Prevention of Otitis Media by Adenoidectomy in Children Younger Than 2 Years

Petri S. Mattila, MD; Veli-Pekka Joki-Erkkila, MD; Terhi Kilpi, MD; Jukka Jokinen, MSc; Elja Herva, MD; Heikki Puhakka, MD

**Objectives:** To test the effect of adenoidectomy in connection with tympanostomy compared with tympanostomy only in preventing otitis media in children younger than 2 years.

**Design:** Prospective trial with randomized and nonrandomized arms.

**Setting:** Primary care study clinics.

**Participants and Interventions:** The study participants were selected from 2497 children who had been enrolled in the Finnish Otitis Media Vaccine Trial at the age of 2 months. A total of 306 children, aged 1 to 2 years, who had experienced recurrent episodes of otitis media were randomized into 2 treatment groups: tympanostomy with or without adenoidectomy. Of the 306 children, 137 were operated on according to random basis (randomized trial). The 169 children whose parents declined participation in the randomized trial were operated on according to the parents' preferences (nonrandomized trial). All children were followed up until 2 years of age. The mean follow-up time was 7 months.

**Main Outcome Measure:** The rate of acute otitis media episodes.

**Results:** The average reduction in the rate of all acute otitis media episodes in the adenoidectomy group was 19% (95% confidence interval [CI], −14% to 43%) among children enrolled in the randomized trial and 25% (95% CI, −13% to 50%) in the nonrandomized trial. The reduction in the randomized trial was mainly due to reduction in the rate of pneumococcal otitis media (58%, 95% CI, 16%-79%).

**Conclusion:** In children younger than 2 years, concurrent adenoidectomy during the insertion of tympanostomy tubes does not seem to have a major advantage over the insertion of tympanostomy tubes alone in preventing otitis media.

Diagnosis of Acute Otitis Media

Each time a child in the FinOM Vaccine Trial experienced symptoms of acute infection that required medical attention, the child was evaluated in one of the outpatient study clinics. Diagnosis of acute otitis media was made when there were signs of effusion in the middle ear cavity and symptoms related to acute otitis. These symptoms included fever, ear pain, signs of upper respiratory tract infection, irritability, diarrhea, vomiting, or discharge from the ear.

When no tympanostomy tube was present, a visually abnormal membrane (eg, abnormal color, position, and/or mobility), suggesting middle ear effusion, was considered as a sign of acute otitis media. The ear was evaluated each time by tympanometry. A flat B-type tympanogram supported the diagnosis of otitis media. Middle ear fluid was obtained by aspiration through the tympanostomy tube. If the tympanostomy tube was not patent, acute otitis media was diagnosed by otorrhea, and middle ear fluid was obtained by aspiration through the tympanostomy tube. If the tympanostomy tube was not patent, acute otitis media was diagnosed by aspiration through the tympanostomy tube. Middle ear fluid was obtained by aspiration through a myringotomy incision. After the insertion of tympanostomy tubes, the presence of middle ear effusion was diagnosed by otorrhea, and middle ear fluid was obtained by aspiration through the tympanostomy tube. If the tympanostomy tube was not patent, acute otitis media was diagnosed by aspiration through a myringotomy incision. Specimens of middle ear fluid were immediately plated on agar plates for isolation, identification, and serotyping of bacterial pathogens as described previously.14,15

Amoxicillin was used as the first-choice antibiotic and was given at 40 mg/kg twice a day for 7 days. Children allergic to amoxicillin were given trimethoprim-sulfadiazine (8 mg/kg of trimethoprim and 25 mg/kg of sulfadiazine twice a day for 7 days), cefaclor (40 mg/kg twice a day for 7 days), or azithromycin (10 mg/kg for a single dose for the first day and thereafter 5 mg/kg once a day for 4 days). In the case of bacteria resistance to the antibiotic, treatment was changed to an antibiotic that was effective in vitro against the microbe. In this case, one of the aforementioned antibiotics or amoxicillin-clavulanic acid (40 mg/kg of amoxicillin and 10 mg/kg of clavulanic acid twice a day for 7 days) was used.

