A COMPARATIVE STUDY ON EFFICACY OF POLYMYXIN B, NEOMYCIN AND POLYMYXIN B, NEOMYCIN, HYDROCORTISONE IN THE TREATMENT OF OTITIS EXTERNA AT NEPAL MEDICAL COLLEGE AND TEACHING HOSPITAL, KATHMANDU

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ABSTRACT

Introduction

Acute otitis externa (AOE) is a common but preventable ear condition. Tenderness with movement of the tragus or pinna is a classic feature of Otitis Externa. Polymyxin B, neomycin, hydrocortisone preparations are the choice for first-line therapy when the tympanic membrane is intact. This study attempted to compare the efficacy of polymyxin B, neomycin and polymyxin B, neomycin, hydrocortisone in the treatment of Otitis Externa.

Objective

To compare the efficacy of polymyxin B, neomycin and polymyxin B, neomycin, hydrocortisone in the treatment of Otitis Externa.

Methodology

To evaluate the efficacy of polymyxin B, neomycin and polymyxin B, neomycin, hydrocortisone in the treatment of Otitis Externa, a hospital based, randomized, prospective study was conducted in Nepal Medical College and Teaching Hospital (NMCTH), Attarkhel, Kathmandu from August 2012 to May 2014. 70 outpatients suffering from Otitis Externa who met the inclusion and exclusion criteria were included. Patients were randomized into group A and group B with lottery system. Odd number patients were included in group A and even number patients in group B. Group A patients received pack soaked with ribbon gauge in polymyxin B, neomycin ointment and Group B patients received pack soaked with ribbon gauge in polymyxin B, neomycin, hydrocortisone ointment. The patients were called for follow up after 48 hours and 96 hours to assess the improvement on the basis of tragal and circumduction tenderness either present or absent (present 1 or absent 2). A decrease in the clinical signs and symptoms (i.e. tragal and circumduction tenderness) was noted. Absence of pain was considered as clinically cured.

Results

In comparison to polymyxin B, neomycin group, hydrocortisone group exhibited statistically significant effectiveness after 48 hours of treatment ($p<0.05$), but in cure rates after 96 hours, no statistical significant difference was observed between two groups ($p>0.05$).

Conclusion

Polymyxin B, neomycin, hydrocortisone group showed higher and faster cure rates than polymyxin B, neomycin group in the treatment of Otitis Externa at 48 hours follow up.

KEY WORDS

Acute otitis externa, hydrocortisone, polymyxin B, neomycin

INTRODUCTION

Otitis externa (OE) is very common condition encountered in outpatient services. It is a common but preventable ear condition, involving inflammation of the ear canal.[1,2] The severity of the disease can range from mild inflammation to life-threatening infection. OE can be categorized as localized or diffuse, if it persists for more than 6 months, it is considered chronic and is more commonly bilateral.[3] The predisposing factors for Otitis Externa include high humidity, and loss of the canal's protective coating of cerumen, eczema, glandular obstruction and local lipid/acid disbalance.[4] It is also commonly seen in swimmers, particularly in the summer months.[5,6]

Combination of topical drugs that is neomycin, polymyxin B, and a corticosteroid was approved by the United States of America Food and Drug Administration (FDA) for the treatment of otitis externa.[7-9] Neomycin is a bactericidal antibiotic active against S. aureus but has minimal activity against P.aeruginosa.[10] Polymyxin B is active against P. aeruginosa but not against S. aureus. Thus, combining neomycin and polymyxin B broadens the spectrum of antimicrobial activity.[11]

On perusal of literature, it is evident that many antimicrobials have been used and their effectiveness has been compared in foreign countries. However, in Nepal such comparative study has not been carried out so far. Thus, it was to study the comparative effectiveness of treatment of otitis externa by steroid-antibiotic with antibiotics alone.

Therefore, in the present study a comparison of efficacy between topical polymyxin B and neomycin with a combination of polymyxin B, neomycin and hydrocortisone was done in patients of otitis externa.

METHODOLOGY

A prospective study was conducted from August 2012 to May 2014 in patients attending Department of Otorhinolaryngology, Head and Neck Surgery (HNS) of Nepal Medical College and Teaching Hospital. Each of the patients was assigned with a serial number in terms of lottery system. All the patients were randomized into two groups: Group A and Group B. Odd number patients were included in Group A and even number patients in Group B. Clinical diagnosis was made and pain was assessed (Present-1, Absent-2). Group A patients received pack soaked with ribbon gauge in Polymyxin B, Neomycin ointment and Group B patients received pack soaked with ribbon gauge in Polymyxin B, Neomycin, Hydrocortisone Ointment.

