A randomized study of four different types of tympanostomy ventilation

tubes – Full-term follow-up

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A B S T R A C T

Objective: To evaluate the impact of tympanostomy ventilation tube material (silicone vs fluoroplastic) and shape (short vs long) regarding time to extrusion, occurrence of otorrhea, occlusion, tube removal and occurrence of persistent perforation.

Methods and material: Four different types of ventilation tubes were used; Long Armstrong tubes, Donaldson tubes, Shepard tubes and straight tubes, representing four specific combinations of VT material (silicone or fluoroplastic) and shape (short, double flanged or long, single flanged). Four hundred children scheduled for bilateral tube insertion were included in a randomized trial. The patients received one type of tube in the right ear and another type in the left ear. The incidence of tube extrusion and complications were monitored postoperatively every third month by an otolaryngologist.

Results: Twenty-two children were excluded during surgery. Out of the studied 378 children the mean age was 35.3 months. 63.8% were boys. Short tubes extruded earlier than long tubes; hazard ratio (HR) 4.84 (95% CI 3.50–6.69, p < 0.001). Long Armstrong tubes were least prone to extrude. Silicone tubes resulted in significantly longer time to first infection in a VT ear, HR 1.68 (95% CI 1.03–2.76, p=0.039). Donaldson tubes rendered the longest mean time to first infection (p=0.025). Infections did not affect tube extrusion rates significantly (p=0.879). No significant differences were found regarding tube occlusion, tube extraction or persistent perforation.

Conclusions: Long tubes are less prone to extrude early. Long Armstrong tubes have the least propensity to extrude early. Silicone tubes render significantly longer time to first infection. Donaldson tubes result in least infections. Infection does not affect extrusion rates significantly.

Level of evidence: 1b

1. Introduction

It has been estimated that more than seventy percent of all children

experience at least one episode of acute otitis media [1]. Transmyringeal

ventilation tube (VT) insertion is a treatment option for recurrent

acute otitis media (rAOM) as well as for secretory otitis media (SOM)

causing hearing impairment.

Insertion of VTs is one of the most common surgical procedures

during childhood. It was reported that by the age of three, 6.8% of

North American children had VTs inserted [2]. VT insertion may

prevent rAOM and restore hearing impaired by SOM [3,4]. In 77% of

children receiving VTs, the quality of life was improved [5].

Time to tube extrusion vary and VT treatment can result in complications:

otorrhea; tube blockage; tympanosclerosis; and persistent

tympanic membrane perforation [6]. Even though VTs are by far the

most common implant in pediatric patients, the knowledge about the

clinical outcomes of different types of VTs is sparse. There is a plethora

of commercially available VTs, differing in design and material, but

very few have been tested in randomized controlled trials (RCTs). A

systematic review of the literature concluded that there is a lack of evidence of whether the VT design or material have any impact on possible tube-associated complications [7].

The present study compared four different types of VTs. The hypotheses were that the two basic features of the VT, i.e. shape and material, cause different time to tube extrusion and different complication rates.

2. Material and methods

Children between one and ten years of age planned for bilateral VT insertion for rAOM or SOM were eligible for inclusion in the study. Exclusion criteria were previous VT treatment, on-going acute otitis media, Downs's syndrome and craniofacial malformations such as cleft palate. Informed consent was obtained from the caregivers.

Four hundred children were randomized by the use of non-transparent consecutively numbered envelopes to receive different types of VTs in each ear. Four different types of tubes were used representing four different combinations of the basic tube features; shape (short or long tubes) and material (fluoroplastic or silicone). Details are shown in Table 1. Statistical software was used to arrange the pre-randomization preparation, so that in each child only one parameter, i.e., shape or material, differed between the ears.

The VT insertions were performed under general anesthesia in an academic tertiary referral ENT department. All surgeons at the unit, including young residents (with supervision when needed) contributed to the study and performed the VT insertion. The VTs were inserted in the anterior portion of the tympanic membrane. At the end of surgery, three drops of oxytetracycline, hydrocortisone and polymyxin B (Terracortril with polymyxin B®, Pfizer) were installed in the inner part of the external ear canal. If the surgeon failed to insert the intended type of VT the patient was excluded from the study. The children were

examined postoperatively by an otolaryngologist every third month, and at extra visits in between if the caregiver requested that, until six months had passed since the extrusion of the last remaining VT. Maximum follow-up time was set at 45 months. The otolaryngologist filled out a form at all postoperative examinations regarding presence of VT for each ear, purulent otorrhea, observed VT occlusion, VT extraction and persistent perforation.

Prior to study start, the Regional Ethical Review Board in Stockholm approved this study (ref. 2008/69–31/3). The study was registered at ClinicalTrials.gov (NCT00809601).

2.1. Outcomes

Time to VT extrusion was measured as the time from surgery to the first observation of the whole VT inner flange appearing lateral to the tympanic membrane. Time to a first event of a complication and the total number of complications were also measured.

