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Original Article

Differences between children and adults with otitis media with effusion treated with CO_2 laser myringotomy

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Abstract

Background: The safety and advantages of CO_2 laser myringotomy for otitis media with effusion (OME) are well described. The goal of such treatment is to avoid unnecessary ventilation tube insertion. Comparisons between different age groups treated with this modality are lacking, and prognostic factors for treatment outcomes are not available.
Methods: We conducted a retrospective cohort study that included 130 children (160 ears) and 96 adults (108 ears) with OME persisting after conservative antibiotic treatment. In eligible patients, we performed laser myringotomy in the affected ear. Follow-up was scheduled every week for 1 month and then every month for 6 months. Results for 233 ears were available for analysis; 24 ears were excluded (19 due to cancer, four due to a cleft palate, and one due to Down syndrome) and 10 patients (11 ears) were lost during follow-up. A logistic regression model was used for analysis, with success of therapy as the binary outcome.
Results: Adult patients had more unilateral lesions ($p < 0.001$) and serous fluid effusions ($p < 0.001$) than did the pediatric patients. However, there was no significant difference in the cure rate (children: 58.1%; adults: 64.7%) and positive culture rate (children: 15.1%; adults: 14.3%) between patient groups. Three factors were found to be associated with a poor prognosis: multiple occurrences in children ($p < 0.001$), mucoid effusion ($p = 0.04$), and a history of ventilation tube use in adults ($p < 0.001$). No other variables predicted treatment outcome.
Conclusion: Our findings suggest that CO_2 laser myringotomy is a useful treatment modality for OME in children and adults, except for children with multiple occurrences and in adults with mucoid effusions and a history of ventilation tube use.

Keywords: adults; children; CO_2 laser; effusion; logistic regression model; myringotomy; otitis media; pediatrics

1. Introduction

Otitis media with effusion (OME) is one of the most common infectious diseases worldwide, both in children and adults. Treatment methods include watchful waiting, antibiotic treatment, and surgical intervention. Ventilation tube insertion (VTI) for OME persisting for more than 3 months is a well-accepted treatment method and is one of the most frequently performed operations in children. In the United States, yearly expenditures for this disease exceed $5 billion,[1,2] comprising more than 24 million doctor visits. Although watchful waiting for 3 months is recommended, concern has been raised regarding a child's quality of life and language development during this time. Conventional myringotomy heals after 1–2 days, which is too short of a time to achieve a therapeutic effect. Armstrong and Armstrong, who reintroduced the ventilation tube in the 1950s, regarded a 3-week period of transtympanic ventilation as adequate for OME.[3]

Although inserting a ventilation tube is a minor procedure, a major disadvantage associated therewith is the need for general anesthesia in children and complications such as chronic perforation, chronic tympanic granuloma, tympanic membrane atrophy, atelectasis, cholesteatoma, and chronic discharge.[4–6]

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Laser-assisted myringotomy (LAT) in the human ear was first introduced by Goode in 1982,[7] and coupled to a handheld otoscope by DeRowe and colleagues in 1994[8]; a flashscanner connected to the otoscope has subsequently made LAT a safer technique.[9] The safety and advantages of CO_2 laser myringotomy have been well described.[10] This treatment allows intermediate-duration middle-ear ventilation (16.35 days)[11] and can be performed under topical anesthesia in an office setting.[12,13]

However, the indications for this treatment and its effectiveness in different age groups are not yet known. Therefore, the purpose of this study was to evaluate characteristics of OME treated with CO_2 laser myringotomy in children and adults. We reveal differences between age groups and examine prognostic factors associated with treatment outcome.

2. Methods

2.1. Patients

Children (aged $\leq$ 14 years) and adults (aged $\geq$ 15 years) with OME of varying duration were included in this study. CO_2 laser myringotomy was indicated when conservative treatment, i.e., oral antibiotic therapy for more than 2 weeks, had failed.

Patients were either referred to us from local medical clinics or came to our clinic *ab initio*. We verified their previous antibiotic treatment history and prescribed a 2-week course of oral antibiotics for those who had not used antibiotics for this episode of OME. Prior to enrollment, we explained the treatment choices to the patient, or parents of the patients, which included watchful waiting, laser myringotomy, and VTI (for OME lasting 3 months or longer, or persistent OME in children at risk). The final choice was made by the patient (or the parents of the patient). Patients who chose laser myringotomy were enrolled in this study.

OME was defined as an accumulation of effusion in the middle ear without signs of acute inflammation. The diagnosis was made by an otolaryngologist with video telescopy as the mainstay of conformation[14] in combination with a type B tympanogram or pure-tone audiometry.

