Eustachian Tube Function Before Recurrence of Otitis Media With Effusion

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Objective: To study the role of eustachian tube function in the development of recurrent otitis media with effusion (OME) in children treated with tympanostomy tubes for OME.

Design: Prospective cohort study.

Setting: Three academic and general hospitals.

Patients: Children aged 2 to 7 years with a first clinical episode of OME that persisted for at least 3 months; 136 (81%) of 168 eligible children participated. All children received tympanostomy tubes for bilateral OME at study entry.

Main Outcome Measure: Recurrence of OME within 6 months of tube extrusion.

Results: No statistically significant differences were present in eustachian tube function test results between ears that developed recurrent OME and those that did not.

The difference in passive ventilatory function between ears with and without OME recurrence was 10 daPa (95% confidence interval, −24 to 43 daPa) for opening pressure and −3 daPa (95% confidence interval, −18 to 11 daPa) for closing pressure. The overall difference in the proportion of ears with and without OME recurrence that could not equilibrate positive and negative applied pressures was 12% (95% confidence interval, −2% to 26%). The proportions of ears with and without OME recurrence that induced negative pressure in the middle ear by forcefully sniffing were 22% and 31%, respectively (P = .75).

Conclusion: Measurement of ventilatory and protective eustachian tube function using the forced response test, the pressure equilibration test, and the sniff test has no value in predicting whether children have an increased risk of OME recurrence.

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Otitis media with effusion (OME) is highly prevalent in young children; at least 80% of children experience 1 or more episodes of OME by age 4 years.1,2 This condition is characterized by a high rate of spontaneous recovery but also by a high rate of recurrence. At present, it is not possible to distinguish children who will develop persistent or recurrent OME from those who will develop transient OME. Predisposing factors for recurrence are probably related to etiology. Otitis media with effusion is a multifactorial-generated condition in which eustachian tube (ET) function is believed to play a crucial role.3 The ET has 3 important functions with respect to the middle ear: ventilation, protection (ie, against nasopharyngeal pressure variations, ascending secretions, and microorganisms), and clearance of secretions.3 Studies4-9 that involve different populations of children have indicated that ET function is impaired in children with OME. These cross-sectional studies, however, have not clarified whether ET dysfunction is a cause or a result of middle ear effusion. We hypothesized that differences in ET function between children will determine why some develop recurrent or chronic OME and others have transient OME. The aim of this study is to test this hypothesis in a group of children treated with tympanostomy tubes for OME. These children underwent the forced response test (passive ventilatory ET function), the pressure equilibration test (active ventilatory ET function), and the sniff test (protective ET function). By comparing the results in ears that developed OME recurrence after spontaneous tympanostomy tube extrusion with those in ears that did not, we aim to establish whether ET function predisposes children with OME to recurrence of this condition.

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METHODS

In the Netherlands, health insurance companies require referral by a general practitioner (GP) before refunding specialist care costs. Therefore, nearly all patients with OME are first seen by their GP. In Dutch general practice, the diagnosis of OME by GPs is generally based on the combination of medical history and otoscopic evidence of fluid in the middle ear. Otoscopic competence is an important issue in the training of GPs, including validation by otomicroscopic and otolaryngologic examination. According to the guidelines of the Dutch College of General Practitioners, children with chronic OME should only be referred to an otolaryngologist after repeated observations of middle ear effusion for at least 3 months. Children were eligible for the study if they were aged 2 to 7 years, had a GP-documented first clinical episode of bilateral OME that persisted for at least 3 months, and had been referred for the first time to the Department of Otorhinolaryngology of 1 of the 3 participating hospitals in Nijmegen or Winterwijk (the Netherlands) between December 1, 1999, and March 31, 2002. The otolaryngologist confirmed the presence of bilateral OME. Because of compliance with the ET function tests, a minimum age of 24 months was defined for participation in the study. Children with Down syndrome, cleft palate, cystic fibrosis, or daily treatment with inhalation or topical corticosteroids for at least 1 month per year were excluded from the study, as were children with documented immunodeficiency, previous adenoidectomy, myringotomy, or treatment with tympanostomy tubes. All of the children who fulfilled the inclusion criteria were sequentially asked to participate in the study. The medical ethical committees of the 3 participating hospitals approved the study protocol. Signed informed consent was obtained from the parents or legal guardians.

