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ORIGINAL ARTICLE

Successive Medical Treatment Versus Watchful Waiting in Chronic Otitis Media with Effusion

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Objective: Management of otitis media with effusion (OME) is still an unresolved problem. Although watchful waiting gained popularity, it may not be applicable in the developing countries where medical and surgical treatments are being used more promptly. The aim of our study was to compare consecutive use of medical therapies with watchful waiting.

Materials and Methods: A randomized and prospective study was planned. One group of patients with chronic OME was treated with a 3-step treatment protocol consisting of amoxicillin, amoxicillin clavulanic acid and trimethoprim sulfamethoxazole along with decongestants and antihistamines. The other group of patients was followed on a basis of watchful waiting.

Results: A total of 70 patients were included in the study, 36 of them were in the watchful waiting group and 34 of them were in the treatment group. The recovery rate in the treatment group (65%) was found to be significantly higher than the watchful waiting group (36%) (p=0,032).

Conclusion: Considering worldwide increase in the antibiotic resistances and economical concerns, watchful waiting should be chosen in uncomplicated patients. Successive medical treatment may provide a viable alternative when watchful waiting is not applicable and surgery is anticipated.

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Introduction

Otitis media with effusion (OME) is a very common problem of childhood, however there are still unclear points, including the pathophysiology and the treatment of the disease.

Decongestants and antihistamines, once very popular for OME, were shown to be ineffective in many studies.[1,2] Promising results were obtained by antibiotics in many studies however these results were found to be short-lived due to high recurrence rate of the OME. [3-10] Currently recommended approach to the uncomplicated OME is watchful waiting in the literature. [11] However antibiotics, decongestants and antihistamines are being widely used for the same diagnosis especially in the developing countries.

There are a number of factors that would limit the applicability of watchful waiting approach. In the developing countries, availability of the medical services and documentation is unfavorable and follow-up is not optimal both on behalf of medical services and patients. Moreover, in patients who are prone to complication, watchful waiting may not be a viable option.

The aim of the present study was to compare the outcome of the medical treatment adapted as a stepped modality with watchful waiting.

Although there are several studies on the efficacy of antibiotics, [3-10] studies questioning the successive treatment are limited [12-14] and as far as we know this is the first study to use 3 different agents, amoxicillin,

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amoxicillin clavulanic acid and trimethoprim sulfamethoxazole consecutively along with antihistamine and decongestant for the treatment of OME.

Materials and Methods

This study was conducted in a university hospital clinic (Permission of Hacettepe University ethical committee, LUT 02/39-6). A randomized prospective study was planned. Two groups of patients with OME were formed. First group was given medical treatment consisting of antibiotics, antihistamines and decongestants. The other group was followed without any medication for OME.

Patients diagnosed with OME were asked to join the study. Thirty-four patients who accepted to participate in the study between dates of 01.05.2003 and 30.04.2004 were included in the treatment group and 36 patients between 01.05.2004 to 30.04.2005 were included in the watchful waiting group. Thus, randomization was achieved by admission to only one group along a year.

Patients who were documented to have chronic OME (COME) between ages of 2 to 12 were accepted into the study. COME was accepted as the OME of 3 months duration.

Diagnosis of OME was made by pneumatic otoscopy and tympanometry (Interacoustics impedance audiometer AT235h using 226 Hz probe tone). Type B and type C2 tympanograms was accepted to indicate OME. Otomicroscopy was employed in the confliction of the otoscopy and tympanometry. Passive smoking (accepted positive if any of the parents smoke), attendance to daycare facilities or school (accepted positive if it was positive also for a sibling) were questioned in the medical history. Patients were also evaluated with fiberoptic endoscopy for adenoid hypertrophy along with routine otolaryngologic examination. Adenoid hypertrophy was scored arbitrarily, according to the obstruction of posterior nasal aperture in 3 groups as less than 30%, 30 to 60% and greater than 60%. A pure tone audiometry (Interacoustics AC-40 audiometer) was performed to rule out accompanying sensorineural hearing loss. Audiologic evaluation was performed by blinded audiologists.

Patients with nasopharyngeal pathology, barotrauma, systemic diseases, immune suppression, congenital anomalies (cleft lip, cleft palate, Down syndrome, craniofacial malformations), allergic rhinitis, history of antibiotic use in the previous month, hearing loss which cannot be explained by OME, tympanic membrane abnormalities (retraction, adhesion) in the otoscopy and previous tonsillectomy, adenoidectomy and ventilation tube insertion were excluded from the study.

Patients in watchful waiting group were examined in monthly intervals. No treatment towards OME was prescribed however patients were allowed to use necessary treatments due to other diseases like upper respiratory tract infections. Patients were excluded from the study if any complication related to OME was observed. Surgery was proffered if the patient was not recovered by 6 months of follow-up.

