

## Original Research Article

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# A study on the efficacy of prophylactic antibiotics in recurrent acute otitis media

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## ABSTRACT

**Background:** The aim of the study was to study the efficacy of broad spectrum antibiotics in the prophylaxis of recurrent acute otitis media.

**Methods:** 86 patients of age group between 2 and 15 years with history of recurrent otitis media were enrolled to study the efficacy of the prophylactic antibiotics used in this condition. The children were treated with amoxicillin or azithromycin during the acute episode. Then they were divided equally into two groups and assigned to receive amoxicillin in one group and azithromycin in the other group at one third the therapeutic dose as prophylaxis for 6 months. The children were evaluated at the end of every month and recurrent episodes if any, was documented.

**Results:** At the end of 6 months it was observed that prophylactic antibiotics were more effective in the younger age group of 2-7 years. Efficacy rates of 87.5% with azithromycin and 77.4% with amoxicillin were noted.

**Conclusions:** As azithromycin is given once a week compared to amoxicillin which is given daily and was found to be equally effective as a prophylactic drug in recurrent acute otitis media with a better compliance, it is a good alternative to amoxicillin as a prophylactic antibiotic. Proper dosage goes a long way in bringing down resistance to the therapeutic agents.

**Keywords:** Recurrent otitis media, Prophylaxis, Antibiotics, Vaccines

## INTRODUCTION

Acute otitis media (AOM) may be defined clinicopathologically as inflammation of the middle ear cleft of rapid onset and infective origin, associated with middle ear effusion and a varied collection of clinical symptoms and signs.<sup>1</sup> Being one of the most common childhood diseases, AOM is a leading cause of a child's absence from school and also of frequent hospital visits.

AOM can be classified into four major subgroups: sporadic, resistant, persistent and recurrent. A multitude of host, infectious, allergic and environmental factors contribute to the aetiology of otitis media.<sup>1</sup> Among the infectious factors, both viral and bacterial organisms have

been implicated. The bacteria that are known to cause AOM are *Hemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pyogenes* and *Staphylococcus aureus* leading to 78% of all AOM cases.<sup>1,2</sup>

Recurrent otitis media is defined as three or more episodes of AOM occurring within a six month period. *H. influenzae* used to be the most common organism identified in recurrent AOM, and is now being replaced by drug resistant *Streptococcus pneumoniae*.<sup>1,3</sup> Also, 50% of the *H. influenzae* are beta lactamase producing.<sup>1</sup> Infants and young children in the day care and from poor socio economic status associated with poor household and overcrowding are at risk of acquiring recurrent otitis media.<sup>1</sup>

Modifying the risk factors, treatment with analgesics and antibiotics during each acute episode, medical prophylaxis with broad spectrum antibiotics, vaccines against both viral and bacterial organisms and surgical prophylaxis (adenoidectomy, adenotonsillectomy, insertion of ventilation tubes etc) are the measures taken to prevent further episodes of recurrent otitis media.<sup>1,4-9</sup>

In this study, the effectiveness of prophylactic antibiotics to prevent recurrent episodes of AOM in children is studied.

Objectives of the study were to study the efficacy of broad spectrum antibiotics in the prophylaxis and thereby any reduced incidence of recurrent AOM, to compare the efficacy between two broad spectrum antibiotics used in the prophylaxis of recurrent AOM and to determine the age group to which prophylaxis is effective.

## METHODS

**Study design:** Non blinded randomized comparative study.

**Study setting:** Patients attending ENT OP, Government TD Medical College, Alappuzha.

### Study period

1<sup>st</sup> of January 2013 to 30<sup>th</sup> June 30 2015 (2 years and 6 months).

### Method of randomization

Block randomization. Block size of 10 was chosen.

### Inclusion criteria

Inclusion criteria were age 2-13 years. All children between the ages of 2 and 13 years having symptoms and signs of recurrent otitis media were included; sex: male and female; children attending the OP with symptoms and signs satisfying the definition of recurrent AOM; children of parents who gave valid written consent to be included in the study and willing to come for regular follow up every month.

### Exclusion criteria

Exclusion criteria were children who have taken prophylactic vaccines against pneumococcal or influenza organisms; history of hypersensitivity or gastric intolerance to penicillin, penicillin derivatives or macrolide group of antibiotics; treatment with systemic antibiotics for conditions other than AOM within a month of enrolment; presence of tympanostomy tube, retraction pockets and cholesteatoma; known cases of and clinically

significant cardiovascular, renal, hepatic or hematologic diseases; immunocompromised children.

### Study procedure

The study was initiated after getting approval from the institutional research committee institutional ethical committee.

