Early Placement of Ventilation Tubes in Infants with Cleft Lip and Palate: A Systematic Review

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Abstract

Objective. Studies have shown that the majority of cleft lip and palate (CLP) children have middle ear fluid present at the time of lip repair (3-4 months). Despite hearing loss, the majority of children do not undergo ventilation tube treatment if required until the time of palate repair (9-12 months). We aimed to examine the effectiveness and potential complications of early ventilation tube placement prior to palatoplasty in infants with cleft lip and palate.

Data Sources. Medline (1946-2015), Embase (1980-2015), and EBM Reviews (Cochrane Central Register of Controlled).

Review Methods. Data sources were searched for publications that described the results of early ventilation tube placement in children with CLP prior to cleft palate repair. Two independent reviewers appraised the selected studies.

Results. Of 226 studies identified, 6 studies met the inclusion criteria. Early ventilation tube insertion in CLP gave similar speech and audiology outcomes to non-CLP children undergoing ventilation tube insertion and better outcomes than those children with CLP having later ventilation tube insertion at or after the time of palate closure. The main reported side effect was otorrhea, being higher for children with CLP having early ventilation tube insertion (67% vs 33%), with a reduction in otorrhea with increasing age. Larger studies with longer-term outcome reporting are required to fully address the study objectives.

Conclusion. Published data are limited but appear to support early insertion of ventilation tubes in children with CLP to restore middle ear function and maximize audiologic and speech outcomes.

Keywords
cleft lip and palate, ventilation tubes, OME
the key determinants of the timing of palatoplasty. Speech and language development begins before 1 year of age, and palatoplasty is aimed at ensuring a functioning mechanism in place for speech production. Early palatoplasty, performed by 1 year and ideally between 9 and 12 months, facilitates normal speech development and helps reduce the establishment of compensatory articulation errors.

Studies have shown that over 90% of children with cleft lip and palate (CLP) have middle ear fluid present at the time of lip repair (3-4 months). Despite this, it is our experience that the majority of children, as per clinical practice guidelines, do not typically undergo VT insertion until the time of palate repair, if required (9-12 months).

The objective of this systematic review is to identify, appraise, and summarize the available evidence for the effectiveness and outcomes of early VT placement prior to palatoplasty in infants with CLP.

Methods
The study was exempted from ethical approval from the University of British Columbia/Children’s and Women’s Health Center Research Ethics Board as it did not involve patients or review of patients’ records. The systematic review protocol, including search strategy and inclusion/exclusion criteria for studies, was developed a priori.

Literature Search Strategy
A systematic search of relevant, published, and peer-reviewed literature was performed using the following sources:

1. Embase (1980-2016)
2. EBM Reviews—Cochrane Central Register of Controlled Trials (January 2016)
3. Medline In-Process & Other Non-Indexed Citations, Ovid Medline Daily, Ovid Medline, and Ovid OldMedline (1946 to January 2016)

To maximize search results, no limits were applied to the initial search. The MeSH headings used and combined for the literature search were as follows:

[Cleft palate (42569) OR cleft lip (32208)] AND [Child* (4302349)] AND [Tympanostom* (3976) OR Grommet (762) OR Ventilation tube (2255) OR Myringotomy (2772) OR Middle ear ventilation (3526)]

Selection Criteria
The search strategy results were reviewed for randomized controlled trials, clinical controlled trials, and cohort and case-control studies. Initial eligibility of studies was based on the title and abstract content and was assessed independently and in duplicate by 2 authors (M.F. and J.W.L.). Any disagreement between the two reviewers was adjudicated by a third author (D.D.B.). Only studies of infants with CLP with early VT placement (at 3-6 months of age) prior to cleft palate repair were included. Studies of children with cleft lip only were excluded. No language restrictions were applied. Reference lists of all studies selected for full paper review were searched for any additional studies not retrieved by the primary literature search.

Data Extraction
For each full-text study reviewed, we recorded patient demographic data, number of participants, exclusion criteria, outcome measures, length of follow-up, and overall study outcome and conclusions.

