Laser Myringotomy versus Ventilation Tubes in Children with Otitis Media with Effusion: A Randomized Trial

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Objectives: Insertion of ventilation tubes in children with otitis media with effusion (OME) is an accepted and common treatment procedure. The majority of patients require general anesthesia. Although laser myringotomy can be performed in local anesthesia, evidence is lacking that this treatment modality is an alternative for tubes, and outcome predictors for laser myringotomy are not available. Study Design: Prospective randomized trial. Methods: We screened 1,403 children with chronic OME that were indicated for placement of ventilation tubes. In the eligible patients, we performed laser myringotomy in one ear and placed a tube in the other ear, both within the same patient. Follow-up was scheduled each month for 6 months. Success was defined as absence of effusion or aural discharge. A logistic regression model was used with success of the therapy as binary outcome. This model was based on base-line variables, asked for in a parent’s questionnaire. Results: Two hundred eight children received the allocated intervention, and no complications occurred. The mean closure time of the laser perforation was 2.4 weeks, and the mean patency time of the ventilation tube was 4.0 months. The mean success rate was 40% for laser and 78% for tubes. Ten known variables were found to predict middle ear status after therapy. Conclusion: Laser myringotomy is a safe but less-effective procedure than insertion of a ventilation tube in the treatment of chronic OME. The logistic regression model enables the otolaryngologist to choose the surgical treatment for the child that benefits most: laser myringotomy or ventilation tube. Key Words: Randomized trial, laser myringotomy, ventilation tube, otitis media with effusion, children, logistic regression model.

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INTRODUCTION

Otitis media with effusion (OME), or glue ear, is the most common cause hearing loss (HL) in children today with a bimodal curve at 2 and 5 years of age.1 Therapy consists of watchful waiting, antibiotic treatment, or surgical intervention. Insertion of ventilation tubes for OME persisting for more than 3 months is well accepted and one of the most frequently performed operation in children.

The minimum time required for a tube to be in place to resolve OME is not known, and, although inserting a ventilation tube is a minor procedure, a major disadvantage is the need for general anesthesia in the majority of children. Complications or side effects of ventilation tubes include periodic aural discharge, atrophy or sclerosis of the tympanic membrane, persistent perforation, development of a retraction pocket, or cholesteatoma.2–4

Laser myringotomy has proven to be a safe method to ventilate the middle ear, and results of up to 70% efficacy have been reported.5–7 However, the indication for laser myringotomy is not yet known, and evidence is lacking that laser myringotomy is an alternative for ventilation tubes. Our present trial was designed to address the following interrelated questions: what is the effectiveness of laser myringotomy compared with the ventilation tube in pediatric patients with chronic OME, and can we create a model to estimate success rates for laser and tube in these patients, taking into account factors which influence the development and course of this disorder?
MATERIALS AND METHODS

Patient Recruitment

The study was conducted between July 1999 and September 2001 in seven Dutch hospitals, with screening of all children with OME. Referrals came from local physicians, medical health care workers, school screening programs, or from parents' own initiative. OME was defined as otitis media with middle ear effusions of any color, but without fever, otalgia, or otorrhea. The diagnosis was made by an otolaryngologist with binocular otoscopy as the mainstay of conformation, in combination with a type B tympanogram or pure tone audiometry. A bilateral tympanogram type C1 or C2, classified after Jerger, was considered to support the diagnosis of OME. If the child was too young or failed at audiometric testing, the diagnosis was based solely on otoscopic findings and history.

Children or parents were questioned for baseline characteristics and known environmental factors of influence for the occurrence and treatment outcome of OME (Table I). If duration of HL reported by the parents was more than one year, we recorded a period of HL of 12 months.

Inclusion criteria were children aged less than 11 years, impaired hearing noticed by parents during at least 3 successive months, and bilateral OME. The following exclusion criteria were applied: unilateral OME, poorly cooperative children, clinically admitted patients, asymmetric perceptive HL, and previously operated ears with other than myringotomy or ventilation tubes.

Informed Consent

The parents of the children gave written informed consent before enrolment. An otolaryngologist explained the potential risks and benefits of each surgical intervention. Their freedom to choose an alternative treatment or to withdraw from the study at any time was emphasized.

