

# Management of Eustachian Tube Dysfunction With Nasal Steroid Spray

## *A Prospective, Randomized, Placebo-Controlled Trial*

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**Objective:** To determine the efficacy of intranasal aqueous triamcinolone acetonide in treating the tympanometric signs and symptoms of eustachian tube dysfunction, such as otitis media with effusion and negative middle ear pressure.

**Design:** Randomized, placebo-controlled, double-blind prospective clinical trial.

**Setting:** Tertiary referral clinic.

**Patients:** Adults ( $\geq 18$  years) and children (6-17 years) presenting with otitis media with effusion, negative middle ear pressure, or both.

**Interventions:** The 2 treatment arms consisted of aqueous triamcinolone or matching placebo administered once daily intranasally for 6 weeks. All subjects underwent tympanometry, otologic examination, and completion of a symptom questionnaire before and after treatment.

**Main Outcome Measures:** Resolution of abnormal tympanometry and change in symptom scores (severity and frequency).

**Results:** Ninety-one patients presenting from September 1, 2005, through December 31, 2008, with otitis media with effusion or with negative middle ear pressure were enrolled and randomly assigned to treatment or placebo in a double-blind manner. No statistically significant difference in normalization of abnormal tympanometric signs was demonstrated with the active treatment arm compared with placebo on either a per-patient basis (19% vs 32%;  $P = .18$ ) or a per-ear basis (22% vs 35%;  $P = .15$ ). There was also no significant difference in the overall poststudy symptom score between the 2 treatment arms, after adjusting for the prestudy overall symptom score in an analysis of covariance model ( $P = .27$ ).

**Conclusion:** These findings do not support the use of intranasal steroid sprays to treat the manifestations of eustachian tube dysfunction.

**Trial Registration:** clinicaltrials.gov Identifier: NCT00279916

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**A**CUTE DYSFUNCTION OF THE eustachian tube is encountered commonly by both primary care providers and specialists dealing with disorders affecting the ear, nose, and throat. Otitis media with effusion (OME) and negative middle ear pressure (NMEP) are well-recognized elements of a clinical spectrum that may result from eustachian tube dysfunction (ETD). Although many interventions have been recommended to treat ETD, no single therapy has gained universal acceptance and been shown to be efficacious.<sup>1</sup> Given the potential for inflammatory processes within the nasal cavity and nasopharynx to play a role in the acute development of ETD, it has been hypothesized that intranasal administration of topical corticosteroid medi-

cations may contribute to the management of this condition.

Previous attempts to prospectively study the effectiveness of nasal steroids to treat ETD have been limited to the pediatric population.<sup>2-6</sup> No currently marketed intranasal corticosteroid formulation has been approved for the treatment of ETD or any of its clinical manifestations. Because of the lack of a single accepted medical intervention to deal with ETD and the ostensibly benign nature of this condition, it is common practice for some clinicians to take a "wait and see" initial approach when this clinical entity is encountered in lieu of prescribing unproven or unapproved medications.<sup>7</sup> Some patients with OME or NMEP have spontaneous resolution of symptoms, yet the exact resolution rates and timing have not been clearly defined.

**PART I**  
**Are you experiencing current dizziness or balance problems?** Yes or No (circle one)  
**Are you experiencing current ringing in your ears?** Yes or No (circle one)  
**Are you experiencing current fever (as measured by a thermometer)?** Yes or No (circle one)  
**Are you experiencing current daily drainage from either ear?** Yes or No (circle one)  
 • If yes, please indicate which ear  
**Have you ever had pressure equalization tubes placed in either ear?** Yes or No (circle one)  
 • If yes, please indicate which ear and approximate date of surgery  
**Can you breathe/pass air through both nostrils?** Yes or No (circle one)  
 • If no, please indicate which side is blocked  
**Do you currently feel like you are suffering from a common cold?** Yes or No (circle one)  
**Have you been flying in an airplane within the last week?** Yes or No (circle one)  
**Do you have a history of any of the following medical conditions or therapies?**  
 • **Cholesteatoma (ear)?** Yes or No (circle one)  
 • **Radiation therapy to the head and/or neck region?** Yes or No (circle one)  
 • **Nasopharyngeal mass or tumor?** Yes or No (circle one)  
 • **Cancer?** Yes or No (circle one)  
 • If yes, please indicate type and location of cancer  
 • **Chemotherapy?** Yes or No (circle one)  
 • **Immunodeficiency?** Yes or No (circle one)  
 • **Cystic fibrosis?** Yes or No (circle one)  
 • **Previous ear surgery other than pressure equalization tube placement?** Yes or No (circle one)  
 • If yes, please indicate type of surgery including note of which ear  
 • **Adenoidectomy?** Yes or No (circle one)  
 • **Neuromuscular disease?** Yes or No (circle one)  
 • **History of allergic rhinitis?** Yes or No (circle one)  
 • If yes, do you suffer from allergic symptoms always or only during certain seasons?  
**Are you currently taking any antibiotics, decongestants, or nasal sprays?** Yes or No (circle one)  
 • If yes, please list medications  
**Do you currently smoke tobacco products?** Yes or No (circle one)  
 • If no, are you exposed to smoke tobacco products in the household, car, or other living environment? Yes or No (circle one)