The patients were called for follow up at 48 hours and 96 hours to assess the improvement or otherwise. Every case was assessed for the improvement on the basis of tragal and circumduction tenderness either present or absent. A decrease in the clinical signs and symptoms was noted. Absence of pain was considered as clinically cured.

Statistical analysis of all the collected data was carried out using Statistical Package for Social Sciences (SPSS) version 20.0. The data was analyzed for age, sex, and cure rates. Descriptive statistics and Chi-square test were used to analyze socio-demographic data. The mean age between two study groups were compared using Chi- square test. Cure rates at the end of 48 hours and 96 hours were compared by using Non parametric McNemar test. The p value less than 0.05 was considered statistically significant, less than 0.01 as highly significant and less than 0.001 as very highly significant.

RESULTS

The following observations were made in the present hospital based prospective study. A total of 77 patients of acute otitis externa who visited Nepal Medical College and Teaching Hospital (NMCTH) were enrolled in the study. Five patients were excluded from this study because of overt fungal acute otitis externa and the other two were excluded because they removed their ribbon gauze before 48 hours. Therefore, at exclusion of seven patients, the observations presented in the results have a total of 70 patients divided into two groups of 35 patients each. One study group was treated with polymyxin B, neomycin whereas the other group received polymyxin B, neomycin, hydrocortisone.

Out of 70 patients, 37 (52.6%) were male and 33 (47.4%) were female. The mean age of the patients under study was 21.54±15.99 years (range 5-70 years). The most commonly involved age group was 5-14 years (29 patients). The results of age and sex wise distribution of Otitis Externa patients are summarised in table 1.

Table 1. Age and sex wise distribution of Otitis Externa

Age group (years)	Gender				Total	
	Male		Female			
	N	%	N	%	n	%
5-14	17	24.3	12	17.1	29	41.4
15-24	9	12.8	9	12.9	18	25.7
25-34	4	5.7	7	10.0	11	15.7
35-44	2	2.8	2	2.9	4	5.7
45 54	2	2.8	1	1.5	3	4.3
55-64	2	2.8	1	1.5	3	4.3
65-74	1	1.4	1	1.5	2	2.9
Total	37	52.6	33	47.4	70	100

Table 2 shows the age wise distribution of patients in different drug groups. In polymyxin B, neomycin group, the mean age was 21.0± 15.71 years (range 5-70 years) while in the polymyxin B, neomycin, hydrocortisone group, it was 22.08±16.47 years (range 5-65 years). There was no statistically significant difference in age wise distribution of Otitis Externa in two drug groups (p>0.05).

Table 2. Age wise distribution of patients in different drug groups

Age groups (years)	Drug groups			
	Polymyxin B, Neomycin		Polymyxin B, Neomycin, Hydrocortisone	
	N	%	n	%
5-14	14	40.0	15	42.8
15-24	10	28.6	8	22.8
25-34	4	11.4	7	20.0
35-44	3	8.5	1	2.9
45-54	2	5.7	1	2.9
55-64	1	2.9	2	5.7
65-74	1	2.9	1	2.9
Total	35	100	35	100

Table 3 shows the association between gender and different drug groups and it was statistically not significant (P>0.05).

Table 3. Gender wise distribution of patients in different drug groups

Drug groups	Female		Male		p-value
	n	%	n	%	
Polymyxin B, Neomycin	20	60.6	15	40.5	>0.05
Polymyxin B, Neomycin, Hydrocortisone	13	39.4	22	59.5	
Total	33	100	37	100	

Efficacy of the study drugs- polymyxin B, neomycin and polymyxin B, neomycin, hydrocortisone were compared on the basis of cure rates. Cure rates are the percentage of subjects completely cured from OE i.e the signs of tragal tenderness and circumduction tenderness were the main criteria. Cure rates were observed at 48 hours and at 96 hours of treatment with the drugs.