<p>| TABLE I. Characteristics of Patients with Otitis Media with effusion and Comparison between Different Groups. |
|---------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|</p>
<table>
<thead>
<tr>
<th>Excluded Patients (n = 371)</th>
<th>Nonparticipating Patients (n = 420)</th>
<th>Participating Patients (n = 208)</th>
<th>P Value*</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female (n) (male %)</td>
<td>229/141 (61.9)</td>
<td>232/188 (55.2)</td>
<td>108/100 (51.9)</td>
<td>.02</td>
</tr>
<tr>
<td>Mean age (years ± SD [range])</td>
<td>4.2 ± 2.2</td>
<td>4.4 ± 2.2</td>
<td>4.2 ± 2.3</td>
<td>.94</td>
</tr>
<tr>
<td>Median duration of hearing loss (months [range])</td>
<td>4 (1–12)</td>
<td>5 (3–12)</td>
<td>6 (3–12)</td>
<td>.002</td>
</tr>
<tr>
<td>Ethnic origin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (n, [%])</td>
<td>284 (76.8)</td>
<td>351 (83.6)</td>
<td>170 (81.7)</td>
<td>.01</td>
</tr>
<tr>
<td>Mediterranean (n, [%])</td>
<td>61 (16.5)</td>
<td>42 (10.0)</td>
<td>16 (7.7)</td>
<td></td>
</tr>
<tr>
<td>Negroid (n, [%])</td>
<td>11 (3.0)</td>
<td>15 (3.6)</td>
<td>13 (6.3)</td>
<td></td>
</tr>
<tr>
<td>Asian (n, [%])</td>
<td>9 (2.4)</td>
<td>7 (1.7)</td>
<td>4 (1.9)</td>
<td></td>
</tr>
<tr>
<td>Other (n, [%])</td>
<td>5 (1.4)</td>
<td>5 (1.2)</td>
<td>5 (2.4)</td>
<td></td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoidectomy (n, [%])</td>
<td>133 (38.2)</td>
<td>128 (30.5)</td>
<td>51 (24.5)</td>
<td>.001</td>
</tr>
<tr>
<td>Tonsillectomy (n, [%])</td>
<td>48 (12.9)</td>
<td>58 (13.8)</td>
<td>23 (11.1)</td>
<td>.001</td>
</tr>
<tr>
<td>Cleft palate (n, [%])</td>
<td>26 (7.1)</td>
<td>15 (3.6)</td>
<td>17 (8.2)</td>
<td>.65</td>
</tr>
<tr>
<td>Ever grommets (n, [%])</td>
<td>176 (47.4)</td>
<td>128 (30.5)</td>
<td>49 (23.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Allergies (n, [%])</td>
<td>8 (2.2)</td>
<td>18 (4.3)</td>
<td>7 (3.4)</td>
<td>.25</td>
</tr>
<tr>
<td>Smoking exposure (n, [%])</td>
<td>66 (24.4)</td>
<td>102 (29.2)</td>
<td>62 (29.8)</td>
<td>.19</td>
</tr>
<tr>
<td>Parents history of otitis (n, [%])</td>
<td>76 (29.9)</td>
<td>125 (36.5)</td>
<td>80 (38.5)</td>
<td>.053</td>
</tr>
<tr>
<td>Siblings</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>0 (n, [%])</td>
<td>79 (20.5)</td>
<td>85 (20.2)</td>
<td>59 (28.4)</td>
<td></td>
</tr>
<tr>
<td>1–2 (n, [%])</td>
<td>175 (47.2)</td>
<td>238 (56.7)</td>
<td>135 (64.9)</td>
<td>.21</td>
</tr>
<tr>
<td>≥3 (n, [%])</td>
<td>120 (32.3)</td>
<td>97 (23.1)</td>
<td>14 (6.7)</td>
<td>.51</td>
</tr>
<tr>
<td>Breast feeding &gt; 3 months (n, [%])</td>
<td>86 (32.0)</td>
<td>130 (37.1)</td>
<td>78 (37.5)</td>
<td></td>
</tr>
<tr>
<td>Current school</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None (n, [%])</td>
<td>58 (41.0)</td>
<td>51 (14.5)</td>
<td>35 (16.8)</td>
<td>.21</td>
</tr>
<tr>
<td>Daycare (n, [%])</td>
<td>67 (24.3)</td>
<td>91 (25.9)</td>
<td>52 (25.0)</td>
<td>.51</td>
</tr>
<tr>
<td>Preschool (n, [%])</td>
<td>151 (54.7)</td>
<td>209 (59.5)</td>
<td>121 (58.2)</td>
<td></td>
</tr>
<tr>
<td>Season at time of inclusion</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Spring (n, [%])</td>
<td>123 (33.4)</td>
<td>127 (30.4)</td>
<td>38 (18.3)</td>
<td></td>
</tr>
<tr>
<td>Summer (n, [%])</td>
<td>40 (10.9)</td>
<td>49 (11.7)</td>
<td>44 (21.2)</td>
<td></td>
</tr>
<tr>
<td>Fall (n, [%])</td>
<td>77 (20.9)</td>
<td>104 (24.9)</td>
<td>72 (34.6)</td>
<td></td>
</tr>
<tr>
<td>Winter (n, [%])</td>
<td>128 (34.8)</td>
<td>138 (33.0)</td>
<td>54 (26.0)</td>
<td></td>
</tr>
</tbody>
</table>