Study sample was calculated based on a similar study by Marchissio et al.<sup>11</sup> A total of 86 patients were enrolled. Initial sample size estimated was 43 in each group.

On enrolment day 1 when a child with recurrent AOM came to the OP with an acute episode, medical history, physical examination and otoscopy findings were recorded. Diagnostic criteria included previous history of AOM, symptoms and signs like ear pain within the last 24 hours, purulent ear discharge, a red bulging tympanic membrane and a perforated tympanic membrane. These findings were documented. Environmental factors like attending day care schools, poor socioeconomic factors, poor hygiene, overcrowding, poor dietary habits and exposure to smoke were noted.

Choice of antibiotics which was determined by national recommendations was amoxicillin of the penicillin group of antibiotics or azithromycin of the macrolide group.<sup>1</sup> The child was given antibiotics (oral amoxicillin 15 mg/kg/dose as syrup or dispersible tablet three times a day for 10 days or oral azithromycin 10 mg/kg/dose once daily for 5 days as syrup or tablet) along with saline nasal drops and analgesics.

Resolution of the acute stage was monitored by recording the history and examination findings. The patient was then put on prophylactic antibiotic.

The selection of prophylaxis was based on block randomization. A block size of 10 was randomly chosen; half was given amoxicillin and other half azithromycin. 15 mg/kg oral amoxicillin once daily was given to one group and 10 mg/kg oral azithromycin once a week to the other group. The prophylactic antibiotics were administered for 6 months.

Patients were asked to come for follow up at the end of every month. They were instructed to use the hospital and our personal contact numbers in case of any adverse effects or in case an acute episode recurred.

Whenever a patient developed an acute episode in between, a full dosage schedule of the antibiotic was given and prophylaxis was continued as before. The patients, among whom the acute infection had not resolved even after 10 days, were considered to have persistent AOM and were excluded from the study.

Efficacy was based on clinically evaluable symptoms and signs. The clinical response was recorded as cure or failure.

At the end of 6 months, the total number of episodes of AOM if any was counted. For bilateral AOM, it was taken as 2 episodes. If the patient had a maximum of 2 or less than 2 episodes in the past 6 months, they were said to have been relieved and cured from recurrent AOM.

Compliance was verified from the empty drug packets/syrup bottles. All drugs were given free of cost from the hospital pharmacy thus bearing no cost to the patient. Adverse reactions if any were categorised as mild, moderate and severe and managed accordingly.

### Statistical analysis

Means, percentages and proportion were used for the qualitative variables. Chi square test was used for testing the significance. Analysis was done with SPSS 16.6.

## RESULTS

The study began with 43 patients in each group. 3 of the amoxicillin group and 2 patients of the azithromycin group did not return at the end of 4 months. 4 patients of the amoxicillin group were excluded during the study period as they had to take systemic antibiotics for other illnesses (2 for bronchopneumonia, 1 for appendicitis and 1 for gastroenteritis). Persistent otitis media was noted in

1 patient of the amoxicillin group and was also excluded. 1 patient of the azithromycin group developed mumps during the study period and was excluded. By the end of the study period, 35 patients who were treated with amoxicillin and 40 patients with azithromycin were included in the final analysis. None reported any severe adverse drug reaction apart from one or two episodes of mild diarrhoea.

Among the 75 patients, 43 were male and 32 were female patients. The youngest child was 2 years old and the oldest one was 13 years. Mean age was 5.0667 with a standard deviation of 2.1592. In the amoxicillin group, the mean age was 5.2 with a standard deviation of 0.5 and in the azithromycin group; the mean age was 5.075 with a standard deviation of 1.96. The demographic and clinical characteristics appeared similar in both the groups of study.

Among the 43 male patients, 20 received amoxicillin and 23 received azithromycin as prophylaxis. 6 among the amoxicillin group and 3 patients among the azithromycin group had recurrent episodes of AOM during the 6 month period of the prophylactic treatment (Table 1).

Among the 32 females, 15 received amoxicillin and 17 received azithromycin. 4 in the amoxicillin group and 2 in the azithromycin group had recurrent episodes of AOM during the prophylactic treatment (Table 1).