Table 4 : Cure rates from baseline (zero hour) and at 48 hours in Group A and Group B*

Groups	Drug groups	Baseline (zero hour)		At 48 hours Cure rates		p value
		n	%	n	%	
Group A	Polymyxin B, Neomycin	35	100	12	34.3	<0.001
Group B	Polymyxin B, Neomycin, Hydrocortisone	35	100	22	62.9	<0.001

**McNemar test*

Table 5: Cure rates from baseline (zero hour) and at 96 hours in Group A and Group B*

Groups	Drug groups	Baseline (zero hour)		At 96 hours Cure rates		p value
		n	%	n	%	
Group A	Polymyxin B, Neomycin	35	100	32	91.4	<0.001
Group B	Polymyxin B, Neomycin, Hydrocortisone	35	100	34	97.1	<0.001

**McNemar test*

Table 6: Comparison of cure rates at 48 hours in two drug groups*

Drug groups	At 48 hours Cure rates			p value
	N		% of cured patients	
	Cured Number	Uncured Number		
Polymyxin B, Neomycin	12	23	34.3	<0.05
Polymyxin B, Neomycin, Hydrocortisone	22	13	62.9	

**McNemar test*

Table 7: Comparison of cure rates at 96 hours in two drug groups*

Drug groups	At 96 hours Cure rates			p value
	N		% of cured patients	
	Cured number	Uncured Number		
PolymyxinB, Neomycin	32	3	91.4	>0.05
PolymyxinB, Neomycin, Hydrocortisone	34	1	97.1	

**McNemar test*

Table 8: Cure rates at 48 hours treatment in male and female patients in two drug groups*

Gender	Drug groups		p value
	Polymyxin B, Neomycin	Polymyxin B, Neomycin, Hydrocortisone	
Male	46.7%	68.2%	>0.05
Female	25%	53.8%	>0.05

**McNemar test*

Table 9: Cure rates at 96 hours treatment in male and female gender in two drug groups*

Gender	Drug groups		p value
	Polymyxin B, Neomycin	Polymyxin B, Neomycin, Hydrocortisone	
Male	93.3%	100%	>0.05
Female	90%	92.3%	>0.05

**McNemar test*

Table 10: Age wise cure rates at 48 hours treatment in between two drug groups*

Age group (years)	Drug groups				p value
	Polymyxin B, Neomycin		Polymyxin B, Neomycin, Hydrocortisone		
	N	%	N	%	
5-20 (21 patients in each groups)	7	33.33	14	66.67	<0.05
21-74 (14 patients in each groups)	5	35.71	8	57.14	>0.05

**McNemar test*

Table 11: Age wise cure rates at 96 hours treatment in between two study groups*

Age group (years)	Drug groups				p value
	Polymyxin B, Neomycin		Polymyxin B, Neomycin, Hydrocortisone		
	n	%	n	%	
5- 20 (21 patients in each groups)	19	90.48	21	100	>0.05
21-74 (14 patients in each groups)	13	92.85	13	92.85	>0.05

**McNemar test*

DISCUSSION

Acute otitis externa (AOE) is characterized by inflammation of the external auditory canal accompanied by itching, otorrhea, hearing loss or a blockage of ear for less than three weeks. The incidence of AOE in humid tropical areas is higher. Diagnosis of AOE is based on symptoms, signs, and microbial findings. It is mostly caused by bacteria and triggered by moisture.[12,13]

The present study intended to compare the effectiveness of polymyxin B, neomycin and polymyxin B, neomycin, hydrocortisone ointment combination. Drops are potentially ototoxic and have more incidence of hypersensitivity reaction compared to ointment.[14,15] Therefore, aural packing impregnated with topical (ointment) preparation was used in this study.

In the present study, the number of males and female patients suffering from OE were 37 and 33, respectively. The male patients were 1.12 times higher than female patients in the study. The result obtained in the present study is in agreement with the study conducted by Jamalullah et al where male patients were 2.45 times higher than female patients. Similarly, study conducted by Joseph et al revealed that number of male patients was 1.07 times higher than female patients. In a study by Shrestha et al observed that the incidence was 1.05 times higher in female patients.[16-18] However, the study of Gercek et al showed no correlation between genders and AOE as the pathology of OE is not influenced by hormones.[19] Therefore, the result of this study supports the observation of numerous workers who reported higher incidence of OE in male patients. However, this assumption is not supported by statistical analysis due to small sample size.

The incidence of OE is higher in younger age groups. The number of OE patients was higher in the age group 5-14 years (29 patients) in the present study. The mean age of the patients was 21.54±15.99 years (range 5-70 years). The results obtained were somewhat similar to study done by Frieden et al who reported the most commonly involved age group for OE to be 5-14 years.[20] Study done by Shrestha[18] et al showed that the persons between 10-20 years were most commonly affected. Another study conducted by Cantrell et al showed that age group between 2-11 years have higher incidence of OE.[17] Therefore, the result of this study corroborates the reports by other workers who reported that the incidence of OE is higher in younger age.