At study entry, all of the children received the same type of tympanostomy tube, bilaterally, for OME under general anesthesia. Adenoidectomy was not performed in these children. Checkup visits were scheduled for 1 week after tube insertion and every 3 months thereafter. At each checkup, ET function tests were performed on ears with patent tympanostomy tubes. The risk period for the development of OME started with the first checkup in which spontaneous tube extrusion was observed (per ear). Follow-up ended at the checkup at which OME was diagnosed or 6 months after spontaneous tube extrusion.

At study entry and at the checkup visits, OME was determined according to the Maastricht Otitis Media With Effusion Study algorithm, which is based on the results of tympanometry and nonpneumatic otoscopy. Tympanograms were classified according to the algorithm of Jerger, in which OME was considered to be present when tympanometry resulted in a type B or C2 tympanogram combined with otoscopic findings that suggested the presence of effusion in the middle ear (eg, glue and fluid lines or bubbles) and no signs of acute ear infection. If tympanometry could not be performed, otoscopic findings that suggested effusion in the middle ear were used to diagnose OME. We refer to ears that developed recurrent OME within the maximum follow-up period of 6 months after spontaneous tube extrusion as rOME+ ears, whereas ears that did not develop OME during follow-up are referred to as rOME– ears. Both ET function tests and tympanometry were performed using a middle ear analyzer (model Tym 87; Rexton Danplex A/S, Copenhagen, Denmark). Pressure applied by the pump ranged from 600 to –600 daPa, at a pump rate of 50 daPa/s.

EUSTACHIAN TUBE FUNCTION TESTS

First, the presence and patency of the tympanostomy tubes were confirmed otoscopically. Each child was seated comfortably and given instructions. The external ear canal was then sealed airtight with the probe of the middle ear analyzer. Both ears were measured, starting with the right ear.

**Forced Response Test**

The forced response test was used to assess ventilatory function of the ET, with opening pressure (Po) and closing pressure (Pc) as the outcome variables. Passive ET ventilatory function was assessed by gradually increasing the pressure in the middle ear using the pressure pump until the ET opened, as indicated by a sudden decrease in the pressure (Figure 1). The maximum pressure was recorded as the Po. After the ET had opened, the pressure pump was turned off so that the ET could close, as indicated by stabilization of the pressure. This residual pressure was recorded as the Pc. To reduce measurement errors, Po and Pc were recorded 3 times in each session of 3 minutes or less, and the means of the 3 measurements were used for further analysis.2 The difference between Po and Pc was calculated. When the ET did not open before the maximum pressure of 600 daPa was applied, Po was arbitrarily recorded as 700 daPa. The corresponding Pc could not be assigned in these cases because no reliable estimate of Pc could be made. The Po reflects the resistance to the tubal opening and consequently reflects the total closing forces of the ET, that is, the luminal forces (mucosal factors, surface tension, viscosity of secretions, etc) and the extraluminal forces (elasticity of cartilage and pressure of surrounding tissues). The Pc reflects the extraluminal forces of the ET, that is, the forces that keep the ET closed in rest. When the ET is opened actively, these forces must be overcome. Extremely high Po and Pc values thus indicate poor ET ventilatory function. Very low Po and Pc values, however, do not automatically indicate good ET function because they may be associated with impaired protective function.