**PART II**  
 Please indicate the **FREQUENCY** and **SEVERITY** at which you have been experiencing the following symptoms **OVER THE PAST WEEK** (circle one):

**1. Fullness or pressure in your ear(s) — OVER THE PAST WEEK**  
**FREQUENCY (circle one):**  
 1 = Never  
 2 = Rarely (once a week)  
 3 = Occasionally (few times a week)  
 4 = Frequently (daily)  
 5 = Constantly  
**SEVERITY (circle one):**  
 1 = None at all  
 2 = Minimum severity—barely noticeable  
 3 = Moderate severity  
 4 = Very severe  
 5 = Maximum severity—could not be more severe

**2. Pain in your ear(s) — OVER THE PAST WEEK**  
**FREQUENCY (circle one):**  
 1 = Never  
 2 = Rarely (once a week)  
 3 = Occasionally (few times a week)  
 4 = Frequently (daily)  
 5 = Constantly  
**SEVERITY (circle one):**  
 1 = None at all  
 2 = Minimum severity—barely noticeable  
 3 = Moderate severity  
 4 = Very severe  
 5 = Maximum severity—could not be more severe

**3. Plugged sensation in your ear(s) — OVER THE PAST WEEK**  
**FREQUENCY (circle one):**  
 1 = Never  
 2 = Rarely (once a week)  
 3 = Occasionally (few times a week)  
 4 = Frequently (daily)  
 5 = Constantly  
**SEVERITY (circle one):**  
 1 = None at all  
 2 = Minimum severity—barely noticeable  
 3 = Moderate severity  
 4 = Very severe  
 5 = Maximum severity—could not be more severe

**4. Popping sensation in your ear(s) — OVER THE PAST WEEK**  
**FREQUENCY (circle one):**  
 1 = Never  
 2 = Rarely (once a week)  
 3 = Occasionally (few times a week)  
 4 = Frequently (daily)  
 5 = Constantly  
**SEVERITY (circle one):**  
 1 = None at all  
 2 = Minimum severity—barely noticeable  
 3 = Moderate severity  
 4 = Very severe  
 5 = Maximum severity—could not be more severe

**SEVERITY (circle one):**  
 1 = None at all  
 2 = Minimum severity—barely noticeable  
 3 = Moderate severity  
 4 = Very severe  
 5 = Maximum severity—could not be more severe

**5. Dampened hearing or hearing loss worse than usual — OVER THE PAST WEEK**  
**FREQUENCY (circle one):**  
 1 = Never  
 2 = Rarely (once a week)  
 3 = Occasionally (few times a week)  
 4 = Frequently (daily)  
 5 = Constantly  
**SEVERITY (circle one):**  
 1 = None at all  
 2 = Minimum severity—barely noticeable  
 3 = Moderate severity  
 4 = Very severe  
 5 = Maximum severity—could not be more severe

**PART III**  
 While enrolled in this study, have you taken any of the following medications?  
 • **Antibiotics?** Yes or No (circle one)  
 • **Oral decongestants (ie: Sudafed, Actifed, Contac, Tylenol Cold, etc)?** Yes or No (circle one)  
 • If yes, please indicate name of medication taken  
 • **Nasal sprays other than the study medication?** Yes or No (circle one)  
**Did you use the prescribed nasal spray for the entire 6-week period?** Yes or No (circle one)  
 • If no, please indicate how long you used the nasal spray  
**Was the prescribed nasal spray difficult to use or have any unpleasant side effects?** Yes or No (circle one)  
 • If yes, please explain  
**Would you use the nasal spray again if prescribed to you by a doctor in the future?** Yes or No (circle one)  
**Did you experience any of the following while using the nasal spray?**  
 • **Nose bleeding?** Yes or No (circle one)  
 • **Throat infection?** Yes or No (circle one)  
 • **Cough?** Yes or No (circle one)  
**Please choose one of the following 3 choices:**  
**A. I think I was treated with the study medication (triamcinolone acetonide)**  
**B. I think I was treated with a placebo medication**  
**C. I have no idea if I was treated with the study medication (triamcinolone acetonide) or if I was treated with a placebo**