Values are number of subjects (n), or mean ± SD. A chi-square test or Student’s t test was used for intergroup comparisons as indicated. A two-sided P < .05 was considered statistically significant.

*Excluded patients compared with eligible participating patients.
†Eligible nonparticipating patients compared with eligible participating patients.
any moment was reaffirmed. The medical ethical review commit-
tees of all the participating hospitals approved the protocol.

Surgical Procedure
To compare the results of the laser myringotomy with the
results of a ventilation tube, we wanted to exclude possible con-
 founding factors. Therefore, both interventions were performed in
one patient, during one procedure, and under general anesthesia.
Without preparing the ear with any topical liquid, in one ear a
ventilation tube was inserted using cold-knife myringotomy, and
in the other ear laser myringotomy was performed. A ventilation
tube with a 1.1 mm internal diameter (Aero-Tymp 904830
Donaldson Silicone/B, Entermed BV, Linschoten) was used. In
case of OME with atelectasis of the middle ear, a Goode-T Tube
(Aero-Tymp 904860 Goode-T-Tube Silicone/B, L = 6 mm, En-
termed BV, Linschoten) was inserted. The laser myringotomy
was performed with a Sharplan CO2-flashscanner laser using a
handhold device and video screen (ESC Sharplan Medical Sys-
tems, Tel Aviv, Israel). The power setting varied from 7 to 20 W,
and the diameter of the circular perforation varied from 1.8 to 2.6
mm, with an aim for the largest diameter as possible (2.6 mm in
159 of 208 patients). The laser myringotomy and insertion of the
ventilation tube were performed in the anteroinferior part of the
tympanic membrane. Fluid was not aspirated from the middle ear
at the laser side, thereby mimicking future office setting proce-
dures of avoiding distress by noise. Children, in whom an ade-
noidectomy was indicated, underwent this procedure using a
sharp curette, according to known guidelines.10 No antibiotics or
eardrops were given before, during, or immediately after the
operation because, in The Netherlands, antibiotics are not con-
sidered common practice in the treatment of otitis media.11

Follow-Up Procedures
Follow-up visits by an otolaryngologist were scheduled every
month, except for the first 90 children, who were scheduled
each week to determine the mean closure time of the laser per-
formation. After closure, the follow-up continued on a monthly
basis until a total follow-up of 6 months. Interval visits were
encouraged if the child had any ear symptoms or was ill. Otorrhea
persisting for more than 1 week was treated by ear drops consist-
ing of either dexamethasone/framycetine/gramicidin or ofloxacin,
depending on the culture, whereas otorrhea with fever was
treated with oral antibiotics only (amoxicillin). During adminis-
tration of medication, the child was seen weekly until recovery. At
follow-up, the parents and child were blinded to the type of
surgery at either side.

Statistical Analysis
Assignment of the side for laser myringotomy or tube inser-
tion was made randomly by computer-generated lists in balanced
blocks of six to assure an even distribution of surgical procedure
for left and right ears. The main outcome variable was the absence
of effusion or otorrhea documented by binocular otoscopy.
This was defined as success. Presence of otorrhea or effusion was
considered as failure.