**Pressure Equilibration Test**

The pressure equilibration test is a qualitative method to measure active ET ventilatory function. The results reflect the ability to equilibrate positive and negative pressures. Positive and negative pressures (+100 and –100 daPa, respectively) were applied to the middle ear, and the residual pressure was...
recorded after several deglutitions (the children were asked to swallow a small amount of water) (Figure 1). Based on the residual pressure, each ear was classified into 1 of 4 tubal function groups according to the methods of Elner et al.14 Group 1 ears equilibrated positive and negative pressures completely (residual pressure <−10 daPa and ≥−10 daPa, respectively). Group 2 ears equilibrated positive and negative pressures partially (residual pressure >−10 daPa and ≤−10 daPa, respectively). Group 3 ears equilibrated positive pressure completely or partially but could not equilibrate negative pressure. Group 4 ears could not equilibrate positive and negative pressures. We considered a single measurement sufficient to obtain reliable results.12

Table 1. Characteristics of 136 Children Treated With Tympanostomy Tubes for OME

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, % boys</td>
<td>50</td>
</tr>
<tr>
<td>Ethnicity, % white</td>
<td>95</td>
</tr>
<tr>
<td>Age at study entry, median (range), y</td>
<td>5.3 (2.1-7.5)</td>
</tr>
<tr>
<td>Low birth weight (&lt;2500 g), %</td>
<td>6</td>
</tr>
<tr>
<td>Premature birth (&lt;37 wk), %</td>
<td>9</td>
</tr>
<tr>
<td>Breastfeeding (&gt;4 mo), %</td>
<td>63</td>
</tr>
<tr>
<td>Diagnosis of OM in the first year of life, %</td>
<td>8</td>
</tr>
<tr>
<td>Diagnosis of OM in the year before study entry, %</td>
<td>43</td>
</tr>
<tr>
<td>Otorrhea in the year before study entry, %</td>
<td>31</td>
</tr>
<tr>
<td>Aged 2-4 y at study entry, %</td>
<td>41</td>
</tr>
<tr>
<td>Attending day care at study entry, %</td>
<td>21</td>
</tr>
<tr>
<td>Aged 2-4 y and attending day care at study entry, %</td>
<td>18</td>
</tr>
<tr>
<td>Siblings, %</td>
<td>93</td>
</tr>
<tr>
<td>Family members with a history of OM, %</td>
<td>61</td>
</tr>
<tr>
<td>Exposure to passive smoking at home, %</td>
<td>34</td>
</tr>
</tbody>
</table>

Abbreviations: OM, otitis media; OME, otitis media with effusion.

Sniff Test

The sniff test is a measure of the capacity of the ET to protect the middle ear cavity against extreme nasopharyngeal pressure variations.15,16 Children were asked to sniff forcefully 5 times. When the negative nasopharyngeal pressure exceeds the closing forces of the ET, there is a pressure breakthrough, and the middle ear space is evacuated. Subsequently, the ET closes, and negative pressure is established in the middle ear (Figure 1).15 Because the ET should remain closed to protect the middle ear against negative pressures created in the nasopharynx, opening of the tube implies poor protective function. If the middle ear pressure decreases once or more after sniffing, this is regarded as poor protective ET function.

STATISTICAL ANALYSIS

All analyses were performed using a statistical software program (SAS version 8.0; SAS Institute Inc, Cary, NC), with children’s ears as the unit of analysis. Because ears and ETs in a child do not behave independently, we conducted statistical analyses that account for this interdependency. Therefore, a linear mixed model (SAS procedure MIXED) was fitted to calculate the differences in Po, Pc, and the difference between Po and Pc between rOME+ and rOME− ears based on all ET measurements from both ears, excluding those obtained during the first checkup, which took place approximately 1 week after tube insertion. These data were excluded because the middle ear status could not have been stabilized, and surgery may have short-term effects on the mucoid layer and epithelium of the middle ear and ET. Therefore, the results of the forced response test may not adequately represent ET function in a physiologic condition.17 Data from the children with missing values at 1 of the checkups due to obstruction of the tympanostomy tube, otorhea, poor cooperation of the child, or absenteeism were included in the analyses because the occurrence of these missing values was assumed to be random. A variance components
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To study the development of active ET function across time, ears in tubal function groups 1 and 2 were pooled with ears in tubal function group 3 because there were only a few ears that seemed to belong to the 2 former categories. The generalized estimation equation with exchangeable correlation structure (SAS procedure GENMOD) did not show any difference in the results of the dichotomized pressure equilibration test and the sniff test at the longitudinal checkups. Subsequently, a summary measure was defined for the most frequent test outcome per ear. The effect of tubal function group and sniff test results on the recurrence of OME, which accounted for dependency of ears within a child, was tested using the likelihood ratio test. Generalized estimation equation models that include the main effect of the specific ET function test plus adjustment for side were compared with the model that excludes the main effect of ET function.