The primary and secondary outcome measures assessed were as follows:

Primary
1. Prevalence of OME preoperatively
2. Complications of ventilation tubes, including otorrhea, tympanic membrane perforation/retraction, and granulation

Secondary
1. Ventilation tube function/patency
2. Hearing loss (conductive) and speech development

Assessment of Study Quality
The quality of the studies included for full-text review was graded according to the Oxford Centre for Evidence-Based Medicine levels of evidence. We also scored each study for potential bias from 0 (low risk of bias) to 5 (high risk bias) according to the following system:

1. Sample selection: consecutive or not; 1 = no or not stated, 0 = consecutive
2. Diagnostic criteria stated: 1 = not stated, 0 = stated
3. Outcomes measured consistently for all patients: 1 = not consistent, 0 = consistent
4. Outcomes reported consistently for all patients: 1 = not consistent, 0 = consistent
5. Follow-up period: 1 = < 1 year follow-up, 0 = ≥ 1 year

This scoring system was used in previous systematic reviews and based upon the Cochrane Handbook for Systematic Reviews of Interventions. The specific biases that are being appraised with each individual scoring point are as follows: selection bias (1 and 2), classification bias (2 and 3), reporting bias (3, 4, and 5), and recall bias (5).

Results
Of the 226 abstracts that were reviewed, 218 did not meet the inclusion criteria. Eight studies were obtained in full text for review. Studies were excluded if their intervention group did not include children having early intervention with VTs. Two of the studies were excluded after analysis of the full text as they did not include subjects with early VT insertion. The flow of
information through the review and study collection is summarized in Figure 1, and the characteristics of the 6 included studies are summarized in Table 1.

**Discussion**

**Rationale**

The studies included in this review were heterogeneous in terms of study design, control groups, outcome measures, and follow-up, and thus a full meta-analysis of the study results was not possible. The level of evidence for the 6 included studies ranged from 1b to 3b, and the risk of bias in the studies was low (see Table 1).

OME appears to be nearly universally present in children with cleft palate prior to the age of 4 months. Klockars and Rautio reported 94% of infants with cleft palate having OME at 4 months; in Dhillon’s study, 97% had OME at 3 months; and Voltonen et al found 94% having OME at 6 months. Overall, the 3 studies had 148 children (296 ears), with 94% of ears having OME before 6 months. In children with OME having at least a mild conductive hearing loss, VTs are anticipated to normalize hearing. This gives us a rationale for considering early VT insertion in children with cleft palate; however, it is important to consider the potential outcomes from surgery, including the complications and benefits.

**Complications of VT Placement**

Table 2 summarizes the outcomes from the included studies: OME status, ventilation tube complications, and ventilation tube patency/function.

Five of the 6 studies reviewed reported on complications. The rate of otorrhea ranged from 20% to 67%. Most episodes of otorrhea were treated conservatively with ear drops. In the study by Curtin et al, rates of otorrhea were higher in the 6 months prior to CP repair at 67% than in the 6 months after palate repair at 33% (1 episode, 24% vs 27%; ≥2 episodes, 43% vs 6%). By way of comparison, in 2001, Ah-Tye et al studied the extent of otorrhea in otherwise healthy children having VTs placed for persistent middle ear effusion and found that nearly 75% had otorrhea within the first year after surgery. Of 230 VTs, they found that the timing of extrusion of the tubes ranged from 19 days to 38.5 months (mean, 13.8 months). The proportion of children who had VTs in place and who developed 1 or more episodes of otorrhea increased progressively, reaching 74.8% after 12 months and 83.0% after 18 months.

Residual tympanic membrane perforation rates after VT extrusion ranged from 2% to 10% for children with cleft palate. Combining the cases in Voltonen et al, Klockars and Rautio, and Hubbard et al gives an overall perforation rate of 6% in those children with cleft palate having early VT insertion, 16 of 255 ears. In the case-control study by Voltonen et al, the rate of residual perforation for children without cleft palate was 3% vs 6% for children with cleft palate. A previous meta-analysis of VT sequelae showed an overall residual perforation rate of 2.2% for short-term tubes and 16.6% for long-term VT.