Figure 1. Eustachian Tube Dysfunction Subject Questionnaire.

This study attempts to determine whether intranasal aqueous triamcinolone acetonide (TAA-AQ) has an effect on the clinical manifestations of ETD, such as OME and NMEP. This is a novel effort to prospectively study patients (both adults and children 6 years or older) who have reached eustachian tube anatomic maturity. Also, by analyzing the rates of spontaneous short-term resolution of OME and NMEP within a control (placebo) group, this study may improve understanding of the natural history of this clinical entity.

## METHODS

Approval for this study was obtained from the Mayo Clinic Institutional Review Board. Adults ( $\geq 18$  years) and children (6-17 years) presenting to the Department of Otorhinolaryngology at Mayo Clinic (Rochester, Minnesota), with OME, NMEP, or both were candidates for enrollment in this study. Signed informed consent regarding the study's goals, rationale, risks, design, and voluntary nature was obtained.

## PRESTUDY EVALUATION

A questionnaire documenting the characteristics of related symptoms and relevant medical history was completed (Figure 1, part I). Adult subjects completed the questionnaire on their own, pediatric subjects between the ages of 12 and 17 years completed the questionnaire with parental assistance, and the parents of pediatric subjects younger than 12 years completed the questionnaire on their children's behalf. The symptom questionnaire asked each subject to use a 5-point scale to indicate the frequency (1 = never to 5 = constantly) and severity (1 = none at all to 5 = maximum severity) of 5 symptoms in the ear during the preceding week: fullness or pressure, pain, plugged sensation, popping sensation, and dampened hearing or hearing loss worse than usual (Figure 1, part II). For each subject, an overall score was derived as the sum of the mean score for frequency and the mean score for severity.

## INCLUSION AND EXCLUSION CRITERIA

All subjects had OME, NMEP, or both with an intact tympanic membrane as documented on otoscopic examination and

typanometry. *Otitis media with effusion* was defined as an accumulation of fluid within the middle ear space in the absence of prominent acute inflammatory signs suggestive of infection. Adult subjects underwent otoscopic examination as well as flexible fiberoptic nasopharyngoscopy; pediatric patients underwent only otoscopic examination. Tympanograms (with external auditory canal volume measurements) were obtained from both ears. Specific exclusion criteria were tympanic membrane perforation (otoscopy), active cholesteatoma (otoscopy), acute or chronic suppurative otitis media (otoscopy), craniofacial syndromes, cleft palate, and developmental delay.

Among subjects with NMEP and tympanic membrane atelectasis, only those with type 1 retraction (mildly retracted), type 2 retraction (retracted over the incudostapedial complex), or type 3 retraction (retraction onto the promontory), as described by Dornhoffer,<sup>8</sup> were considered for enrollment. Justification for exclusion of type 4 retraction (extent of retraction pocket not visualized) was based on the concern of adhesion formation, occult cholesteatoma, or both—placing these potential subjects in a poorer prognostic category that might have required imminent surgical intervention. In addition, all subjects expressed willingness to return for a scheduled follow-up evaluation at 6 weeks.

## RANDOMIZATION

Subjects who met inclusion criteria were enrolled by the investigators and were then randomly assigned blindly by a third party (clinic pharmacy) to 1 of 2 parallel treatment arms (active treatment arm and control arm). Because subjects with a type B vs a type C tympanogram may represent variations of ETD severity, the randomization schedule was stratified by the tympanogram result for the worse ear (type B or C) and generated using a block randomization scheme. A *type A* tympanogram was defined as having a peaked pressure measurement less negative than  $-100$  kPa. Peaked tympanograms with pressure measurements more negative than  $-100$  kPa were considered *type C*. Nonpeaked or flat tympanograms were considered *type B*. The study was double-blind for study subjects and all individuals involved in performing study-related assessments. The pharmacy oversaw the randomization, and the treatments were bottled in identical containers with the sequence concealed until all participants had been assigned.