**Table 1: Showing the age, sex distribution and recurrence following prophylactic treatment with azithromycin and amoxicillin in recurrent AOM.**

Age group (years)	No. of males in amoxicillin group	No. of patients of recurrence of AOM	No. of females in amoxicillin group	No. of cases of recurrence of AOM	No. of males in azithromycin group	No. of cases of recurrence	No. of females in azithromycin group	No. of cases of recurrence
<b>2 to 4</b>	8	2	6	2	10	0	7	0
<b>5 to 7</b>	10	2	7	1	9	0	8	1
<b>8 to 10</b>	2	2	2	1	4	3	1	0
<b>11 to 13</b>	0	0	0	0	0	0	1	1
<b>Total</b>	20	6	15	4	23	3	17	2

**Table 2: Sex distribution of children who received the prophylactic drugs and their comparison to determine the efficacy.**

Drug used	Sex	Recurrence+	Recurrence-	Total
<b>Amoxicillin</b>	Male	6	14	20
	Female	4	11	15
	Total	10	25	35
<b>Azithromycin</b>	Male	3	20	23
	Female	2	15	17
	Total	5	35	40

Amoxicillin group: Chi square=0.0467, p=0.8286 Azithromycin group: Chi square=0.0146, p =0.903.

Comparison between the sex distribution in the recurrent cases of the amoxicillin group (chi square=0.0467, p=0.8286) and of the azithromycin group (chi square=0.0146, p=0.903) showed that sex distribution was not a factor in determining the efficacy of the prophylactic antibiotic (Table 2).

**Table 3: Age distribution and percentage efficacy of the prophylactic drugs.**

No of patients in each age group (years)	Name of the drug used in prophylaxis	
	Amoxicillin	Azithromycin
No of patients in the 2-7 years of age group	31	34
No of patients in the 8-13 years of age group	4	6
Total no in both the groups together	35	40
No of patients with cure in the 2-7 years of age group	24	33
No of patients with cure in the 8-13 years of age group	1	2
Percentage of cure in the 2-7 years of age group (%)	77.4	97
Percentage of cure in the 8-13 years of age group (%)	25	33.3
Percentage of cure in both the groups together (%)	71.4	87.5

At the end of 6 months of this study period, 71.4% of patients in the amoxicillin group and 87.5% in the azithromycin group who did not have more than 2 episodes of AOM, were considered to have satisfied the efficacy criteria for cure (Table 3).

Children were categorized into groups of 2-7 and 8-13 years and the percentage efficacy of these two antibiotics was calculated separately in both these groups (Table 3).

**Table 4: Efficacy of amoxicillin between the two age group of children.**

Age group (years)	Recurrence	Recurrence	Total
	+	-	
2 to 7	7	24	31
8 to 13	3	1	4
<b>Total</b>	<b>10</b>	<b>25</b>	<b>35</b>

Chi square=4.7702, p=0.028957.

**Table 5: Efficacy of azithromycin between the two age group of children.**

Age group (years)	Recurrence	Recurrence	Total
	+	-	
2 to 7	1	33	34
8 to 13	4	2	6
<b>Total</b>	<b>5</b>	<b>35</b>	<b>40</b>

Chi square=18.93, p=0.05.

**Table 6: Comparison of efficacy between amoxicillin and azithromycin in prophylaxis of recurrent AOM.**

Drug	Recurrence	Recurrence	Total
	+	-	
Amoxicillin	10	25	35
Azithromycin	5	35	40
<b>Total</b>	<b>15</b>	<b>60</b>	<b>75</b>

Chi square=2.04, p=0.15.

**Table 4: Efficacy of amoxicillin between the two age group of children.**

Age group (years)	Recurrence	Recurrence	Total
	+	-	
2 to 7	7	24	31
8 to 13	3	1	4
<b>Total</b>	<b>10</b>	<b>25</b>	<b>35</b>

Chi square=4.7702, p=0.028957.

**Table 5: Efficacy of azithromycin between the two age group of children.**

Age group (years)	Recurrence	Recurrence	Total
	+	-	
2 to 7	1	33	34
8 to 13	4	2	6
<b>Total</b>	<b>5</b>	<b>35</b>	<b>40</b>

Chi square=18.93, p=0.05.

**Table 6: Comparison of efficacy between amoxicillin and azithromycin in prophylaxis of recurrent AOM.**

Drug	Recurrence	Recurrence	Total
	+	-	
Amoxicillin	10	25	35
Azithromycin	5	35	40
<b>Total</b>	<b>15</b>	<b>60</b>	<b>75</b>

Chi square=2.04, p=0.15.

In the group of 2-7 years, the amoxicillin group had a clinically efficacy rate of 77.4% and only a 25% in the group of 8-13 years (Table 3). Chi square test was done to compare the efficacy in both the groups. The reduced recurrence rate in the younger age group (Table 4) was however, not found to be significant (Chi square=4.7702 p=0.028957). Similarly with azithromycin though the clinical efficacy rate was 97% in the group of 2-7 years, with only 33.33% in the group of 8-13 years (Table 3),

the higher cure rate in the younger group (Table 5) was not statistically significant (Chi square=18.93 p=0.05).