Other reported complications included granulation tissue on the tympanic membrane 3% and retraction or atelectasis of the tympanic membrane (8%-15%). Interestingly,
<table>
<thead>
<tr>
<th>Author (Year, Country)</th>
<th>Journal</th>
<th>Study Design</th>
<th>Level of Evidence</th>
<th>Sample Size (n)</th>
<th>Age</th>
<th>Intervention and Comparisons</th>
<th>Follow-up</th>
<th>Bias Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brgoch et al,2015, United States</td>
<td>Eplasty</td>
<td>Retrospective cohort</td>
<td>2b</td>
<td>94</td>
<td>Not reported</td>
<td>VTP prepalate repair vs at palate repair vs postpalate repair VTP at CL repair vs TTP at CL repair</td>
<td>Not reported</td>
<td>1/5</td>
</tr>
<tr>
<td>Klockars and Rautio, 2012, Finland</td>
<td>International Journal of Pediatric Otorhinolaryngology</td>
<td>Prospective randomized case-control</td>
<td>1b</td>
<td>93 (44 case, 49 control)</td>
<td>3-4 months</td>
<td>VTP at CL + soft palate repair (case) vs TTP at CL only repair (control)</td>
<td>8 months</td>
<td>2/5</td>
</tr>
<tr>
<td>Curtin et al, 2009, United States</td>
<td>Archives of Otolaryngology–Head and Neck Surgery</td>
<td>Prospective cohort</td>
<td>2b</td>
<td>33</td>
<td>4.2 months</td>
<td>VTP at CL repair or stand-alone procedure (4.2 months), observation after CP repair</td>
<td>12 months</td>
<td>1/5</td>
</tr>
<tr>
<td>Valtonen et al, 2005, Finland</td>
<td>Laryngoscope</td>
<td>Prospective case-control</td>
<td>3b</td>
<td>72 (39 case, 33 control)</td>
<td>6 months</td>
<td>VTP at 6 months prior to CP repair vs non-CLP children with OME/TTP</td>
<td>6 years</td>
<td>0/5</td>
</tr>
<tr>
<td>Dhillon, 1988, England</td>
<td>Journal of the Royal Society of Medicine</td>
<td>Prospective cohort</td>
<td>2b</td>
<td>50</td>
<td>3 months</td>
<td>Bilateral myringotomy and random unilateral VTP at CL repair or stand-alone procedure (3 months)</td>
<td>2 years</td>
<td>0/5</td>
</tr>
<tr>
<td>Hubbard et al, 1985, United States</td>
<td>New England Journal of Medicine</td>
<td>Prospective case-control</td>
<td>3b</td>
<td>48 (24 case/ 24 control)</td>
<td>3 months</td>
<td>VTP at 3 months vs observation ± later myringotomy (mean, 30 months)</td>
<td>8 years</td>
<td>1/5</td>
</tr>
</tbody>
</table>

Abbreviations: CL, cleft lip; CR, cleft palate; OME, otitis media with effusion; TTP, tympanostomy tube placement; VTP, ventilation tube placement.

a As per Oxford Centre for Evidence-Based Medicine.
in the case-control study by Voltonen et al,\textsuperscript{15} the rate of retraction or atelectasis was 18% for children without cleft palate vs 8% for children with cleft palate.\textsuperscript{17} This likely reflects the higher repeat VT insertion rate in the cleft palate group and more aggressive management of their middle ear effusions.

\textbf{VT Outcomes}

VT patency rates and repeat VT insertion rates were discussed in 5 of the studies reviewed. VT patency was 56\% at 8 months in Klockars and Rautio\textsuperscript{11} with short-term VTs and 80\% at 2 years in Dhillon\textsuperscript{10} with long-term VTs. Curtin et al\textsuperscript{16} showed an improvement in patency after palate repair and an assumed improvement in eustachian tube function (63\% pre-palatoplasty vs 79\% postpalatoplasty). Due to persistent eustachian tube dysfunction, repeat VT insertion rate would be anticipated to be higher for children with cleft palate than children without cleft palate. Over a 6-year follow-up period, Voltonen et al\textsuperscript{15} showed a higher repeat VT insertion rate of 69\% for children with cleft palate treated with early VTs compared to 39\% for non–cleft palate controls. Brgoch et al\textsuperscript{20} showed that children with cleft palate having early VT insertion had a mean of 1.4 tubes vs 0.7 tubes for those waiting to have VTs until the time of palate repair.\textsuperscript{20} The rate of early middle ear effusions was not documented in this study, only the rate of effusions at the time of palate repair (91\%).

