allocated to two groups (A: Boric acid and B: polymyxin NH ear drops) and Painkiller was prescribed and administered orally for all patients and in the presence of fever, cellulitis around the ears and neck adenopathy, broad-spectrum systemic antibiotics were used besides topical treatment. Symptoms of patients who were evaluated by a physician includes pain, discharge from

the ear, swelling of the ear canal, auricle swelling, tenderness, and ear itching. In addition, pain was evaluated in patients and was recorded by Macgill Pain Questionnaire, in the first, third, seventh and tenth days.

**Results:** Results showed that itching on third day ( $p=0.007$ ) and swelling of the ear canal in the examination of the third day ( $p=0.006$ ) and the seventh day ( $p=0.001$ ) in the polymyxin NH group was more than those of boric acid group. Overall mean pain based on McGill questionnaire was  $11.10\pm1.49$  in boric acid group in the examination on the first day and was  $4.05\pm0.22$  in the examination on the tenth day and in the polymyxin NH group, it was  $10.9\pm0.99$  on the first day and  $4.20\pm0.40$  on the tenth day. In both groups, pain relief was the same and there was no significant difference between two groups ( $p=0.075$ ).

**Conclusion:** The findings of this study showed slight differences in the effectiveness of the boric acid drug and combination of polymyxin, neomycin and hydrocortisone in the treatment of patients with acute otitis externa that is of clinical significance.

**Keywords:** Drug therapy, Inflammation, Otolaryngology

## INTRODUCTION

Otitis externa is the inflammation of external ear canal. Epidemiologically, the prevalence is four in every thousand children and/or adults per year, of which 80% occurs in summer [1]. The most common bacterial causes of ear infections include *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Streptococcus pyogenes* and some coliform bacteria [2,3].

Treatment of this disease may be simple and it is cured in one visit [4], but sometimes it is likely to be life-threatening and has fatal complications. In most cases, the treatment is topical therapy [1]. Several drugs have been used for topical treatment of the disease. Some of these drugs are neomycin and hydrocortisone ear drops or ciprofloxacin drops [5].

Another drug that is locally used in the treatment of acute otitis externa is combination drug of polymyxin B, neomycin and hydrocortisone or polymyxin NH [6]. Of other drugs used in the treatment of this disease is the solution of boric acid in ethyl alcohol 95% or that of acetic acid 2% [7].

There is no agreement upon the use of prescribed drugs in the treatment of acute otitis externa and different drugs have been introduced in various reference books for its treatment but none of them has been identified as the drug of choice because no significant difference has been reported in the effectiveness of drug treatments. One of the compounds widely used in the treatment of acute otitis externa is polymyxin NH combination, although this combination is effective in many external otitis, but it can trigger some complications. For example, neomycin and polymyxin can

be ototoxic in patients with perforated tympanic membrane and cause damage to the inner ear. On the other hand, neomycin is the most common drug that causes contact dermatitis in the outer ear [4].

Polymyxin NH is relatively expensive. Another drug that has been used in the treatment of otitis externa is boric acid and no specific side effect has been reported for it [6, 7]. It is a cheaper drug than polymyxin NH thus important in terms of reducing health care costs for patients.

In addition, one of the predisposing factors of fungal otitis externa is the history of local antibiotics intake. As boric acid is a drug that not only prevents fungal otitis externa but also is effective in treatment of it. Regarding the epidemiological differences in response to treatment with these drugs in patients, this study could be helpful in determining which drug is more effective for patients in this region.

## AIM

The aim of this study was to compare the effect of boric acid and polymyxin, neomycin and hydrocortisone compound in the treatment of acute otitis externa.

## MATERIALS AND METHODS

This double blind clinical trial study was carried out in 2013. A total of 80 patients aged more than 17 years old were included. The IRCT code of this study is 201409256252N6. The patients were selected among those who were referred to Kashani hospital clinic with a diagnosis of acute otitis externa by otolaryngologist.