The power calculation was based on a two-sided alpha of
0.05 and a power of 0.80, minimally, to detect a difference in
success rate between the two ears. With the assumption of a
success rate of 70% for laser12,13 and a functional ventilation tube
in 90% of the population after 6 months,14 at least 72 patients
were needed. All data were entered into a database (Microsoft
Access 97, Redmond, WA), and statistical analysis was performed
using SPSS 9.0 (Chicago, IL) for Windows and SAS (Cary, NC) on
an intention to treat basis.

A logistic regression model was used, with success of the
therapy as binary outcome. Repeated measurements of this out-
come variable were available within a single patient, generated
by the two differently treated ears observed at a number of
control visits. With 208 patients included in the study, the rule of
thumb was used that the number of simultaneously estimated
coefficients in the model may not become much larger than 14.
The effects were estimated by fitting a generalized linear model
using a procedure for fitting generalized linear models (PROC
GENMOD) with the generalized estimating equations (GEE)
method to account for the correlated outcomes.

RESULTS
Patient Characteristics and Preoperative Evaluation
One thousand four hundred three (1,403) children with
signs and symptoms of otitis media were seen during the
study period. Of this group, 999 children suffered from
OME persisting for more than 3 months, and they were
indicated for surgical therapy. Three hundred seventy-one
children did not meet the inclusion criteria. Of the remain-
ing 628 eligible children, 420 did not join the study for
several reasons: 398 refused to participate, 8 did not ap-
pear at time of surgery, 11 received no laser myringotomy
at time of surgery, and, in 3 children, the OME spontane-
ously resolved. Two hundred eight children agreed to par-
ticipate and were enrolled in the study to receive the trial
intervention (Fig. 1).

Baseline characteristics of participating and eligible
nonparticipating patients were comparable for most of the
stratification criteria except for cleft palate, siblings, and
season of onset, whereas excluded patients more fre-
quently had a history of (adenotonsillectomy and ventilation tubes (Table I). Tymanometry could be performed in 385 ears. Type B was found in 362 ears (172 bilateral), type C1 in 5 ears, and C2 in 18 (3 bilateral) ears. The time interval between the indication and the operation procedure was on average 32 (range 1–160, median 28) days.

The Donaldson-type ventilation tube was used in 196 (94%) of the children and the Goode-T tube in 12 (6%) children, 8 of them having a cleft palate. A total of 97 children underwent an adenoectomy as a combined procedure. Adenoectomy in combination with tonsillectomy was performed in 16 children. None of the 208 children had any complication at time of the procedure.

**Follow-Up**

The mean number of the scheduled monthly follow-up visits for all children was 4.6. Thirty-seven percent (77) of the children kept all 6 follow-up appointments. The number of children that did not appear at scheduled visits increased with the number of follow-up visits, and this reached a maximum at the fifth control visit. At the 5-month visit, 94 patients did not appear compared with 72 patients at the 6-month control visit. One hundred seven additional unscheduled visits were made between regularly visits because of intercurrent illness or complaints, leading to two withdrawals. A total of 55 (26%) children quit the study (41 lost to follow-up, 14 failures). The frequency of control visits was the main reason for discontinuation of follow-up.

**Outcome**

The mean closure time of the laser perforation was 2.38 (range 0.86–5.57) weeks and was calculated from 84 of the 90 patients mentioned previously who appeared weekly until closure of the laser perforation. The diameter of the laser perforation in these patients of 2.4 (n = 34) and 2.6 mm (n = 50) did not lead to a significant difference in closure time. In 94 patients, the tube was extruded after a mean time of 3.88 (range 0.4–6.2, median 3.9) months.

An effusion-free middle ear at the laser side was observed in 46.6% of patients after 1 month and in 35.5%, 37.1%, 38.6%, 41.6% and 39.1% after 2, 3, 4, 5, and 6 months, and for the tube side, this was noticed in 87.4%, 81.9%, 81.5%, 75.5%, 68.5% and 70.7% of patients, respectively. Adenoectomy performed as combined procedure and older age both had a positive significant influence on the success rate ($P = .006, P = .01$). A significant negative influence was found in patients with one or more siblings ($P = 0.03$), parental smoking ($P = .01$), school admittance ($P < .001$), and a parents’ history of otitis media ($P = .006$). No significant effect was found for history of tubes, time of HL, sex, ethnic origin, history of adenoectomy or adenotonsillectomy, season, breast feeding, cleft palate, syndrome, and tonsillectomy performed as combined procedure. During follow-up, otorrhoea occurred more frequently at the tube side than at the laser side ($P = .002$). Of the 140 patients that appeared at the last control visit at 6 months, four ears showed a functional laser perforation, and in 65 ears the ventilation tube was still in place.