When the efficacy rates of azithromycin and amoxicillin as a prophylactic drug were compared (Table 6), the lower recurrence rate noted in the azithromycin group was not found to be statistically significant (chi square=2.04 p=0.15).

## DISCUSSION

An acute episode of otitis media may subside completely with or without antibiotics. Or may persist or recur. It can also progress to middle ear effusions, tympanic membrane perforation, hearing impairment and affect speech and language development. Both intracranial and extra cranial complications are documented occasionally. Hence it is important to take measures to prevent recurrent episodes of otitis media.<sup>1</sup>

Environmental factors play a major role in recurrent AOM.<sup>1</sup> AOM increases with increased contact with other children and the length of time spent in the day care.<sup>1</sup> Younger children are more affected.<sup>1</sup> The parents of these children should be advised to modify these risk factors.

Though antibiotic prophylaxis can potentially create problems, they should be considered in recurrent otitis media. The incidence of recurrent AOM is only one in eight.<sup>1</sup> But meta-analysis does show the benefit of medical prophylaxis in reducing the number of episodes of AOM.<sup>1</sup>

Viral and bacterial vaccines are effective, but the wide range of causative organisms, the varied serotypes and other technical difficulties make immunisation a difficult option for prophylaxis.<sup>1,6,7</sup>

Amoxicillin still remains the drug of choice in AOM used at many centres and macrolides in penicillin sensitive cases.<sup>1</sup>

The azalide antibiotic azithromycin has a half-life of 68 hours and therefore achieves sustained tissue concentration in a number of body sites which includes the middle ear, even with a once daily dose, making it ideal to administer as a prophylactic drug with a periodic administration and higher compliance.<sup>10</sup>

Among the 75 patients, 66 children were in the 2-7 years of age group and 9 in the 8-13 years of age group. 40 were males and 35 females. The difference in age and sex distribution in both the groups was studied which was statistically not significant (Table 2, p>0.05).

Both prophylactic antibiotics were more effective in the group of 2-7 years of age than the group of 8-13 years (p<0.05). As both the antibiotics were equally effective in preventing further episodes of AOM (87.5% efficacy rate with azithromycin and 71% with

amoxicillin), the once weekly dosage makes azithromycin a better alternative to amoxicillin. A comparative study between azithromycin and amoxicillin as prophylactic drugs in recurrent otitis media by Marchisio, Pricipi et al and by Prim et al also came to a similar conclusion.<sup>10,11</sup>

Review study by Cheong et al which compares the effects of interventions by prophylactic antibiotics, tympanostomy tube insertion and adenoidectomy concluded that prophylactic antibiotics are effective in reducing otitis media recurrence, recurrence frequency and total recurrence time.<sup>12</sup>

There are several studies where a single antibiotic versus placebo control or comparison between antibiotics like amoxicillin, septran, macrolides etc. have been made with a result that prophylactic antibiotics are effective in the management of recurrent AOM.<sup>4,10,13</sup>

Some of the modalities of treatment that have been tried for recurrent AOM are adenoidectomy and myringotomy with grommet insertion.<sup>1,8,9</sup> Others include pneumococcal vaccines, intranasal fluticasone during viral infection, intranasal *H. Influenza* vaccine etc.<sup>5,6,11</sup> In these studies the more successful treatment was the use of grommet insertion which reduced the incidence of OME.<sup>13</sup>

Though latest studies do not advocate the routine use of antibiotics for treating AOM and as prophylaxis in recurrent AOM, considering the risk outcome ratio and the fact that there are no major adverse effects involved in this treatment, its use may be justified in situations associated with environmental risk factors.<sup>1,14</sup> Marchisio et al obtained similar statistics (69% success for amoxicillin and 85.1% with azithromycin).<sup>10</sup> Other antibiotics that have been tried as prophylactics are trimethoprim-sulphamethoxazole and cefprozil.<sup>3,14</sup>

Priority should be given to altering the risk factors associated with recurrent otitis media like overcrowding, contact with younger children in the day care, exposure to smoke and household dust and poor nutrition. Mothers should be advised regarding the correct posture while breastfeeding. Broad spectrum antibiotics when used appropriately help in preventing further episodes of otitis media and emergence of resistant organisms. Culture and sensitivity of ear discharge should be done in cases of persistent otitis media and also in children where antibiotic prophylaxis has failed in recurrent AOM.

## CONCLUSION

A multidisciplinary approach is necessary for reducing the incidence of AOM as well as recurrent AOM. The latest treatment modality for recurrent acute otitis media advocates the use of pneumococcal vaccines, intranasal influenza vaccine etc., but these are still unavailable to the poorer segment of the society where the prevalence of

otitis media is common and are not effective against multiple organisms.

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