Inclusion criteria of this study were, male and female patients aged more than 17 years old with a diagnosis of acute otitis externa. Exclusion criteria included treatment with topical treatment within the last two weeks or received oral antibiotics, diabetic patients, people with immunodeficiency, those who received oral corticosteroids or immunosuppressive drugs, patients who had perforated eardrum, those whose external otitis lasted more than three weeks and patients with furunculosis of external ear canal. After that eligible patients were diagnosed according to inclusion and exclusion criteria, written consent forms were distributed among the participants by doctor's physician. All participants signed consent forms. Finally, information of about 80 patients was analysed.

In this study, patients were randomly divided into two groups based on the even and odd numbers of reception, or based on their turn of examination that was in odd and even days and interventions were conducted by a colleague. The first group was given boric acid 3%, and the second group was given polymyxin NH ear drops. The dosage for both the groups was, three drops into the ear canal, three times a day. For all patients, oral palliative were prescribed and administered. In the case of fever, cellulitis around the ears and neck lymphadenopathy, broad-spectrum systemic antibiotics was used alongside topical therapy [8]. In the first visit, the patients were examined by an otolaryngologist. Symptoms that were recorded were as follows: pain, ear discharge, the inflamed ear canal, auricle swelling. Tenderness was recorded based on the severity of symptoms in McGill Pain questionnaire that has acceptable validity and reliability. The subsequent examination was done on the days 3, 7 and 10. Furthermore, patients were asked at each visit for the presence of symptoms such as itching and hearing loss and the presence or absence of cellulite around the ears. Cervical lymphadenopathy and fever were also recorded at each visit. In patients suffering from severe inflammation of the ear canal so that the drug was unable to reach the ear canal, cotton wick dipped in anti-inflammatory ointment was used and was placed inside the ear canal and in the second visit, the wick was removed and if necessary, another cotton wick was re-laid. In the case of presence of discharge inside the ears canal, it removed from the ear canal for all patients at each visit.

This research was a double-blind study, i.e., neither the patients nor the researchers were aware of the medications prescribed. Drug drops were packaged identically and were tagged by pharmacologist and were separated from each other. A researcher-designed questionnaire were used to gather data like age, sex, clinical symptoms consisting of ear discharge, pain, tenderness, itching, hearing loss, the inflamed ear canal, auricle swelling, cellulitis, neck lymphadenopathy, fever. The first part of McGill questionnaire was also used in gathering information.

The first part of the questionnaire consisted of four criteria: the Descriptive criterion [description of pain by the patient], evaluation criterion (evaluation of patient conditions and the limitations that the pain has caused in his life), behavioural criterion (change that pain has caused in his behaviour), examination criterion (clinical examination was done by a physician). The first three criteria was scored from 0 to 5 and the last criterion i.e. examination criterion was from 0 to 3. Thus, the score of the first part was between 0 and 18.

This questionnaire was first used by Melzack (1973) on 297 patients who suffered from various types of pain [9]. After numerous studies and research, this questionnaire was introduced and recommended as a reliable tool for research and pain assessment with various clinical methods.

Besides, Ibrahim Nejad et al., examined the validity and reliability of this questionnaire in Iran and were shown its Cronbach's alpha coefficient equal to 90, indicating that this questionnaire is of high reliability [10,11].

## STATISTICAL ANALYSIS

After completing the questionnaires, the data were analysed through SPSS software 17.0. Mean, standard deviation and frequency distribution data were analysed using descriptive statistics and correlation between variables in 2 groups were analysed using independent t-test (age) and chi square (sex). Besides, to compare the clinical symptoms in the 2 groups, the chi-square test and to compare criteria of McGill pain questionnaire in two groups, Mann-Whitney test was used with respect to non-normality of the data.

## RESULTS

In this study, the age of patients in the first group (BA) ranged between 19 and 65 years with a mean and standard deviation of  $43.3 \pm 15.11$  respectively and was in the range of 21 to 63 years with a mean and standard deviation of  $45.45 \pm 12.7$  in the second group (PNH group). According to independent t-test, no significant difference was observed between the two groups in terms of age of subjects ( $p=0.102$ ). In the first group, 45% ( $n = 18$ ) were female and 55% ( $n=22$ ) were male and in the second group, 60% ( $n=24$ ) were female and 40% ( $n=16$ ) were male. The chi-square test showed no significant difference between the groups in terms of sex ( $p =0.179$ ). The results of the statistical analysis of patients' symptoms during examination on days zero, third, seventh and tenth in two groups is shown in [Table/Fig-1].