**Predictive Outcome Assessment**

After modeling with backward elimination, 10 of 17 recorded baseline variables (age, sex, current school, adenoidectomy, parents’ history of otitis media, nicotine exposure, siblings, season at time of inclusion, syndrome, duration of HL) with a $P$ value smaller than 0.35 were accepted and used as covariables to adjust the estimate of the predictive percentage of failure and success for the laser myringotomy and the ventilation tube for 6 successive months (Fig. 2). This model more properly takes account of subjects missing at random, and it shows slight differences in outcome compared with the raw observed percentages. It shows that the predicted lower success rate for laser myringotomy of 40% is fairly constant during 6 months, whereas the success rate for the tube decreases with time ($P = .0042$).

Table II shows the covariables and their effects in the logistic model to predict the outcome for laser myringotomy and tubes for the individual patient at 3 and 6 months, respectively. According to the logistic formula $Pr (failure) = exp(z)/1 + exp(z)$, with $z = \alpha + (\beta_1 x_1) + (\beta_2 x_2) + (\beta_3 x_3) + \ldots + (\beta_n x_n)$, $Pr (success) = 1 – Pr (failure)$, the predictive outcome can be calculated.

For example, the predictive success for laser myringotomy after 3 months follow-up for a 4 year-old male patient with HL for 4 months who goes to school and is seen in summer and has no siblings is $z = 0.5909 + (1* - 0.1864) + (4* - 0.1392) + (4* - 0.0094) + (1*0.9707) + (1*0.2544) = 1.0352; P failure = .73; P success = .27.

**Complications during Follow-Up**

One patient suffered from severe otalgia during the first 2 days after laser myringotomy, without signs of inflammation, and was treated with oral analgesics. All but four laser perforations closed spontaneously within 6 months. In one laser-treated ear, an epidermal pearl of the
therapy (syndrome 0 decrease from 87.4% after 1 month to 70.7% at 6 months success rate of the ventilation tube showed a significant constant over the rest of the follow-up period, whereas the first month after the procedure and remained fairly approximately 40% (range 46.6–35.5%) was reached in 81 children.

The laser myringotomy success rate in this trial of 46% to 83%, reported by other authors, could be ascribed to season of onset and siblings. A possible explanation for the difference in season might be that the seven hospitals did not start the study simultaneously, leading to more inclusions in fall and winter, and this may have had some influence on the outcome. The higher participation rate of smaller families may have contributed to a higher rate of success for both therapies. We conclude that our study population is a good reflection of children with OME receiving ventilation tubes. We compared risk factors for OME between the participating and eligible nonparticipating patients and checked for demographic differences between them to increase the generalizability of the study to the reference population. We showed that there were no significant differences except for season of onset and siblings. A possible explanation for the difference in season might be that the seven hospitals did not start the study simultaneously, leading to more inclusions in fall and winter, and this may have had some influence on the outcome. The higher participation rate of smaller families may have contributed to a higher rate of success for both therapies. We conclude that our study population is a good reflection of children with OME receiving ventilation tubes.

The mean closure time of the laser perforation of 2.4 weeks is in accordance with the findings of others. Cohen et al.6 reported a closure time of 2 to 3 weeks after 21 myringotomies in children aged 1 to 5 years, and Sedlmaier et al.18 found an mean closure time of 16.3 days in 81 children. The laser myringotomy success rate in this trial of approximately 40% (range 46.6–35.5%) was reached in the first month after the procedure and remained fairly constant over the rest of the follow-up period, whereas the success rate of the ventilation tube showed a significant decrease from 87.4% after 1 month to 70.7% at 6 months (range 87.4–68.5%). The effect of the laser myringotomy can therefore be determined 1 month after the procedure.

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children with chronic OME between these two surgical methods.

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BIBLIOGRAPHY