2.2. Power analysis

The statistical power analysis indicated a need of a study population of four hundred children to test the primary hypothesis (time to VT extrusion) with 80% power at a 5% significance level.

2.3. Statistical analyses

For descriptive statistics, categorical data are presented as frequencies and percentages, n (%), while discrete and continuous data are given as means and standard deviations (SDs). Differences between two independent groups were tested using Pearson's χ^2-test for categorical data and the Mann-Whitney U test for discrete and continuous data. To take the dependence between right and left ear on the same individual into account, time to VT extrusion, treated as interval-censored data, was analyzed using shared gamma frailty Cox regression models clustered

on individuals. The models applied a penalized likelihood on the hazard function using splines with 8 knots and smoothing parameter κ=10000. These regression models used either tube type, tube shape, tube material, or both tube shape and tube material as independent variables. The results are presented as hazard ratios (HRs) with accompanying 95% confidence intervals (CIs). Time to VT extrusion was illustrated graphically using Kaplan-Meier curves. Persistent perforation, defined as having a perforation lasting at least 90 days, was analyzed using Generalized Estimating Equations (GEE) logistic regression models with an independent working correlation matrix structure and within-subject effect for ears. These regression models used either tube type or both tube shape and tube material as independent variables. The statistical analyses were performed using IBM SPSS Statistics 24 and the R package 'frailtypack'. For all statistical analyses, a two-sided p-value<0.05 was considered statistically significant.

3. Results

Out of the 400 children included in the study, twenty-two (5.5%) were withdrawn during surgery due to protocol violation or due to an acute otitis media finding at myringotomy. Thus, 378 children continued the study, 64.3% boys and 35.7% girls. The reason for VT insertion was rAOM in 44.7% of the children, SOM in 41.0% and a combination of rAOM and SOM in 14.3%. Mean age at surgery was 35.3 (SD 19.5) months for all children. The mean age at insertion for each type of VT is presented in Table 2 as well as the number of inserted VTs, diagnosis and gender distribution for each tube type.

3.1. Time to extrusion

The short tubes extruded significantly earlier than the long tubes; hazard ratio (HR) 4.84 (95% CI 3.50–6.69, p < 0.001). When adjusted for tube material, the HR was 4.80 (95% CI 3.46–6.64, p < 0.001).

Fluoroplastic tubes extruded significantly earlier than silicone tubes; HR 1.33 (95% CI 1.04–1.72, p=0.025) according to the univariable analysis. When adjusted for tube shape no significance was found; HR 1.30 (95% CI 0.99–1.69, p=0.056).

When comparing the individual tube types, the Armstrong tube was least prone to extrude. Median time to extrusion is presented in Table 3 and Fig. 1 (Kaplan-Meier curve). The differences between all different tube types were significant except between Shepard and Donaldson tubes. Infection did not cause significantly higher extrusion rate (p=0.879).

3.2. Infections

In total, 13.8% of all ears had an infection at least once. 3.1% had more than two periods of infections (total range 0–6). The percentage of tubes that had a least one infection is presented in Table 4.

Since a tube infection could only occur while the tube was in situ, adjustments were made for the differences found regarding time to extrusion. Neither tube shape, nor tube material caused statistically significant differences regarding total occurrence of infections.

3.3. Time to first infection

Silicone tubes had significantly longer time to first infection, HR 1.68 (95% CI 1.03–2.76, p=0.039). The HR did not change when adjusted for tube shape. No significant differences were found when comparing long tubes with short tubes, HR 0.93 (95% CI 0.56–1.55, p=0.78). The HR did not change when adjusted for tube material. The analysis for the individual tube types identified the Donaldson tube to have the longest time to first infection, but this finding was only significant when comparing with the Shepard tube (HR 2.54 (95% CI 1.12–5.77, p=0.025)), Table 5.

3.4. Tube occlusion

In total, 10.5% of all VTs had a least one occurrence of occlusion. The propensity of each VT type is presented in Table 6. No significant differences were found regarding time to first event of tube occlusion with regard to either tube shape, HR 1.46 (CI 95% 0.85–2.50) or tube material, HR 1.38 (CI 95% 0.83–2.31).

3.5. Tube extraction

Twenty-five of the tubes were by the otolaryngologist recommended to be extracted. The reasons were parental request, pain and intractable tube infection or occlusion. There were no significant differences between the VT types. Neither tube shape, HR 0.95 (CI 95% 0.28–3.17) nor tube material HR 0.86 (CI 95% 0.26–2.84) significantly affected these results.

3.6. Persistent perforation

Only ten ears (1.32%) had a perforation recorded to last at least 90 days. Four of the perforations were found after a Shepard tube. Armstrong tubes resulted in three perforations and straight tubes two. One persistent perforation was found after a Donaldson tube. The differences between tube types were not statistically significant.