A new episode of otitis media regardless of origin was considered to start when at least 30 days had elapsed since the beginning of the previous episode. A new episode of acute otitis media due to Streptococcus pneumoniae was considered to start when at least 30 days had elapsed since the beginning of the previous culture-confirmed pneumococcal episode. Analogous definitions were used for episodes of acute otitis media caused by Haemophilus influenzae and Moraxella catarrhalis.

Randomization and Enrollment

The criteria for admitting the child for operative treatment to the Department of Otorhinolaryngology, Tampere University Hospital, were more than 3 to 5 events of acute otitis media during the last 6 months or 4 to 6 events of acute otitis media during the last year. Each time a child from the pneumococcal vaccine study who was older than 10 months but younger than 23 months was referred for operative treatment at the Department of Otorhinolaryngology, Tampere University Hospital, he or she was randomized into one of the 2 treatment groups: tympanostomy tube placement without adenoidectomy or tympanostomy tube placement with adenoidectomy. Children older than 10 months but younger than 12 months underwent surgery at the age of 12 months. Of the 2497 children enrolled in the pneumococcal vaccine study, 306 children were randomized to undergo tympanostomy either alone (162 children) or combined with adenoidectomy (144 children). Thus, the design of the trial was unconventional in that the eligible children were randomized before the study subjects were enrolled.

The allocated treatment was not exposed to the parents or to the operating surgeon before the study was introduced and explained to the parents. However, if the parents expressed willingness to participate, the randomly allocated treatment was revealed to them. At this point, the parents were given the chance not to participate. After the allocation was revealed, those children whose parents gave written consent were enrolled in the randomized trial and operated on according to the allocation of the randomization.

Of the 306 children randomized, 137 were enrolled in the trial. Of those enrolled, 63 were assigned to be treated with tympanostomy tube placement (39% of the 162 children randomized to have tympanostomy only) and 74 were assigned to be treated with concurrent tympanostomy tube placement and adenoidectomy (51% of the 144 children randomized to have concurrent tympanostomy and adenoidectomy). Five of the 63 children who were initially randomized to have tympanostomy alone and were operated on according to the allocation of the randomization had adenoidectomy performed later (before the follow-up ended at the age of 2 years). These 5 children were included in the analysis by using a time-dependent treatment covariate. Thus, in the analysis, the 5 children were transferred from the tympanostomy group to the tympanostomy and adenoidectomy group at the time of adenoidectomy.

The 169 of the 306 randomized children whose parents refused to participate in the randomized trial underwent either tympanostomy alone (45 children) or tympanostomy with adenoidectomy (124 children). The decision of which of the 2 treatments the child would receive was largely influenced by the parents’ wishes. These 169 children constitute the study subjects of the nonrandomized trial.

Surgery

All the operations were performed with the patients under general anesthesia. Tympanostomy tube placements were performed by anterior radial myringotomy, aspiration of effusion, and insertion of the tympanostomy tube. Adenoids were visualized using velotraction and a mirror. Adenoidectomy was then performed under visual control using a Beckmann ring curette and smaller curettes to remove residual tissue. Adenoid tissue in the fossae of Rosenmüller was routinely removed. Altogether 8 surgeons were involved.
FOLLOW-UP

Follow-up of the children up to 2 years of age was performed at the study clinics of the FinOM Vaccine Trial. Acute otitis media was diagnosed as described herein. After the diagnosis of acute otitis media, the parents were given a follow-up card to record the duration of middle ear discharge during the following 7 days. The data on this card were transferred to study forms during the follow-up visit, which occurred 4 weeks later.

OUTCOME MEASURES

The main outcome measures were the rate of all acute otitis media episodes and the rates of otitis media episodes caused by S pneumoniae, H influenzae, and M catarrhalis. The secondary outcome measure was the number of days with otitis media as recorded on the follow-up cards.