## INTERVENTION

Subjects aged 12 years or older in the active treatment arm received TAA-AQ (Nasacort AQ Nasal Spray; sanofi-aventis US, LLC, Bridgewater, New Jersey), 2 metered sprays in each nostril once daily ( $55$   $\mu$ g per spray), and those in the control arm received the same amount of placebo nasal spray consisting of an identical aqueous solution that lacked triamcinolone (2 sprays in each nostril once daily). Subjects younger than 12 years in the treatment arm received TAA-AQ, 1 metered spray in each nostril once daily ( $55$   $\mu$ g per spray), and those in the control arm received the same amount of matching placebo nasal spray. Subjects were instructed not to use oral or topical decongestants during the study. Intranasal TAA-AQ was chosen for its properties as an odorless aqueous preparation that was projected to cause relatively less mucosal irritation and burning compared with some other nasal steroid preparations, thereby improving the likelihood of maintaining the trial's blinding.

## FOLLOW-UP

At 6 weeks, subjects were asked to complete the symptom frequency and severity questionnaire again (Figure 1, part II) and

a new questionnaire related to compliance, quality of blinding, and adverse treatment effects (Figure 1, part III). Otologic examination and tympanometry were repeated.

## OUTCOME MEASURES

The primary outcome measure was tympanogram normalization by 6 weeks, defined as a change in tympanogram from a pretreatment type B or C to a posttreatment type A. Our hypothesis was that administration of daily intranasal TAA-AQ would result in a higher rate of tympanogram normalization compared with the rate resulting from administration of placebo. Analysis of the primary outcome measure was based on an intent-to-treat principle; that is, subjects were analyzed according to the assigned treatment that was undertaken. Subjects who were treated with antibiotics or oral or topical decongestants or who had tympanostomy tube placement while enrolled were considered to have treatment failures in a secondary analysis of this measure. In addition, the change in the overall frequency and severity symptom score was evaluated.

## STATISTICAL ANALYSES

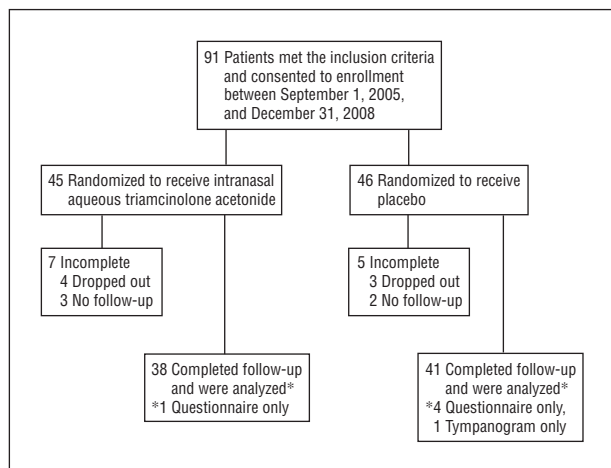
The targeted sample size of 73 patients per treatment arm was determined to be sufficient to provide 80% power to detect a difference of 25% (placebo arm) vs 50% (treatment arm) in the percentage of patients with complete resolution of symptoms at 6 weeks, assuming a 10% dropout rate. The primary analysis was made on a per-subject basis. Both ears needed to have a type A result on the follow-up tympanogram for the subject to be classified as having normalization. The proportion of subjects who experienced normalization was compared between the 2 treatment arms using a  $\chi^2$  test. In addition, a 95% confidence interval (CI) was calculated for the difference in proportions between the 2 treatment arms. A subgroup analysis of the primary outcome was also undertaken for patients between 6 and 17 years of age. As a secondary analysis, tympanometric normalization was evaluated on a per-ear basis using all ears with type B or type C tympanogram results at baseline. The comparison on the proportion of ears with normalization was evaluated on the basis of a logistic regression model that was fit using generalized estimating equations to take into account the correlation between ears of the same subject.

Finally, the responses at 6 weeks to the symptom frequency and severity questionnaire were compared between the 2 treatment arms using Wilcoxon rank sum tests. In the case of treatment failures, the subject's data points were assigned the worst rank before calculation of the rank sum test. In addition, an overall score was derived as the sum of the mean score for frequency and the mean score for severity. The poststudy overall symptom score was compared between the 2 treatment arms, after adjusting for the prestudy overall symptom score in an analysis of covariance model.