Furthermore, additional analyses were performed. A generalized estimation equation based on the longitudinal measurements was used to study the possible interaction effect of the sniff test with either the pressure equilibration test or the forced response test on the risk of OME recurrence. The timing of OME recurrence in relation to the pressure equilibration test and the sniff test was tested using the Fisher exact test.

RESULTS

A total of 168 children met the criteria for inclusion in the study; 136 of them (81%) participated. The reasons for refusal to participate in the study were not related to ET function. In most of the included children, the diagnosis of bilateral OME at study entry was confirmed by a bilateral type B tympanogram. Median participant age at study entry was 5.3 years (range, 2.1-7.5 years), and 50% were boys (Table 1).

Tympanostomy tubes were inserted bilaterally in 135 children and unilaterally in 1 child. Thus, 271 ears had tympanostomy tubes in situ at study entry. Figure 2 shows the profile of the checkups at which ET function was measured (patent tympanostomy tubes) and the checkups at which ears were at risk of OME recurrence (after spontaneous extrusion of the tubes). Tympanostomy tubes were extruded a median of 9 months after insertion. The documentation data of tube extrusion (range, 3-30 months) were the same in rOME+ and rOME− ears.

At the predetermined end of the study (August 15, 2003), 90 children had completed the follow-up. The OME recurrence rate was high: 56 children had bilateral recurrence, 17 had unilateral recurrence, and only 17 did not develop recurrent OME. The children who subsequently developed bilateral, unilateral, or no OME recurrence were of comparable sex and age at study entry.

Complete follow-up data up to a maximum of 6 months after tube extrusion were obtained from 210 ears; 61 ears (29%) did not develop OME recurrence, whereas 149 ears (71%) did (Figure 2). In most of the rOME+ ears (87%), the diagnosis was based on a type B tympanogram.

In 62 ears, OME recurrence could not be assessed because of loss to follow-up, censored data that indicated that the tympanostomy tubes were still in situ at the end of the study, or the follow-up period of 6 months had not yet elapsed. The ET function test results in these ears corresponded with those in ears with known OME status. In the following sections, the total number of ears may differ because of missing values for the various ET function tests.

FORCED RESPONSE TEST

Figure 3 shows the results of the forced response test in rOME+ and rOME− ears at the 3-, 6-, 9-, and 12-month checkups after insertion of the tympanostomy tubes. The ETs of 17 ears did not open at 600 daPa at 1 or more of the checkups. There was no statistically significant difference in Po or Pc between rOME+ and rOME−.
ears. The overall difference between rOME+ and rOME– ears was 10 daPa (95% confidence interval, −24 to 43 daPa) for Po and –3 daPa (95% confidence interval, −18 to 11 daPa) for Pc. When Po and Pc per visit were subtracted (difference between Po and Pc), a small but non-significant difference was discernible 6 months after tube insertion (Figure 3C). The overall difference between Po and Pc was 10 daPa (95% confidence interval, −8 to 29 daPa) higher in rOME+ than in rOME– ears.

PRESSURE EQUILIBRATION AND SNIFF TESTS

Most ears in the rOME+ and rOME– groups had poor active ET function (tubal function group 3 or 4) (Table 2). No statistically significant differences were detected in the distribution of the 4 tubal function groups between rOME+ and rOME– ears (P = .70). Tubal function group 4 applied slightly, but consistently, more often to rOME+ ears than to rOME– ears: 12% more (95% confidence interval, −2% to 26%) in all ears and 8% and 13% more in left and right ears, respectively.