Several studies had different duration of treatment and the efficacy of study drugs had also varied depending upon the duration of treatment.

In the present study, at 48 hours follow up of treatment, 34.3% were cured in polymyxin B, neomycin group while 62.9% were cured in polymyxin B, neomycin, hydrocortisone group. Polymyxin B, neomycin, hydrocortisone group had statistically significant ($p<0.05$) higher and faster cure rates than polymyxin B, neomycin group at 48 hours of treatment. Faster relief in the later group may be due to anti-inflammatory action of hydrocortisone. However, at 96 hours follow up of treatment, 91.4% were cured with polymyxin B, neomycin while 97.1% were cured with polymyxin B, neomycin, hydrocortisone group. At 96 hours, the cure rate was found to be statistically not significant ($p>0.05$).

At 96 hours, both study drug combinations were equally effective, as inflammation subsided following elimination of infections in both study groups.

In the study by Mosges et al polymyxin B + neomycin + hydrocortisone cured OE patients within 10 days of topical therapy.[21] Shrestha et al in a study observed that steroid –antibiotic was more effective than 10% icthammol glycerine on seven day visit.[18] The study cured all patients within ten days of treatment but no statistically significant differences in cure rates were recorded between the two groups.

Topical antimicrobials, with or without topical corticosteroids are highly effective compared to placebo. Kaushik et al assessed the effectiveness of topical antimicrobials containing steroids with placebo for AOE.[22] The study concluded that topical antimicrobials containing steroids were significantly more effective than placebo drops on statistical analysis. The findings of these studies are in agreement with the finding of the present study that polymyxin B + neomycin + hydrocortisone are effective in OE.

There are several studies that have compared the efficacy of Polymyxin B + neomycin + hydrocortisone with other antimicrobials and steroid drugs, and the results were equivocal.

A study done by Mosges et al showed the efficacy of Polymyxin B sulphate + neomycin + hydrocortisone was better than that of bacitracin alone.[23] Similarly, Shrestha et al revealed that steroid antibiotics (neomycin and betamethasone valerate) produced statistically significant reduction in pain and edema as compared to 10% ichthammol glycerine.[18] The finding of these studies support the result obtained in the present study that polymyxin B +

neomycin + hydrocortisone is significantly effective than other antimicrobials in OE.

Similarly, there are several studies that have compared the efficacy of Polymyxin B + neomycin with other antimicrobials and the results were equivocal. Mosges et al in a study compared polymyxin B + neomycin + gramicidin (PS) group with glycerol (non pharmacologic treatment).[24] This study proved that PS exhibited significantly higher effectiveness than glycerol. Another study done by Tempera et al compared polymyxin B + neomycin with ciprofloxacin group.[25] The study proved that neomycin + polymyxin B achieve the maximum effect in the minimum time. The finding of these studies support the result obtained in present study that combination of polymyxin B + neomycin is more effective in AOE than other antimicrobials.

The results of this study indicated that AOE is common in age group 5-14 years. Men are more prone to AOE. Both study drug combination were effective in the treatment of AOE but the cure rates was significantly higher in Polymyxin B, neomycin, hydrocortisone group as compared to Polymyxin B, neomycin group by 48 hours of treatment. In this study, polymyxin B, neomycin, hydrocortisone group provided faster relief which can be explained on the basis of potent anti-inflammatory activity of hydrocortisone. Therefore, the addition of hydrocortisone with polymyxin B, neomycin causes early resolution of inflammation and faster cures rates as judged by tragal and circumduction tenderness.

LIMITATION OF THE STUDY

In this study duration of time was limited and sample size was also small therefore multicentre studies with large sample size are required.

RECOMMENDATION

In this study, sample size was small. Therefore, multicentre studies with large sample size may give better results. This study comprises the patients suffering from acute OE. However, patients of chronic OE can be taken into consideration in other studies. This study did not assess the adverse effects of the drugs. So, further studies are warranted to assess both efficacy and adverse effect of these drugs.

CONCLUSION

In this study it is concluded that Otitis Externa was common in age group 5-14 years. Men were more prone to suffer from Otitis Externa. On comparison, the efficacy of polymyxin B, neomycin, hydrocortisone group was significantly higher at 48 hours of treatment. However, no statistical significant difference was observed at 96 hours of treatment.

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CONFLICT OF INTEREST

None

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