All calculated *P* values were 2-sided, and *P* < .05 was considered statistically significant. Statistical analyses were performed using SAS, version 9.1 (SAS Institute, Inc, Cary, North Carolina).

## RESULTS

Ninety-one subjects met the inclusion criteria and provided consent for enrollment from September 1, 2005, through December 31, 2008. Of the 91 subjects, 45 (49%) were male, and the mean (SD) age at enrollment was 41.7 (29.5) years, with a range of 6.1 to 95.8 years. The total number of patients screened during the subject recruit-



**Figure 2.** Flow chart of subject enrollment and participation.

ment process was not recorded. Thirty-four subjects (37%) were from 6 to 17 years old. On the basis of a randomization schedule stratified by tympanogram type (B or C) for the more severely affected ear, 45 subjects were randomly assigned to receive TAA-AQ and 46 to receive placebo. Enrollment and participation are outlined in **Figure 2**. Because of a slow rate of subject recruitment, the target enrollment number of 146 was not met.

### SUBJECTIVE ASSESSMENTS

Each subject completed a general questionnaire before starting the study. Twenty subjects (22%) reported balance problems, 27 (30%) reported tinnitus, and 24 (26%) reported “common cold” symptoms experienced before the study. These complaints occurred in equal numbers in both arms of the study. The prestudy overall symptom frequency and severity score was not significantly different between the 2 treatment arms (median overall score, 4.8 vs 4.3 for TAA-AQ vs placebo;  $P = .17$ , Wilcoxon rank sum test).

### OBJECTIVE ASSESSMENTS

Tympanometry data were used as an objective measure of improvement or normalization of eustachian tube function.

### PRIMARY OUTCOME MEASURE

Thirty-seven of 45 subjects randomized to TAA-AQ had a follow-up tympanogram; of these, 7 (18.9%) had complete normalization (type A tympanogram for both ears). Of the 37 subjects who were randomized to placebo and had a follow-up tympanogram, 12 (32.4%) had complete normalization (difference in proportions,  $-13.5\%$ ; 95% CI,  $-33.2\%$  to  $6.2\%$ ;  $P = .18$ ). These results are summarized in **Table 1**.

Similar results were observed among the subset of pediatric subjects. A total of 34 subjects between 6 and 17 years old were enrolled, of whom 30 had a follow-up tympanogram. On follow-up, the complete normalization rates in the pediatric subjects were 1 of 15 (7%) in the TAA-AQ

**Table 1. Summary of Complete Resolution of Abnormal Tympanometry**

Treatment Group <sup>a</sup>	Complete Normalization of Abnormal Tympanometry	
	Regardless of Additional Treatment	Considering the Subjects Who Took Additional Treatment as Having Incomplete Resolution
Intranasal aqueous triamcinolone acetonide, No. (%)	7/37 (18.9)	5/37 (13.5)
Placebo, No. (%)	12/37 (32.4)	9/37 (24.3)
Difference in proportions, % (95% CI)	-13.5 (-33.2 to 6.2)	-10.8 (-28.5 to 6.9)
<i>P</i> value	.18	.24

Abbreviation: CI, confidence interval.

<sup>a</sup>Of the 38 subjects in the triamcinolone arm with complete follow-up, 37 had a follow-up tympanogram. Of the 41 subjects in the placebo arm with complete follow-up, 37 had a follow-up tympanogram.

arm and 4 of 15 (27%) in the placebo arm (difference in proportions,  $-20.0\%$ ; 95% CI,  $-45.7\%$  to  $5.7\%$ ;  $P = .14$ ). When the pediatric subjects treated with antibiotics or oral decongestants while enrolled in the study were handled as having treatment failures (ie, nonnormalization of symptoms), then the complete normalization rates in the pediatric subjects were 1 of 15 (7%) in the TAA-AQ arm and 3 of 15 (20%) in the placebo arm (difference in proportions,  $-13.3\%$ ; 95% CI,  $-37.2\%$  to  $10.5\%$ ;  $P = .28$ ).

### SECONDARY OUTCOME MEASURES

Among the 37 subjects randomized to TAA-AQ, 7 reported taking antibiotics ( $n = 5$ ) or oral decongestants ( $n = 2$ ) while enrolled in the study. Two of these 7 subjects had complete tympanometric normalization.