STATISTICAL ANALYSIS

The comparison of the risk of acute otitis media between the treatment groups was made by the Cox proportional hazards model for multivariate counting process to allow for multiple episodes for the same child.12 The correlation between recurrent episodes was addressed using the robust variance estimation for the regression variables.13 To account for the possible unbalance of the PncCRM and PncOMPC vaccines between treatment groups, the Cox model was adjusted with the vaccination status. In addition to the vaccination status, the model was adjusted for sex, number of siblings, and the preoperative number of otitis media episodes. The reduction in the rate of acute otitis media episodes in the group of children who underwent concurrent adenoidectomy and the insertion of tympanostomy tubes compared with children who underwent the insertion of tympanostomy tubes only (ie, efficacy of concurrent adenoidectomy) was calculated as 1 minus the relative risk, with the corresponding 95% confidence interval (CI).

Because of the association of the age of the child with the risk of acute otitis media, the follow-up time was age specific. Each child entered the risk set immediately after the operation and was followed up until the age of 2 years (the close-out visit of the FinOM Vaccine Trial). In addition, the child was absent from the risk set for 30 days from the diagnosis of otitis media according to the definition of the acute otitis media episode as described herein. The age-specific cumulative intensity was presented by plotting a Nelson-Aalen estimate of cumulative hazard through age.

RESULTS

RANDOMIZED TRIAL

Of the 137 children enrolled in the randomized study, 74 had adenoidectomy combined with tympanostomy tube placements, and 63 had tympanostomy tube placements only (Figure 1). The mean age at the time of operation was 17 months, and the mean follow-up time was 7 months (Table 1). Because the randomized treatment was revealed to the parent(s) before their consent was obtained, it was a potential source of a selection bias, and it resulted in a difference between the 2 treatment groups in the number of children recruited. However, this did not result in apparent differences between the 2 treatment groups in risk factors for acute otitis media, such as sex, the proportion of children without any siblings, day care attendance, the number of acute otitis media episodes before surgery, and the age at the time of the operation (Table 1).

Among the children who participated in the randomized trial, the rate of all acute otitis media episodes per person-year was 2.40 in the tympanostomy group and 2.05 among children who underwent both adenoidectomy and the insertion of tympanostomy tubes (Figure 2 and Table 2). To minimize the effect of confounding factors, the analysis of the risk of otitis media associated with concurrent adenoidectomy was adjusted for sex, number of siblings, the preoperative number of otitis media episodes, and the pneumococcal vaccination status. The estimate of efficacy of adenoidectomy together with tympanostomy vs tympanostomy alone was 0.19 (1 relative risk; 95% CI, 0.14 to 0.43; Table 2).

We then analyzed whether the presence of fluid in the middle ear at the time of surgery was a factor that predicted the outcome of concurrent adenoidectomy. In those children who had fluid in the middle ear at the time of surgery, the rate of otitis media was 2.73 per person-year among those who had adenoidectomy together with the insertion of tympanostomy tubes and 2.36 per person-year among those who had insertion of tympanostomy tubes only (efficacy, −0.13; 95% CI, −1.06 to 0.38). Among those children in the randomized trial who did not have fluid in the middle ear at the time of surgery, the rate of otitis media was lower (1.58 per person-year) among those who had adenoidectomy together with the insertion of tympanostomy tubes compared with those who had in-
The study design allowed the detection of the effect of concurrent adenoidectomy in preventing pathogen-specific episodes of otitis media. Among the children who participated in the randomized trial, concurrent adenoidectomy was followed by a lower rate of acute otitis media episodes caused by *S pneumoniae* (Table 2). Concurrent adenoidectomy did not have any significant effect on the rate of otitis media episodes caused by *H influenzae* or *M catarrhalis* (Table 2).

There was no statistically significant difference between the randomization groups in the frequency of days with purulent ear discharge. The number of days with ear discharge per person-year was 3.45 days among children who underwent the insertion of tympanostomy tubes alone and 3.62 days among children who underwent both the insertion of tympanostomy tubes and adenoidectomy.

**NONRANDOMIZED TRIAL**

Of the 169 children who did not participate in the randomized trial, 124 had adenoidectomy combined with tympanostomy tube placements, and 45 had tympanostomy tube placements only (Figure 1). The estimate of the efficacy of concurrent adenoidectomy in preventing otitis media was 0.25 (95% CI, –0.13 to 0.50). As opposed to the randomized trial, concurrent adenoidectomy in the nonrandomized trial was not associated with a decrease in the rate of pneumococcal otitis media (Table 2).