Ear discharge was reported more in the BA group than the PNH group at the baseline examination ( $p=0.012$ ). Itching on the first ( $p =0.011$ ) and the third day of examination ( $p=0.007$ ) was more in the second group than the first group and swelling of ear canal in the examination on the third day ( $p=0.006$ ) and seventh day was more in the PNH group ( $p=0.001$ ) than the BA group.

Regarding the four criteria of assessment of pain, on the first and third days of examination, there was no significant difference between the two groups ( $p\geq 0.05$ ). On the seventh day, no significant difference was observed between the scores of examination criteria ( $p=0.001$ ) and evaluation criteria ( $p=0.041$ ), thus, the severity of pain were reported less in BA group than PNH group regarding to the examination criteria and evaluation criteria. On the tenth day of examination, descriptive criteria ( $p=0.044$ ) between the two groups showed significant difference. So, in the case of descriptive criteria, the severity of pain was reported less in BA group compared with PNH group [Table/Fig-2]. Overall pain severity on the seventh day ( $p =0.001$ ) and the tenth day ( $p=0.044$ ) in BA group were reported less than that of PNH group.

## DISCUSSION

Otitis externa is one of the most common types of ear infection and is estimated to be present between 5-20 percent of all patients with ENT (ear, nose, throat) problems [12]. Topical antibiotic treatment is very effective for improvement of patients with acute otitis externa. It is reported that, about 15% of patients with acute otitis externa recover without receiving any treatment within 10 days i.e. recovery rate is increased 65 to 80% with the use of topical antibiotics, steroids, or both [13].

Regarding the findings of this study, clinical symptoms of patients were more reduced in BA group as compared to polymyxin, neomycin, and hydrocortisone group. Clinical trials that assessed symptoms of patients after topical treatment, concluded that ear pain after just one day of treatment was significantly decreased in patients and most of the symptoms including itching, ear discharge were improved after 4 and 7 days [14-16].

Previous studies suggested that hydrocortisone addition to acetic acid significantly reduce ear pain from 8 days to 7 days [14].

Besides, adding hydrocortisone to ciprofloxacin compared with the combination of neomycin, polymyxin B and hydrocortisone can reduce ear pain from the period of 4.7 days to 3.8 days [17].

Group variable		First group		Second group		p-value (chi-square test)
		Absolute frequency	Relative frequency	Absolute frequency	Relative frequency	
Ear discharge	first day examination	34	85	24	60	0.012
	third day examination	12	30	14	35	0.63
	seventh day examination	4	10	4	10	1
	tenth day examination	0	0	0	0	
Itching	first day examination	34	85	40	100	0.011
	third day examination	16	40	28	70	0.007
	seventh day examination	4	10	10	25	0.077
	tenth day examination	0	0	0	0	
Hearing loss	first day examination	30	75	32	80	0.59
	third day examination	2	5	2	5	1
	seventh day examination	0	0	0	0	
	tenth day examination	0	0	0	0	
Swelling ear canal	first day examination	38	95	38	95	1
	third day examination	18	45	30	75	0.006
	seventh day examination	0	0	16	40	0.001
	tenth day examination	0	0	0	0	
Auricle swelling	first day examination	2	5	5	5	1
	third day examination	0	0	0	0	
	seventh day examination	0	0	0	0	
	tenth day examination	0	0	0	0	
Fever	first day examination	2	5	0	0	0.15
	third day examination	0	0	0	0	
	seventh day examination	0	0	0	0	
	tenth day examination	0	0	0	0	
Pain	first day examination	6	15	6	15	1
	third day examination	0	0	0	0	
	seventh day examination	0	0	0	0	
	tenth day examination	0	0	0	0	

[Table/Fig-1]: Absolute and relative frequency of patients' symptoms in both groups (boric acid and combination of polymyxin, neomycin hydrocortisone)

Similarly, in studies comparing neomycin, polymyxin and hydrocortisone, antiseptic alone significantly reduced duration of symptoms from 11.1 days to 9/4 days [18] and decreased average days of inflammation from 7.4 to 5/6 [19].