Among the 37 subjects randomized to placebo, 7 reported taking other relevant medicines: antibiotics ( $n = 3$ ), oral decongestants ( $n = 1$ ), nasal spray ( $n = 1$ ), combination ( $n = 1$ , antibiotics/oral decongestants; and  $n = 1$ , combination oral decongestants/nasal spray) while enrolled in the study. Three of these 7 subjects had complete tympanometric normalization.

When the subjects treated with antibiotics or oral decongestants while enrolled in the study were handled as having treatment failures (ie, nonresolution of symptoms), then 5 subjects (13.5%) randomized to TAA-AQ had complete tympanometric normalization compared with 9 subjects (24.3%) randomized to placebo (difference in proportions,  $-10.8\%$ ; 95% CI,  $-28.5\%$  to  $6.9\%$ ;  $P = .24$ ).

### PER-EAR TREATMENT OUTCOME

Among the 37 subjects randomized to TAA-AQ with a follow-up tympanogram, a total of 55 ears had an initial tympanogram of type B or C; on follow-up, 12 ears (21.8%) had complete normalization. Among the 37 subjects randomized to placebo with a follow-up tympanogram, a total of 57 ears had an initial tympanogram of type B or C; on follow-up, 20 ears (35.1%) had complete normalization.

**Table 2. Tympanogram Results per Ear<sup>a</sup>**

Result	Initial Tympanogram Type	Follow-up Tympanogram Type	Intranasal Aqueous Triamcinolone Acetonide, No. (90 ears)	Placebo, No. (92 ears)
Resolution, total No.	B	A	12	20
	C	A	3	7
No resolution, total No.			9	13
	B	B	43	37
	B	C	17	12
	C	B	6	7
	C	C	8	5
No. (%) of ears with complete resolution			12/55 (21.8)	20/57 (35.1)
Not initially affected, total No.			19	17
	A	A	15	15
	A	B	0	0
No follow-up tympanogram, total No.	A	C	4	2
			16	18
	A	...	5	4
	B	...	4	7
		7	7	

<sup>a</sup>A description of the tympanography type is given in the "Randomization" subsection of the "Methods" section.

This difference was not statistically significant ( $P = .15$ ). These results are summarized in **Table 2**.

When the subjects treated with antibiotics or oral decongestants while enrolled in the study were handled as having treatment failures (ie, incomplete resolution), then 8 of the 55 ears (15%) of subjects randomized to TAA-AQ had tympanometric normalization compared with 16 of the 57 ears (28%) of subjects randomized to placebo ( $P = .16$ ).

### SYMPTOM QUESTIONNAIRE OUTCOMES

Subjects who were randomized to TAA-AQ tended to have more moderate severity in fullness or pressure in their ears ( $P = .07$ ), as well as more frequent ( $P = .02$ ) and more severe ( $P = .03$ ) plugged sensation in their ears, than did subjects randomized to placebo, after 6 weeks of treatment. In addition, the overall poststudy symptom score tended to be higher for subjects randomized to TAA-AQ compared with the score for those randomized to placebo ( $P = .07$ ). After adjusting for the prestudy overall symptom score in an analysis of covariance model, the poststudy overall symptom score was not significantly different between the 2 treatment arms ( $P = .27$ ).

**Table 3** summarizes the change (from pretreatment to posttreatment) in symptom frequency and severity after categorization of the change scores as same, better, or worse. The percentage of subjects with improved symptoms was not significantly different between the 2 treatment arms for any of the 5 symptoms ( $P > .05$ ,  $\chi^2$  test).

### ADVERSE EVENTS

Although both cough and nosebleeds were reported as adverse events in both arms of the study, no severe events occurred and no subject was removed from the study as a result.

### COMMENT

The ideal treatment strategy for management of ETD in adults is not well understood. Watchful waiting may be a reasonable, conservative initial option to manage ETD in uncomplicated cases. Yet, analysis of data derived from the placebo arm of this study demonstrates that only approximately one-third of cases seemed to undergo spontaneous normalization of tympanometric findings at a 6-week follow-up interval. Notwithstanding this low rate of spontaneous resolution, severe adverse consequences of watchful waiting were not encountered. This new information about natural disease history in adults should prove valuable for patient counseling.