The percentage of ears that developed negative pressure in the middle ear by sniffing forcefully varied from approximately 10% to 39% during follow-up. No overall statistically significant differences could be demonstrated between rOME+ and rOME– ears (P = .75) (Table 3).

Because we did not demonstrate any differences in ET function between rOME+ and rOME– ears using each ET function test separately, we investigated whether rOME+ ears were more likely to have a combination of 2 unfavorable test results. No noticeable differences were detected between the 2 study groups with the combination of poor protection based on the sniff test and poor ventilatory function based on the forced response test or with the combination of the sniff test and the pressure equilibration test (data not shown). We also studied the timing of OME recurrence in relation to ET function test results. Differences were found in the timing of OME recurrence among the tubal function groups (P = .03) (Table 2). In tubal function group 4, 64% of the ears had developed OME recurrence at the first checkup after the checkup with documented extrusion of the tubes, whereas in group 3, this had occurred in only 39% of the ears (P = .01). No differences were seen in the timing of checkups with OME recurrence for ears with good and poor protection as reflected by the results of the sniff test (P = .18) (Table 3).

**ADDITIONAL ANALYSES**

This prospective cohort study was designed to gain more insight into factors that contribute to OME recurrence by comparing the results of 3 different ET function tests in ears with and without OME recurrence after initial treatment with tympanostomy tubes. Passive ventilatory ET function did not differ between ears with and without OME recurrence within 6 months of spontaneous tube extrusion: the distribution of Po and Pc and the difference between Po and Pc during follow-up were similar for ears with and without OME recurrence.

We expected that a higher proportion of rOME+ ears would be in tubal function groups 3 and 4 than in groups 1 and 2 because groups 3 and 4 indicate poor active ventilatory ET function. The data from this study provide some support for this hypothesis: ears in group 4 were more likely to develop recurrent OME, and they did so at an earlier date, but the effects were fairly small. Note
that the study population contained a high proportion of ears with poor active ET ventilatory function. In the study by Elner et al, group 4 frequencies were 7% in healthy adults compared with 45% in healthy children and 72% in children with recurrent ( > 11) acute otitis media episodes.

We hypothesized that more rOME+ ears would induce negative pressure after forceful sniffing than rOME− ears. Less than one third of all ears developed negative pressure in the middle ear. These figures are comparable with those reported in other populations of children with OME. No differences in sniff test results were found in our study between rOME+ and rOME− ears.

In conclusion, the results of this study show that there are no substantial differences in ET function between ears that develop OME recurrence and ears that do not. An earlier study posed the question of whether the forced response test and the pressure equilibration test are responsive enough to middle ear conditions and sufficiently discriminative in children with various degrees of middle ear effusion. In the present study, we did not demonstrate any convincing consistent differences in ET function between rOME+ and rOME− ears. This does not mean that the ET does not play a role in the development of OME. On the contrary, in our population of children with a minimum of 3 months of bilateral OME, active ET ventilatory function and protective function were poor. Therefore, we must conclude that in a population of children treated with tympanostomy tubes for OME, the discriminative power of these tests is too low to distinguish those who will develop recurrent OME from those with transient OME. It is also likely that in this group of children with preexisting poor ET function, other factors, such as the immune response to respiratory pathogens, play a more important role in distinguishing children with recurrent OME from children with transient OME.

In this prospective cohort study based on a population of children with a minimum of 3 months of bilateral OME before study entry, no differences were found in ET dysfunction between ears that developed OME recurrence and ears that did not develop OME recurrence after treatment with tympanostomy tubes. Consequently, we conclude that the forced response test, the pressure equilibration test, and the sniff test, which measure the ventilatory and protective functions of the ET, have no value in predicting whether a child with a previous episode of OME has an increased risk of OME recurrence.

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