A total of 130 children (160 ears) and 96 adults (108 ears) with OME were enrolled in this trial in the Department of Otorhinolaryngology of the Taipei Veterans General Hospital from January 2006 to December 2009. During the analysis, 24 ears were excluded (19 due to cancer, four due to a cleft palate, and one due to Down syndrome). Ten patients (11 ears) were lost during follow-up. Therefore, assessment of outcomes for 233 ears was possible at the conclusion of the study.

2.2. Interventions

Before CO_2 laser myringotomy, patient demographic data were collected, and tympanometry was performed in all patients. Sound-threshold audiometry was recorded in children over 4 years old, and noise or play audiometry was recorded in younger children. Audiometry was repeated postoperatively. Laser myringotomy was performed using a CO_2 flashscanner laser (OtoLAM; ESC/Sharplan, Tel Aviv, Israel), which creates a round perforation in the tympanic membrane. Patients underwent the procedure in an office setting with the use of 10% lidocaine (Xylocaine) local anesthesia for 30 minutes. The anesthetic solution was infiltrated directly into the ear canal with a 3-mL syringe with the patient lying on the other side. Circular perforations were created in all affected ears in the lower anterior or lower posterior quadrant according to each patient's anatomic structure, with a power of 15 W, single pulse duration of 200 milliseconds, and a scanned area of 1.9 mm in diameter. After creating the fenestration, aspiration of fluid from the middle ear was performed under microscopic control, and the fluid was sent for culturing with a specially designed suction culture bottle. No postoperative eardrops were prescribed.

2.3. Informed consent

Adult patients and parents of participating children gave written informed consent before enrollment. An otolaryngologist explained the potential risks and benefits of the surgical intervention. The medical ethical review committees of our hospitals approved the study protocol.

2.4. Main outcome measures

Postoperative perforation healing time and eardrum condition were evaluated by outpatient clinic examination weekly for 1 month, and then monthly for another 5 months. Resolution of disease was defined as both normal video telescopy findings and a type-A tympanogram. Resolution, persistence, or recurrence of disease was documented at the 6-month follow-up examination.

Additional data collected included patient age, sex, disease duration, underlying disease, past ear interventions, operation date, lesion side, myringotomy location, type of effusion, perforation healing date, disease status, pain score, postoperative tympanic membrane condition, and pre- and postoperative tympanogram and tympanic characteristics.

We define treatment success (cured of disease) as no evidence of fluid after the perforation had healed and no OME recurrence for 3 months. We classified OME recurrence within 3 months as treatment failure. Multiple occurrences were defined as ears that received more than one intervention with a normal interval longer than 3 months.

2.5. Statistical analysis

We first investigated the association between age group and the risk factors listed in Table 1. The Chi-square test was used for categorical risk factors. Two-tailed t test was used for continuous variables.

Secondly, the effect of potential prognostic factors was evaluated using the mixed logit model. In the mixed logit model, $Y = 1$ was defined as an uncured status after undergoing CO_2 laser myringotomy. Repeated measurements were collected for a single patient; thus, the random intercept model was used to assess the effect of prognostic factors on outcomes. Each risk factor was included in the univariate logit

Table 1
Demographic data.

	Children		Adults		*p* value
Total patient number	100		63		
Total ear number	148		85		
	n	%	*n*	%	
Age (yrs)[a]	7.70 (1–14)		56.42 (15–90)		
Sex					
Women	58	39.2	51	60.0	0.002
Men	90	60.8	34	40.0	
Underlying disease					
No disease	107	72.3	65	76.5	0.002
Allergic rhinitis and sinusitis or adenoiditis	36	24.3	9	10.6	
Mastoiditis and previous tympanoplasty	5	3.4	11	12.9	
Mean disease duration (wks)[b]	8.18 (6.75)		6.52 (7.67)		0.215
Uni or bilateral					
Unilateral	61	41.2	68	80.0	< 0.001
Bilateral	87	58.8	17	20.0	
Season					
Winter	38	25.7	24	28.2	0.820
Spring	56	37.8	34	40.0	
Summer	28	18.9	12	14.1	
Autumn	26	17.6	15	17.6	
Fluid appearance					
Serous	51	34.5	66	80.5	< 0.001
Glue-like	49	33.1	10	12.2	
Others	48	32.4	6	7.3	
Multiple occurrence					
No	123	83.1	64	75.3	0.149
Yes	25	16.9	21	24.7	
VTI history					
No	123	83.7	71	83.5	0.977
Yes	24	16.3	14	16.5	
Culture result					
Negative	107	82.3	60	82.2	0.918
Positive	19	14.6	10	13.7	
No culture data	4	3.1	3	4.1	
Treatment result					
Not cured	62	41.9	30	35.3	0.321
Cured	86	58.1	55	64.7	