Patients in the treatment group were also examined in monthly intervals. Patients were given medications in the first half of the month according to the treatment algorithm shown in Figure 1 and they were re-examined after 2 weeks of rest. Dosages of the drugs were shown in Table 1. Patients returned to treatment from the last successful stage, in case of recurrence.

Table 1. Drugs and dosages used in the study.

Drug	Dosage	Duration	Step
Amoxicillin	40 mg/kg/d	15 days	1
Amoxicillin clavulanic acid	45/6,4 mg/kg/d	15 days	2
Trimethoprim sulfamethoxazole	6/30 mg/kg/d	15 days	3
Pseudoephedrine HCl	45 mg/kg/d (2-5y/o) 90 mg/kg/d (5-12y/o)	10 days	All
Clemastine	1 mg/kg/d (2-6y/o) 2 mg/kg/d (6-12y/o)	10 days	All

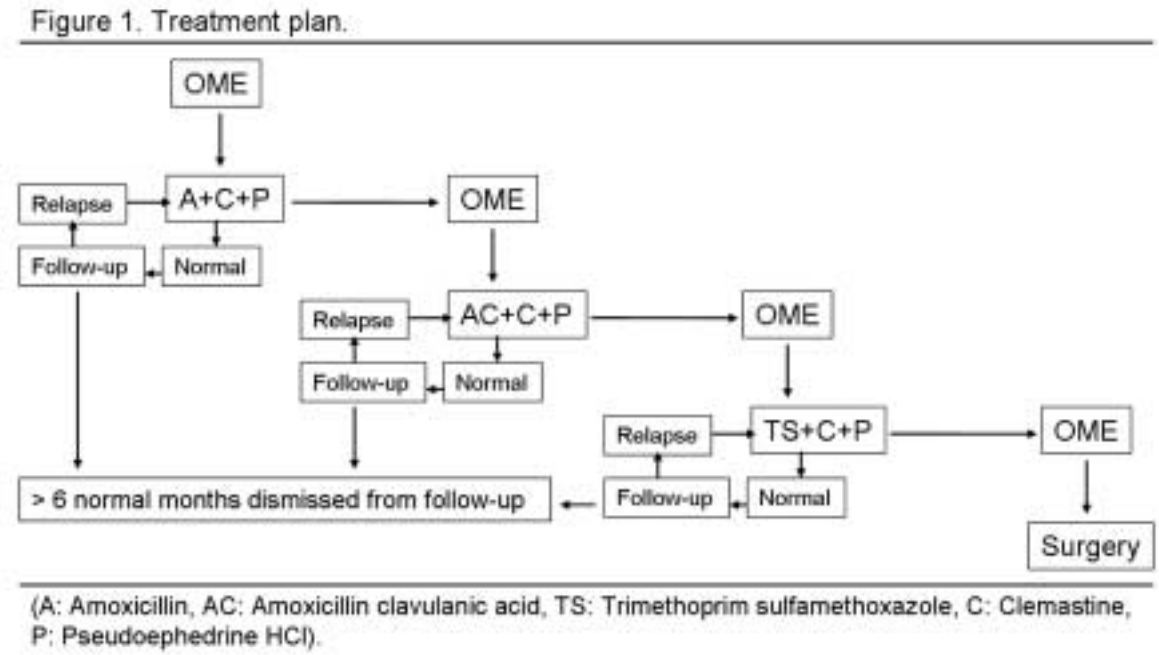

Figure 1. Treatment algorithm.

Patients were continued to follow-up until 6 months were completed. Surgery was proffered to patients who did not recover.

The outcome between groups was compared by using chi-square test. The groups were compared with each other for homology: sex was studied by chi-square test; age, air-bone gap was studied by Student's T test. Adenoid hypertrophy was studied by Mann -Whitney U test, the time of acceptance was first categorized according to seasons, spring and summer; and autumn and winter were combined and studied by Mann - Whitney U test. A p value less than 0.05 was considered statistically significant. Statistical analyses were performed on a personal computer with the SPSS for Windows (version 13.0, SPSS, Chicago).

Results

The age ranges were 2-11 in the watchful waiting group and 2-12 in the treatment group. Age, sex, adenoid vegetation, seasonal variance, attendance to day-care unit or school, passive smoking, unilaterality or bilaterality of the disease and the level of air bone gap in the audiological evaluation, which were considered to be the major confounding factors, were found to be similar in both groups (Table 2).

Table 2. Comparison of confounding factors between treatment and watchful waiting groups.
(* F: female, M: male, † au+wi: autumn+winter, ‡ sp+su: spring+summer).