In 2002, van Heerbeek et al<sup>1</sup> published the results reported for various medical interventions for ETD in both animal models and humans and noted a lack of data from prospective randomized, double-blind, placebo-controlled trials within the medical literature. In particular, evidence to support the use of oral decongestants and antihistamines for OME in children is lacking.<sup>9</sup> Furthermore, a study by van Heerbeek et al<sup>10</sup> demonstrated no effect of single-dose topical application of a nasal decongestant on ETD in children in a randomized, double-blind, placebo-controlled study using sophisticated measures of eustachian tube function.

Publications prospectively addressing the effect of nasal steroids on ETD are limited. Thomas et al<sup>5</sup> systematically reviewed the existing prospective data in 2006 relating to the treatment of OME in children using oral or nasal steroids for the *Cochrane Database*. They concluded that combined therapy with antibiotics and nasal steroids in children may have short-term benefit compared with antibiotics alone but based this on the findings of a single prospective study.<sup>6</sup> They also concluded that data to support the use of nasal steroids alone were insufficient because they were based on the findings in a

**Table 3. Summary of Change in Symptom Scores<sup>a</sup>**

Criterion <sup>b</sup>	Intranasal Aqueous Triamcinolone Acetonide	
	(n=38)	Placebo (n=40)
Fullness or pressure in ears		
Frequency		
Better	11 (28.9)	18 (45.0)
Same	17 (44.7)	17 (42.5)
Worse	10 (26.3)	5 (12.5)
Severity		
Better	13 (34.2)	18 (45.0)
Same	14 (36.8)	13 (32.5)
Worse	11 (28.9)	9 (22.5)
Pain in ears		
Frequency		
Better	11 (28.9)	8 (20.0)
Same	17 (44.7)	23 (57.5)
Worse	10 (26.3)	9 (22.5)
Severity		
Better	9 (23.7)	6 (15.0)
Same	19 (50.0)	25 (62.5)
Worse	10 (26.3)	9 (22.5)
Plugged sensation in ears		
Frequency		
Missing	0	1
Better	10 (26.3)	14 (35.9)
Same	13 (34.2)	21 (53.8)
Worse	15 (39.5)	4 (10.3)
Severity		
Missing	0	1
Better	15 (39.5)	14 (35.9)
Same	8 (21.1)	16 (41.0)
Worse	15 (39.5)	9 (23.1)
Popping sensation in ears		
Frequency		
Missing	0	1
Better	11 (28.9)	8 (20.5)
Same	14 (36.8)	18 (46.2)
Worse	13 (34.2)	13 (33.3)
Severity		
Missing	0	2
Better	9 (23.7)	6 (15.8)
Same	17 (44.7)	19 (50.0)
Worse	12 (31.6)	13 (34.2)
Dampened hearing/loss worse than usual		
Frequency		
Missing	0	1
Better	16 (42.1)	16 (41.0)
Same	14 (36.8)	15 (38.5)
Worse	8 (21.1)	8 (20.5)
Severity		
Missing	0	1
Better	15 (39.5)	14 (35.9)
Same	13 (34.2)	15 (38.5)
Worse	10 (26.3)	10 (25.6)

<sup>a</sup>Data are given as number (percentage) of responses to that question.

<sup>b</sup>The frequency and severity of each of these 5 symptoms were rated by each subject (Figure 1, part II) before starting the study and after 6 weeks using a 5-point scale to indicate the frequency (1 = never to 5 = constantly) and severity (1 = none at all to 5 = maximum severity). The change was categorized as "same" if the same response was provided by the subject during both assessments, "better" if a more favorable response (less frequent or less severe) was provided after 6 weeks, or "worse" if a more unfavorable response (more frequent or more severe) was provided after 6 weeks.

prospective placebo-controlled study involving children with both allergic rhinitis and OME.<sup>4</sup>

A more recent report by Cengel and Akyol<sup>2</sup> prospectively studied 122 children between the ages of 3 and 15 years with OME, adenoid hypertrophy, or both, who were awaiting surgery. Those authors reported a statistically significant higher rate of resolution (42%) in children treated with daily intranasal mometasone furoate monohydrate at 6 weeks compared with those with no treatment at all (14%). Furthermore, they also noted a significant reduction in adenoid size among the treated children.

Our findings, which do not include preschool-aged children, do not demonstrate a statistically significant benefit in normalizing tympanometry when comparing the use of nasal steroid spray with placebo spray at 6 weeks. These findings were contradictory to our hypothesis that nasal steroids would increase the rate of tympanogram normalization.