VTI = ventilation tube insertion.
[a] The mean (range) of age is shown.
[b] The mean (SD) of mean disease duration is shown.

mixed model individually to assess its impact on patient outcomes. However, when a specific category of a factor is rare, the estimate is unreliable and inefficient. In this situation, we calculated the odds ratio based on the observed odds, and we derived the *p* value using the two-tailed Fisher Exact test. In multivariate logistic regression analysis, two variables with a *p* value less than 0.05 in a univariate logit mixed model (VTI history, multiple occurrence) were accepted and combined with two variables that might have clinical significance and confounding effect (sex and disease duration) as covariables to estimate of the predictive effect of treatment failure in Table 3. All statistical analyses were performed using STATA 10.1 (StataCorp, College Station, TX USA).

3. Results

Demographic data are shown in Table 1. Variables that showed no significant differences between age groups included disease duration, the season in which the operation was performed, multiple occurrences, VTI history, and positive culture

Table 2
Odds ratio of each factor in a univariate mixed logic model.

	Children						Adults					
	Cured		Uncured				Cured		Uncured			
	n	%	*n*	%	OR	*p* value	*n*	%	*n*	%	OR	*p* value
Sex:	35	40.7	23	37.1	—		33	60.0	18	60.0	—	
Women												
Men	51	59.3	39	62.9	2.048	0.493	22	40.0	12	40.0	1.228	0.829
Underlying disease:	64	74.4	43	69.4	—		44	80.0	21	70.0	—	
No disease												
Allergic rhinitis and sinusitis or adenoiditis	21	24.4	15	24.2	1.063	0.99[b]	5	9.1	4	13.3	3.788	0.424
Mastoiditis and previous tympanoplasty	1	1.2	4	6.5	5.953	0.15[b]	6	10.9	5	16.7	1.996	0.540
Mean disease duration (wks)[a]	9.64	(8.40)	7.03	(4.85)	1.170	0.055	5.81	(5.17)	6.91	(8.79)	0.933	0.319
Unilateral	38	44.2	23	37.1	—		43	78.2	25	83.3	—	
Bilateral	48	55.8	39	62.9	4.241	0.162	12	21.8	5	16.7	0.620	0.706
Season:	26	30.2	12	19.4	—		12	21.8	12	40.0	—	
Winter												
Spring	30	34.9	26	41.9	2.342	0.442	27	49.1	7	23.3	0.049	0.053
Summer	16	18.6	12	19.4	1.206	0.886	8	14.5	4	13.3	0.097	0.188
Autumn	14	16.3	12	19.4	2.907	0.416	8	14.5	7	23.3	0.633	0.753
Fluid appearance: Serous	29	33.7	22	35.5	—		43	78.2	23	76.7	—	
Glue-like	31	36.0	18	29.0	0.691	0.702	3	5.5	7	23.3	4.362	0.044[b]
Others	26	30.2	22	35.5	1.286	0.799	6	10.9	—	—	0.156	0.414[b]
Multiple occurrence	82	95.3	41	66.1	—		44	80.0	20	66.7	—	
No												
Yes	4	4.7	21	33.9	10.500	< 0.001[b]	11	20.0	10	33.3	3.112	0.321
VTI history	77	89.5	46	75.4	—		52	94.5	19	63.3	—	
No												
Yes	9	10.5	15	24.6	4.006	0.237	3	5.5	11	36.7	10.035	< 0.001[b]
Culture result	59	80.8	48	90.6	—		39	86.7	21	84.0	—	
Negative												
Positive	14	19.2	5	9.4	0.124	0.115	6	13.3	4	16.0	1.000	0.999

VTI = ventilation tube insertion.
[a] The mean (SD) of mean disease duration (wks) is shown.
[b] The *p* value is based on Fisher's Exact test (two-sided).

rate. In contrast, children had a higher percentage of male patients, mucoid fluid, involvement of both ears, and history of allergic rhinitis and/or sinusitis. Treatment results did not differ significantly between the adult and child patient groups.