Factors	Treatment Group	Watchful Waiting Group	Difference
Age	4,94 ± 2,24	5,01 ± 1,94	P=0,907, t=0,118
Sex	19F / 15M*	24F / 12M*	P=0,354, X^2=0,858
Adenoid vegetation	<30% 30-60% >60%	<30% 30-60% >60%	P=0,567, U=567500
	5 15 14	4 15 17	
Air-bone gap	29,1 ± 10,3 dB	23,9 ± 10,9 dB	P=0,117, t=-1,601
Unilaterality	8/36	7/34	P=0,868, X^2=0,028
Season	31 au+wi†, 5 sp+su‡	31 au+wi†, 3 sp+su‡	P=0,506, X^2=0,443
Day-care	10/34	12/36	P=0,724, X^2=0,125
Passive smoking	6/34	6/36	P=0,913, X^2=0,012

Twenty-two out of 34 (65%) patients in the treatment group were free of effusion at the end of the follow-up period, whereas only 13 out of 36 (36%) patients were free of effusion in the watchful waiting group. Thus, outcome was significantly different between the groups (p=0,017).

The effect of the confounding factors on the outcome was also analyzed (Table 3), however, we did not find any correlation.

The stage at which the effusion resolved was also analyzed for both groups. Recoveries were seen in 2 to 6 months (mean=4,09, SD=1,411) in the treatment group. Due to repetitive use of drugs, 2 to 8 courses of antibiotic treatments (mean=3,85, SD=1,617) were used in the treatment group. Four patients recovered with only amoxicillin, 7 patients recovered in the amoxicillin clavulanic acid stage and 11 patients recovered with the use of trimethoprim sulfamethoxazole (Figure 2). In the watchful waiting group, patients recovered in 2 to 5 months (mean=3,31, SD=0,947). Up to 3 courses of antibiotics in 14 patients (mean=0,67, SD=0,986) had to be used in watchful waiting group due to intervening upper respiratory tract infections. Recoveries achieved in the watchful waiting group were earlier than the treatment group however this was not statistically significant (p=0,085, t=-1,772).

Only one complication was encountered in one patient in the treatment group. A mild maculopapular rash was seen in the first day of the amoxicillin clavulanic acid treatment. The medication was replaced with amoxicillin and the symptoms were disappeared. No other complication related to medications was seen.

Figure 2. Success rates of the individual steps.

Table 3. Effect of confounding factors on the outcome.

Factor	Effect on Outcome
Age	p=0,494, t=-0,688
Sex	p=0,461, X^2=0,543
Adenoid vegetation	p=0,748, U=587500
Air-bone gap	p=0,755, t=-0,314
Unilaterality	p=0,145, X^2=2,121
Season	p=0,452, X^2=0,565
Day-care	p=1, X^2=0,000
Passive smoking	p=0,526, X^2=0,402

We also did not observe any complication related to OME except the hearing loss which was in the expected range in all cases. No structural changes in the tympanic membrane, namely retraction pockets or adhesions were discerned in any of the groups.

Discussion

2004 Clinical Practice Guideline presents the new trend in the management of OME. [11] Excluding high risk patients for language development, watchful waiting is recommended unless hearing, language, vestibular problems or deformation of structural integrity of the tympanic membrane occur. Use of decongestants and antihistamines are not recommended. Antimicrobial therapy is presented as an option when the surgery is aversed, however repetitive courses of antimicrobials are strongly not recommended.

The feasibility of this guideline in developing countries is on the other hand questionable. Use of ventilation tubes after a single antibiotic trial is a common approach. Although, it is not recommended in the practice guideline, repetitive use of antibiotics is also used in the management of OME. The results obtained in the present study denote a significantly better outcome in the medical treatment group, compared to watchful waiting group.

Resolution rate of the middle ear effusion was 36% in the watchful waiting group as might be expected for the

chronic OME (persistence of OME for 3 months). [15] Slightly better outcome found in the present study may be related to treatments due to interfering infections.

In the treatment group, 65% of the patients became free of effusion. The effect of antibiotic treatment in OME may be explained either by eradicating the bacteria in middle ear or by reducing the bacteria colonizing nasopharynx. In the literature, antibiotic trials are usually composed of single course of a single antibiotic. Success rates of 31 to 64% were achieved with antibiotics used for 10 to 28 days whereas control groups in these studies using either placebo or decongestants had resolution rates between 14 to 27%. [3-10]

Despite the favorable outcomes achieved by the antibiotics, the main problem with this approach was the frequent relapses which decreased the success of the treatment. [8] We did not encounter this problem in the 3 months of follow-up. Relapses of the OME cannot be precluded until the immune system and Eustachian tube function mature. On the other hand, same approach may be employed again for the relapses in the following year. Patients who are experiencing more frequent relapses may be operated.