A subgroup statistical analysis of pediatric subject outcomes was undertaken; this likewise did not show evidence of a positive treatment effect with use of the study medication. Because the mechanics of ETD may differ between preschool-aged children and older patients as a result of the timing of anatomic eustachian tube maturity and other epidemiologic factors, it is difficult to apply data derived from very young children to adults. For this reason, preschool-aged children were excluded from this study.

#### STUDY WEAKNESSES

The study enrolled 91 rather than the targeted 146 subjects because of a slow rate of subject recruitment. Although the observed rate for complete resolution in the placebo arm was close to what was anticipated (observed 32.4%, anticipated 24.3%), the rate in the TAA-AQ arm was considerably lower than anticipated (observed 18.9%, anticipated 50%). The 95% CI for the difference (TAA-AQ minus placebo) in the observed proportions was -33.2% to 6.2%. Accordingly, the calculated upper range of possible improvement after treatment that could have been undetected by this study is a mere 6%, which is such a small difference that it likely would not provide most clinicians with motivation to treat ETD with TAA-AQ. We note that published data relating to the natural history of ETD and NMEP on which to base our pre-study outcome predictions were sparse.

A second weakness relates to the secondary outcomes, wherein we analyzed the results of a nonvalidated eustachian tube symptom questionnaire (to our knowledge, a validated tool does not yet exist) that also did not demonstrate beneficial treatment effects. We candidly acknowledge that the definitive meaningfulness of these secondary outcomes is in question because they are derived from a nonvalidated questionnaire.

We also acknowledge that nasal septal deviation, turbinate hypertrophy, and adenoid hypertrophy, which could have had a negative effect on drug delivery in some cases, were not assessed.

Finally, this study intentionally did not seek to exclusively include or exclude subjects with allergic rhi-

nitis. Twelve percent of all subjects reported a history of allergic rhinitis, yet subjects were not formally evaluated for confirmation or quantification. However, the number of subjects with self-reported allergic rhinitis was actually slightly higher in the control arm (17% vs 7% in the treatment arm); therefore, it is unlikely that this factor could account for the failure of the active study medication to show a treatment benefit.

Given the inflammatory nature of allergic rhinitis and the established potential negative effect on eustachian tube function,<sup>11</sup> it is certainly possible that nasal steroids may have a role in treating patients with ETD who fall within this specific subcategory. Newer intranasal steroid preparations, such as TAA-AQ, are efficacious and generally safe, as demonstrated in large studies dealing with allergic rhinitis.<sup>12</sup> Future research efforts looking specifically at the impact of nasal steroids on ETD in subjects with established allergic rhinitis are needed.

### STUDY STRENGTHS

First, despite the study's shortcomings, this is to our knowledge the first prospective placebo-controlled study dealing with the effect of nasal steroid sprays on ETD in adults and relatively older children—a patient group that has been generally neglected in clinical trial efforts to study ETD. Second, the primary outcome measure evaluated in this study (tympanogram normalization) is one that is both objective and clinically relevant insofar as tympanometry is commonly used by physicians to evaluate ETD. Finally, the placebo arm of this study provides valuable prospectively acquired data related to the natural history of ETD in older children and adults that is otherwise scarce in the medical literature.

In conclusion, topical intranasal application of TAA-AQ did not increase the likelihood of normalization of the tympanometric manifestations of ETD at 6 weeks in a study group of subjects aged 6 years or older. On the basis of responses to a pretreatment and posttreatment questionnaire, it also appears unlikely to improve ETD-related symptom complaints. Finally, our data portray a natural history of OME and NMEP in this population that undergoes spontaneous resolution by 6 weeks in only approximately one-third of subjects. The study medication was well tolerated without any unexpected adverse effects or serious adverse events reported.

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**Study concept and design:** Gluth, McDonald, and Orvidas. **Acquisition of data:** Gluth, McDonald, Bauch, Beatty, and Orvidas. **Analysis and interpretation of data:** Gluth, Weaver, Bauch, and Orvidas. **Drafting of the manuscript:** Gluth, McDonald, and Weaver. **Critical revision of the manuscript for important intellectual content:** Gluth, Bauch, Beatty, and Orvidas. **Statistical analysis:** Weaver. **Obtained funding:** Gluth and Orvidas. **Administrative, technical, and material support:** McDonald, Bauch, and Orvidas. **Study supervision:** Gluth, McDonald, Bauch, Beatty, and Orvidas. **Financial Disclosure:** None reported.

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