The cure rate was 60.5% (141/233) in all ears, 58.1% in children and 64.7% in adults. Seven patients had multiple occurrences, with visit intervals ranging from 4 to 12 months, at an average of 5.1 months. We obtained a culture report for 206 of 244 ears; the positive rate was 15.1% (19/132) in children and 14.3% (10/74) in adults.

Univariate logistic regression analysis (Table 2) and multivariate logistic regression (Table 3) revealed three predictors of treatment failure. In the adult group, significant predictors of treatment failure were mucoid effusion ($p = 0.04$) and a history of VTI ($p < 0.001$). In children, multiple occurrences ($p < 0.001$) were predictive of a poor prognosis.

Table 3
Odds ratio of each factor in a multiple mixed logic model.

	Children		Adults	
	OR	*p* value	OR	*p* value
Sex	—		—	
Women				
Men	0.568	0.544	1.029	0.986
Mean disease duration (wks)	1.137	0.123	0.937	0.405
Multiple occurrence	—		—	
No				
Yes	85.594	0.013	2.670	0.582
VTI history	—		—	
No				
Yes	11.054	0.084	650.448	0.018

VTI = ventilation tube insertion.

3.1. Complications during follow-up

After LAT, only one ear of a boy aged 5 years developed chronic otitis media from OME. This child had allergic rhinitis, but he did not have a history of VTI. Culture showed no bacterial growth initially; however, pus formation was noted during follow-up. No other complications or postoperative sensorineural hearing loss were observed in any patient.

4. Discussion

Our study confirms the safety of laser myringotomy in both children and adults.[10,13,15] We also showed an equivalent success rate in both patient groups despite a few demographic differences. Further, we determined predictors of poor treatment

outcome in each patient group, which may be used to identify appropriate candidates for LAT.

OME in children and adults has previously been assumed to constitute different conditions.[16] OME epidemiology, disease course, risk factors, and management have been widely studied in children.[17,18] However, little is known about adult-onset OME.[19] Based on the concept that the etiology of OME is multifactorial, many different factors are implicated in the pathophysiology of this disease.[20] Therefore, the impact of different prognostic factors may also differ between age groups.

In the present study, we compared possible prognostic factors for OME between children and adults and examined potential demographic differences between these patient groups. The child group contained a greater number of male patients and had a greater incidence of allergic rhinitis and/or sinusitis history, involvement of both ears, and mucoid effusion. Variables that did not differ significantly between adult and child patients included mean disease duration, the season in which the operation was performed, the percentage of multiple occurrences, and previous VTI history.

Possible explanations for the greater number of unilateral lesions observed in adults are, first, natural prevalence and, second, the adult patient's alertness to a unilateral lesion, which is more dependable than parental suspicion in children.[21] However, selection bias may be partly responsible for this difference, because laser myringotomy is generally preferred to VTI for unilateral lesions. On the other hand, the higher prevalence of serous middle ear effusion may also be a characteristic finding in adult patients, as, unexpectedly, 10 ears with glue-like effusion in adults were observed in unilaterally involved ears, rather than in cases where both ears were involved. To understand the pathophysiology of adult-onset OME, Kariya and colleagues examined inflammatory cytokine expression in adult-onset OME[22] and Chung and others analyzed the composition of mucin in mucoid middle ear effusions.[23] Yung and colleagues concluded that the paranasal sinusitis plays a role in adult-onset OME.[19] Zhao and others found that interleukin-10 and transforming growth factor-β1, as immunoregulatory mediators, participate in the inflammatory response in chronic OME in adults.[24] In our study, mucoid effusion was significantly associated with treatment failure in adults, but not in children; a similar trend for OME recurrence after VTI dropping was observed in a previous study.[6] Therefore, a difference in the pathogenesis of OME may exist not only between age groups but also between fluid types. It is difficult to predict the type of effusion fluid involved in OME before myringotomy. Therefore, estimating the type of effusion involved based on eardrum examination may provide a suitable parameter for determining the choice of treatment in the future.