Among the group of children who were included in the nonrandomized trial and who had concurrent adenoidectomy, the proportion of female children and the proportion of children without any siblings were high compared with the group of children in the nonrandomized trial who underwent the insertion of tympanostomy tubes only and compared with both groups of children in the randomized trial (Table 1).

**COMMENT**

The study children were carefully followed up in a clinic setting by specially trained study physicians, which allowed accurate detection of otitis media episodes. The design of the vaccine efficacy trial allowed us to determine the effect of adenoidectomy in connection with the insertion of tympanostomy tubes compared with tympanostomy only on attacks of acute otitis media caused by each of the major pathogens. Furthermore, the age of the children was ideal for the evaluation of this kind of intervention because the risk of acute otitis media is the highest during the first 2 years of life.1

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**Table 1. Characteristics of Children Who Underwent Tympanostomy With or Without Adenoidectomy**

<table>
<thead>
<tr>
<th>Adenoidectomy</th>
<th>Random Allocation of Treatment</th>
<th>Nonrandom Allocation of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of children</td>
<td>Yes. No. of children</td>
</tr>
<tr>
<td>No. of children</td>
<td>63 (38)</td>
<td>74 (40)</td>
</tr>
<tr>
<td>Female</td>
<td>24 (38)</td>
<td>27 (36)</td>
</tr>
<tr>
<td>Male</td>
<td>39 (62)</td>
<td>47 (64)</td>
</tr>
<tr>
<td>At least 1 sibling</td>
<td>39 (62)</td>
<td>55 (74)</td>
</tr>
<tr>
<td>Day care outside home</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 12 mo</td>
<td>18 (27)</td>
<td>17 (22)</td>
</tr>
<tr>
<td>At age 18 mo</td>
<td>34 (54)</td>
<td>37 (50)</td>
</tr>
<tr>
<td>Mean age at operation, mo</td>
<td>17.4 (40)</td>
<td>16.7 (40)</td>
</tr>
<tr>
<td>Mean No. of previous episodes of otitis media</td>
<td>3.4 (30)</td>
<td>3.5 (30)</td>
</tr>
<tr>
<td>No. of otitis media episodes before the age of 1 y</td>
<td>1.6 (30)</td>
<td>1.8 (30)</td>
</tr>
<tr>
<td>Vaccination status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PncCRM</td>
<td>25 (40)</td>
<td>23 (31)</td>
</tr>
<tr>
<td>PncOMPC</td>
<td>18 (29)</td>
<td>25 (34)</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>20 (32)</td>
<td>26 (35)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Completed</td>
<td>Dropped out</td>
</tr>
<tr>
<td></td>
<td>63 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>74 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>45 (100)</td>
<td>121 (98)</td>
</tr>
<tr>
<td></td>
<td>0 (0)</td>
<td>3 (0)</td>
</tr>
</tbody>
</table>

*Data are number (percentage) of children unless otherwise indicated.
†Includes 5 children who initially underwent tympanostomy tube placements alone but who later underwent adenoidectomy.
Because of ethical reasons, the allocated treatment was revealed to the parents before they gave their final consent to participate. Consequently, some parents withdrew their initial consent once they heard about the treatment group. This resulted in an uneven allocation of the 2 treatment regimens among the study children enrolled in the randomized trial (63 tympanostomy alone vs 74 adenoidectomy with tympanostomy). Therefore, the design of the randomization of the present study was prone to a bias due to possible selection of children in the allocated treatment groups. Such a bias is avoided in conventional trials conducted according to the CONSORT (Consolidated Standards of Reporting Trials) principles. Nevertheless, the design of the present survey may have allowed the detection of a large therapeutic effect. In addition, the possible selection of children in the randomization groups could be evaluated by analyzing the characteristics of the children in the 2 treatment groups. It revealed that in the randomized trial there were no significant differences between the groups treated by random allocation in sex distribution, number of siblings, and the preoperative number of otitis media episodes before the allocated treatment was given.