\textbf{Functional Outcomes (Hearing, Speech)}

Hearing loss and speech development were discussed in 3 of the studies and showed support for early VT insertion. In Curtin et al,\textsuperscript{16} the patients had their VTs inserted at age 4.2 months on average, with palate surgery at 10.5 months on average.\textsuperscript{16} Audiograms showed normal hearing thresholds prior to palate repair with those children benefiting from normal hearing for over 6 months prior to palate surgery. In the case-control study by Voltonen et al,\textsuperscript{15} the children with cleft palate treated with early VTs had hearing thresholds comparable to non–cleft palate age-matched children having VTs for OME at a long-term follow-up of 6 years.\textsuperscript{15}

Hubbard et al\textsuperscript{18} had an 8-year follow-up of 24 children with cleft palate with early VTs (3 months) compared to 24 children with cleft palate with myringotomy later at an average of 30.8 months. They found those children with early VTs had overall better hearing at follow-up, as measured by pure-tone threshold average, than the later intervention group, although this did not reach significance, with both groups overall having normal hearing thresholds. Consonant articulation, measured by the Templin-Darley Tests of Articulation, was significantly better in those having early myringotomy and VTs than those children with cleft palate having later intervention. It was presumed that those having later intervention had continuous OME throughout most or all of their first years of life.

\begin{table}[h]
\centering
\caption{Summary of Study Outcomes.}
\begin{tabular}{|l|l|l|l|}
\hline
Author, Year & OME Status (Preoperative or Follow-up) & VT Complications & VT Patency/Function \\
\hline
Brgoch et al,\textsuperscript{20} 2015 & — & — & Mean of 1.4 VTs if early VTs vs 0.7 if first set at palatoplasty \\
Klockars and Rautio,\textsuperscript{11} 2012 & 87/93 children (94\%) with OME at 4 months old; at 8 months postoperatively, 56\% without tubes had OME & 2\% perforation and 3\% granulation on TM at 8-month follow-up & 56\% VTs patent at 8 months \\
Curtin et al,\textsuperscript{16} 2009 & — & Otorrhea 67\% at 6 months prior to CP repair vs 33\% postrepair 6 months after (1 episode, 24\% vs 27\%; \geq 2 episodes, 43\% vs 6\%) & 63\% patent pre-CP repair vs 79\% 6 months post-CP repair \\
Voltonen et al,\textsuperscript{15} 2005 & 6-year follow-up: study group 64\% healed, 1\% OME, 15\% tubes; control (non-CP) 61\% healed, 12\% OME, 6\% tubes & Study vs control: Retraction TM, 8\% vs 18\% Perforation, 10\% vs 3\% & Repeat VTs, 69\% study vs 39\% control \\
Dhillon,\textsuperscript{10} 1988 & 97\% has OME at 3 months, 80\% still had OME at 2 years if no tube despite palate repair & 20\% (10) otorrhea, 6\% (3) removal & 80\% VTs patent at 2-year follow-up \\
Hubbard et al,\textsuperscript{18} 1985 & 8-year follow-up 4\% OME in study and control & Study vs control: Perforation, 13\% vs 6\% Retraction/atelectasis, 15\% vs 8\% & — \\
\hline
\end{tabular}
\end{table}

Abbreviations: CP, cleft palate; OME, otitis media with effusion; TM, tympanic membrane; VTP, ventilation tube placement; —, not included in study.
Limitations
Although randomized controlled trials are the ideal or accepted standard, only 1 was found in this systematic review, which led to the consideration of observational (cohort studies and case-control studies).
Although no significant publication bias was observed, it is possible that negative or null findings from studies were not published, potentially contributing to publication bias and the small number of studies in this review.

Conclusions
Early VT insertion in CLP enables normal hearing at an early age, with up to 97% having OME at the time of early insertion. The main side effect of early VT insertion was otorrhea, with the majority being either self-resolving or managed with antibiotic drops.
Children with CLP having early VTs appear to have the potential for similar hearing and speech outcomes as children without CLP. We cannot conclude whether early VTs have a benefit over VTs at the time of palate repair from the studies reviewed as no study directly compared long-term outcomes in early VTs vs VTs at time of palate repair. This systematic review gives support to the safety of early VT insertion and facilitates the justification and design of a prospective randomized controlled trial of early VT insertion at the time of lip repair vs later VT insertion at the time of palate repair.

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Julie Pauwels, pediatric otolaryngology research coordinator, BC Children’s Hospital, Vancouver, Canada, coordinated the research team.

Author Contributions
Mark Felton, design, acquisition, analysis and interpretation of work, drafting, revising and final submission; Jong Wook Lee, acquisition and analysis of work, drafting and final approval for submission; Darius D. Balumuka, acquisition and analysis of work, drafting and final approval for submission; Jugpal S. Arneja, conception and design of work, revising and final approval for submission; Neil K. Chadha, conception and design of work, revising and final approval for submission.

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