The difference of the present study from the previous studies is the employment of three different antibiotics along with decongestants and antihistamines consequently. There are a few studies designed in this way. Donaldson et al [12] used single daily dose antibiotics and explained the efficacy of this approach by the prevention of relapses. Daly et al [13] compared stepped regimen of trimethoprim sulfamethoxazole and prednizolone in patients with OME and recurrent AOM which was found to be significantly more successful than placebo. Şafak et al [14] compared azythromycine given 3 times a week, once a week to pseudoephedrine hydrochloride which was used as placebo for up to 3 months. They found the antibiotic groups more successful, however their results did not reached to statistical significance.

The rate of resolution after the first step of the treatment group was only 12%. The success rate might be speculated to increase if an antibiotic other than amoxicillin was employed in this step, Even if, we assume that every step of the treatment was independent from the previous steps, the best result would be 33% with trimethoprim sulfamethoxazole. Therefore, decision of surgery after a single course of treatment would lead to a higher rate of surgery. The cumulative result of the treatment would spare at least another one third of the patients from the surgery.

The protocol of the present study does not allow identifying the most effective antibiotic for the OME. Highest resolution rates were reported by Marks et al [7] with trimethoprim sulfamethoxazole. Sixty-four percent of the cases were free of effusion at the end of 6 weeks. Similarly, the greatest rate of resolution was observed after third step of the present study. However, cumulative effect of the former steps may have a contribution to it.

Duration of the treatment may be more important than the type of the antibiotic chosen for the treatment of the OME. Eradication of the offending microorganisms would lead to resolution of the effusion. However reacquaintance of bacteria to middle ear either by an AOM attack or through a dysfunctional eustachian tube would cause a relapse of the effusion which is the characteristic of OME. The effect of long term antibiotic usage may be justified by avoiding relapses. Antimicrobial prophylaxis studies provided promising results. [16, 17]

The treatment protocol used in the present study is actually the routine OME treatment policy of our clinic. The antimicrobial agents used in this study are commonly used antibiotics in the treatment of AOM. Bacteriologic studies show the same causative microorganisms in AOM and OME. Therefore, it is reasonable to use the same antibiotics for OME. Amoxicillin is recommended as first line drug and amoxicillin clavulanic acid as the second-line drug for AOM. [18] Trimethoprim sulfamethoxazole is used as the last step of the treatment although mechanism of action is not clear, most of the resolutions happened in this third step of management trimethoprim sulfamethoxazole. Cotrimoxazole was shown to be more efficious than amoxicillin potassium clavulanate. [19]

In the era of emerging antibiotic resistance, use of antibiotics should be limited. A major concern regarding the treatment protocol used in the present study is the resistance problem. Widespread use of too many courses of antibiotics may potentially lead to arise of new resistant bacterial strains. For this reason, watchful waiting should be applied whenever possible, leaving successive medical treatment only to selected cases.

Decongestants and antihistamines, although their use is not recommended,[1, 2] were used in the present study to fully simulate the treatment policy of our clinic.

Non-medical, non-surgical treatment alternatives like autoinflation were also employed for OME; however, relapses lower the initial benefit in long term.[20]

The primary aim of the present study is to compare an active treatment approach with watchful waiting approach. This inevitably led to some shortcomings in the study design. One of these shortcomings was that the study was not blinded both on behalf of the patient and on behalf of the physician. To overcome this problem we employed tympanometry as a diagnostic tool which is an objective method and audiologists were unaware of the study protocol. Should there be a confliction between the otoscopic findings and tympanometry, otomicroscopy and a blinded fellow was referred.

There are many confounding factors like passive smoking, daycare, adenoid hyperplasia, seasonal variance, bilateral disease and air-bone gap, affecting the outcome of OME. [21, 22] The groups should be analogous in a treatment trial in order to prevent bias. Both groups in this study were found to be similar for confounding factors which may indicate a successful randomization.

Neither the patients in the watchful waiting group nor the patients in the treatment group developed a complication or progression. We also did not encounter any major side effect related to the medication. Therefore, both approaches were proved to be safe.

Conclusion

Many OME cases would resolve spontaneously without any complication. Considering worldwide increase in the antibiotic resistances and economical concerns, watchful waiting should be chosen when applicable. However, some of these patients may develop complications if the disease is allowed to progress, which would be the case in developing countries. Insertion of ventilation tubes is an effective treatment,[23] however, its associated complications and cost should be considered in decision making. [24] Successive medical treatment may provide a viable alternative when watchful waiting is not applicable and surgery is anticipated.

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