In a study by Slack and colleagues on 27 patients with primary diagnosis of otitis externa who did not receive any topical treatment in the last two weeks, three treatment methods were compared with each other. One group was a combination of antibiotics and

Group		Boric acid	polymyxin, neomycin and hydrocortisone	p-value
Pain assessment criteria	variable	Exam-ination day	Mean ± Standard deviation	Mean ± Standard deviation
	first	0.57±3.35	3.15±0.48	0.08
	third	0.30±2.1	2.20±0.40	0.213
	seventh	0.36±1.85	2±0.32	0.056
Examination criteria	first	0.22±1.05	1.2±0.40	0.044
	third	0.22±1.95	2±0	0.155
	seventh	0.30±1.1	1.55±0.50	0.001
	tenth	0±1	0±1	1
Evaluation criteria	first	0.46±2.70	2.70±0.46	1
	third	0.50±1.50	1.60±0.49	0.372
	seventh	0±1	1.1±0.30	0.041
	tenth	0±1	0±1	1
Behavioral criteria	first	0.57±2.35	2.35±0.48	0.87
	third	0.46±1.30	1.45±0.50	0.169
	seventh	0±1	1±0	1
	tenth	0±1	0±1	1
Overall pain	first	11.10±1.4	10.90±0.99	0.06
	third	1.02±6.85	0.19±7.25	0.185
	seventh	0.50±4.95	0.80±5.65	0.001
	tenth	4.05±0.22	4.20±0.40	0.044

[Table/Fig-2]: Mean and standard deviation of criteria of McGill pain questionnaire in BA and PNH in the examination on the first day to the tenth day.

steroids, the second group combined antibiotics, steroids as well as antifungal agent and the third group received boric acid in alcohol. The results indicated that solutions with antibiotics have no superiority over boric acid in the treatment of acute otitis externa [20]. Based on the results, there was no significant difference in the first and third days, but after seven days, pain was significantly reported lower in the first group. After 10 days, the descriptive criteria in the first group were significantly less than the second group. The severity of pain decreased from 11.10±1.4 in the first group to 4.05±0.22 on the tenth day in the first group and in the second group, it decreased from 10.90±0.99 to 4.20±0.40. Changes in the reduction of pain in the first group was more than those of the second group, but this difference was not significant between the two groups ( $p = 0.075$ ).

In another study, ciprofloxacin plus dexamethasone was more effective in reducing pain in patients with acute otitis externa and it reduced the severity of pain much faster after initiation of treatment [21]. Besides, Kandas stated in his study that trichloroacetic acid 5% (TCA) had more efficacy, fewer side effects and better pain relief as well as significant impact in preventing relapse compared with combination of antibiotics and steroids in the treatment of acute otitis externa [22].

In the study of Psifidis, full recovery of otitis externa was reported in patients treated with polymyxin NH, with ciprofloxacin and hydrocortisone and with ciprofloxacin alone as 84%, 100%, 96.7% respectively [8]. In a study by Mendelsohn, the effect of topical boric acid, acetic acid and placebo on otitis externa in dogs was evaluated, and it was shown that boric acid significantly reduced fungal organisms compared to acetic acid and placebo in dogs [19].

## CONCLUSION

As observed in the study, the effect of boric acid in recovery of symptoms and pain relief in patients with acute otitis externa in

comparison with polymyxin, neomycin hydrocortisone, the use of boric acid is suggested in the treatment of these patients. Boric acid is a mild acid and is mostly used as a disinfectant in inflammation including inflammation of the external ear canal. It does not have antibiotics component, so, there is no concern for predisposition to antibiotic resistance. Hence, it is recommended to use this drug in patients with acute otitis externa.

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