The advantages associated with CO_2 laser myringotomy have been widely studied. However, most previous publications have focused on children,[7,8,10–12,25–29] and only a few studies have examined both children and adults.[13,30] Further, there is no general agreement about the indications for this treatment and prognostic factors. Significant predictors of LAT outcome in children have been shown to include allergic rhinitis, sinusitis, exposure to smoking, disease duration, eardrum condition, mucous fluid, and adenoidectomy.[10,13,26,29] However, little is known about prognostic factors for LAT in adult-onset OME.[30] In our series, we confirmed that several variables are not related to treatment outcome, as shown in previous publications, namely, age, sex, and season. However, we also found that disease duration and history of allergy and/or sinusitis had no impact on treatment efficacy in our study, although these factors have previously been described as being predictive of outcome. Koopman and colleagues[10] found no significant effect of a history of inserted tubes on the treatment outcome in children. In our series, only 12 of the 38 ears with a history of VTI were cured. After a multivariate logistic regression analysis, VTI history was strongly associated with treatment failure in adults, but not in children. This finding is compatible with the report of Koopman and others.[10] A possible reason for the predictive value of VTI history in adults may be that Eustachian tube dysfunction plays a major role in OME in adults, but not in children, which implies that CO_2 laser myringotomy is less effective in patients with a history of VTI because this procedure cannot solve the underlying structural problem. On the other hand, in children with a history of VTI, laser treatment should not be contraindicated because their Eustachian tube function improves during development. Therefore, the CO_2 laser may be particularly useful for children, rather than adults, to avoid the additional insertion of a ventilation tube.

Multiple OME occurrences in children, i.e., more than one intervention with a normal interval (4–12 months in our study), were found to be another significant prognostic factor. A possible explanation for this finding is that children with Eustachian tube dysfunction are vulnerable to OME recurrence, which is compatible with the report of Hogan and colleagues concerning children younger than 3 years.[31] The authors concluded that children who are susceptible to OME tended to have a greater number of separate episodes, rather than an increased overall duration. Such children are primarily distinguished by the likelihood with which they might acquire the disease. Although our patients with multiple occurrences recognized that LAT is helpful for a good hearing interval, we may suggest VTI due to a reduced chance of avoiding it.

OME is not only a disease resulting from Eustachian tube dysfunction, but it is also an infectious disease. The conventional culture rate ranges from 15% to 25%,[32,33] which is compatible with our results of 14.4% in children and 13.7% in adults. Many reports have examined biofilms and isolation of the bacterium *Alloiococcus otitidis*, which have been linked to the development of OME.[34–36] Even when the culture is negative, a metabolically active pathogen may exist,[32] and evidence indicates a role of this pathogenic bacterium in resistance to antibiotics such as beta-lactamase and erythromycin in children with OME.[37] Therefore, a negative culture is no longer a favorable finding, and further investigation is needed to clarify the possible efficacy of simultaneous laser myringotomy treatment and pathogen eradication.

Although underlying tympanoplasty or mastoiditis was not significantly associated with treatment outcome in our study, this finding may be due to the small number of cases included. In our cohort, there were only two ears with a history of

tympanoplasty and 14 with a history of mastoiditis. Our findings in those patients appear to be less than favorable, with only seven cures in 16 ears. Chronic inflammation in childhood may lead to hypopneumatization of the mastoid, which may result in poor OME outcomes in adults receiving nonsurgical treatment.[38] Tympanoplasty changes the normal eardrum structure, similar to the impact of a thickening of the eardrum.[27] Thus, in our opinion, patients with a history of tympanoplasty or mastoiditis are not good candidates for LAT.

Some authors have concluded that it is risky to perform LAT under local anesthesia in children younger than 6 years. In our series, which included 46 patients younger than 6 years [3-year-olds ($n = 8$), 4-year-olds ($n = 15$), and 5-year-olds ($n = 23$)], the cure rate was 83.3%, and only one patient experienced complication of chronic otitis media. Therefore, we believe that young age is not a contraindication to LAT.

Patients were enrolled in our study following referral by a local clinic or the choice of the patient (or parents). No randomized controlled trial comparing watchful waiting and CO_2 laser treatment is currently available. We decided against randomization in our study for ethical reasons. However, due to this lack of randomization, a selection bias may have existed. Therefore, we used a multiple variable logistic regression to assess our results. Further, due to the lack of a control group, we could only compare our findings with the natural course of OME.[31] However, we believe that it would be unethical to randomize patients to laser myringotomy in one ear and not the other, or to randomize some patients to treatment and others to watchful waiting. Interestingly, our study included 18 patients with bilateral lesions who received surgery on only one side. The reason for this discrepancy was inadequate cooperation of the child or spontaneous resolution of OME in the other ear when visiting the clinic for the second surgery. Additional case accumulation may answer the question.

In conclusion, we found that the pathogenesis of OME in children and adults differed, but that the efficacy of LAT was equivalent in both patient groups. Three predictors of treatment outcome were identified in our study, which may help guide the selection of treatment in patients with OME. We believe that CO_2 laser myringotomy may be used successfully in adults and children with OME. Contraindications to this treatment include multiple occurrences in children and mucoid effusion and a history of VTI in adults.

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