Five of the children who were initially randomized to the tympanostomy group underwent adenoidectomy after the initial tympanostomy tube placement and before the follow-up ended at the age of 2 years. These children had recurrent otitis media despite the insertion of tympanostomy tubes, which was the reason for performing adenoidectomy. In the efficacy analysis, the 5 children were not censored at the time of adenoidectomy, because this may have introduced a bias in favor of adenoidectomy, since these 5 children were obviously exceptionally otitis prone having had numerous attacks of otitis media even after tympanostomy. Instead of censoring the children in the analysis at the time of adenoidectomy, we included the children in the adenoidectomy group at the time of adenoidectomy. By doing so, we attempted to minimize a possible bias in favor of concurrent adenoidectomy. However, this may have resulted in an underestimate of the effect of adenoidectomy.

The analysis of the randomized trial suggested that adenoidectomy in connection with the insertion of tympanostomy tubes compared with the insertion of tympanostomy tubes alone seemed not to result in a major advantage in prevention of otitis media before the age of 2 years. If concurrent adenoidectomy in connection with the insertion of tympanostomy tubes provided any effect in preventing otitis media during the average follow-up of 7 months, it may have occurred in children who did not have any fluid in the middle ear at the time of surgery. To gain more information on the effects of adjuvant adenoidectomy, the rate of otitis media was analyzed in children who did not participate in the randomized trial. Although in the nonrandomized trial there was a trend in favor of a beneficial effect of concurrent adenoidectomy, the difference in the rate of otitis media between the treatment groups did not reach significance.

In the randomized trial, concurrent adenoidectomy was associated with a reduction of otitis media specifically caused by pneumococcus. Such an association was not observed in the nonrandomized trial. This apparent discrepancy raises doubts that the observed effect of concurrent adenoidectomy on pneumococcal otitis media in the randomized trial occurred by chance. On the other hand, the nonrandomized trial is prone to errors due to selection of children in the 2 treatment groups, such as those that resulted in the differences between the 2 treatment groups in the sex distribution and distribution of children with no siblings. Therefore, the observed effect of adenoidectomy on pneumococcal otitis media in the randomized trial may represent a true effect.

In a recent trial performed by Paradise et al, adenoidectomy in combination with tonsillectomy low-
ered the recurrence rate of acute otitis media, but adenoidectomy alone had only a modest effect in preventing otitis media. The age of the children in this trial ranged from 3 to 15 years, although the onset of otitis media in most of the children occurred before the age of 3 years. In this trial, the mean annual rate of otitis media during the first follow-up year was 1.8 episodes in the adenoidectomy group and 2.1 in the control group; however, the difference did not reach statistical significance, and during the second and third follow-up years, adenoidectomy had no favorable effect. In our study, during the average follow-up of 7 months, the mean rate of otitis media was 2.05 episodes per person-year in the adenoidectomy with the insertion of tympanostomy tubes group and 2.40 episodes per person-year in the group with the insertion of tympanostomy tubes alone. Thus, the results of our study resemble those of the trial performed by Paradise and coauthors.

Although adenoidectomy has been reported to result in an enhanced resolution of middle ear effusion in children with OME, adenoidectomy in the present study had no effect on the duration of otorhoea. It is possible that the pathogenesis of middle ear inflammation in OME may have distinct characteristics compared with the pathogenesis of recurrent otitis media. These may involve obstruction of the eustachian tube, presence of distinct pathogens in the adenoids, or the inflammatory reactions in the adenoids. Furthermore, it is possible that otitis media in children younger than 2 years compared with older children has unique characteristics because of the immaturity of the immunity of the young child.

We conclude that in children younger than 2 years, concurrent adenoidectomy during the insertion of tympanostomy tubes does not seem to have a major advantage over the insertion of tympanostomy tubes alone in preventing otitis media.

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Corresponding author and reprints: Petri S. Mattila, MD, Department of Otorhinolaryngology, Helsinki University Central Hospital, PO Box 220, 00029 Helsinki, Finland (e-mail: petri.mattila@hus.fi).

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