4. Discussion

The introduction of new pharmacological products is strictly regulated and is normally preceded by rigorous testing through well-designed randomized clinical trials. The regulations regarding medical implants are far less controlled. This has led to a veritable smorgasbord of VTs for the otolaryngologist to choose from, without reasonable scientific evidence to support decision-making. The present study aimed at shedding light on the outcomes of different types of VTs.

4.1. Time to extrusion

Short VTs had a 4.8 times higher risk of extrusion during full-term follow-up as compared with long VTs. This result consolidates the data of the twelve-month follow-up where significantly more of the short VTs had extruded during to first post-operative year compared with the long VTs [8]. Randomized studies of VTs are uncommon and the present study is to date by far the largest. Previously, the Goode T-tube (long VT, silicone, extra-long inner flanges) was found to result in a significantly longer time to extrusion than Shepard, Armstrong and Reuter-Bobbin tubes in a randomized study of 75 patients [9]. In a study of 31 children, titanium grommets stayed significantly longer time than Shepard tubes did [10]. Notably, the titanium tubes had a larger inner flange. Gold-plated tubes were found to extrude earlier than similarly sized Teflon tubes in a randomized study [11]. The Lens tube (short VT with a funnel-shaped outer flange) stayed significantly longer than Donaldson tubes [12]. Apart from these studies, we have found no other randomized ones.

Interestingly, the incidence of infection did not affect the extrusion rate. A major factor behind VT extrusion of double-flanged tubes is believed to be the accumulation of epithelial debris under the outer flange leading to an increased tissue pressure that may compromise the blood flow in the tympanic membrane tissue next to the VT [13]. Since infection sparks inflammation, which includes increased epithelial turnover, we expected to find that infection would cause an increased extrusion rate. This was however not found in the study.

Among the four different VT types tested in the present study, the long silicone VT had the longest time to extrusion. In our opinion however, a long duration is not always preferable. VTs intended for extra length of usage, for example the Goode T-tube, were reported to more often result in persistent perforations [6]. The desirable length of stay of the tube could differ with indication for treatment and individual

patient factors. Therefore, regarding time to extrusion, one cannot claim that one tube type is superior to another, but the results of the present study may support the clinician in better tailoring the treatment for the specific patient. In that decision, other factors must be taken into account, such as complication rates.

4.2. Infections

Infection is the most common complication of VT treatment. In the present study 13.8% of the ears had at least one observed episode of purulent otorrhea. This is in accordance with findings in previous studies, including a meta-analysis that reported otorrhea affecting 17.0% of intubated ears [6,14]. It must be noted, though, that comparisons between studies are of doubtful value since groups may differ regarding preventive measures. Water precautions for example are sometimes advocated and have in a randomized study been shown to slightly decrease the number of otorrhea events [15]. In the present study, no specific instructions were given about avoiding water in the ears when swimming. Water exposition was not controlled for in the present study, but since it was randomized we expect that water exposition was equally distributed between ears with different tube types, therefore not affecting the comparative results.

The short silicone VT had the longest time to first infection. The silicone material may be the main reason, since silicone tubes had significantly longer times to first infection while tube shape did not significantly affect the result. In a randomized study, short fluoroplastic tubes were found to result in less episodes of otorrhea than long silicone tubes, but the study did not have a study arm with short silicone tubes, so it was not possible to draw any conclusion regarding the effect of the material per se, nor of the shape [9].

The material of the VT surface has previously been discussed as a risk factor for tube-related otorrhea. Albumin coating of titanium tubes

reduced VT otorrhea in a prospective study while phosphorylcholine coating did not, when used in fluoroplastic VTs [16,17].

A small inner diameter of the VT was proposed to reduce the risk of swimming induced otorrhea as it would decrease the risk of water entering the ear through the tube, but a randomized study did not confirm this [12]. In the present study, the inner diameter was the same for all types of VTs.

4.3. Tube occlusion

The total occurrence of VT occlusion in the present study was 10.5%, which is in the vicinity of the VT occlusion rate of 6.9% found in a previous meta-analysis [6]. No significant differences between tube types were found in the present study, neither regarding shape, nor material of the VTs. The VT material has in another randomized study been found to affect the occlusion rate; a tube made of stainless steel (Reuter-Bobbin tube) had a greater rate of plugging than Shepard and Armstrong tubes [9]. Phenylephrine coating resulted in less cases of tube occlusions [18]. Gold-plating of VTs did not prevent tube occlusion [11]. A review concluded that there is not any type of VT to which bacterial biofilm will not adhere [19].

4.4. Tube extraction

VT extraction is in the literature mainly discussed in relation to persistent perforations. It has been argued that VT removal increases the chance of spontaneous healing of the tympanic membrane but it has also been reported that VT removal can increase the risk of a persistent perforation [20,21].

In the present study we followed the national guidelines recommending against VT extraction in trouble-free ears [22]. In the few cases where the tube was removed due to chronic infection or other causes, no significant differences were found between the different VT

types. It must be mentioned, though, that no strict protocol was used for the decision-making of VT extraction. The decision was at the discretion of the otolaryngologist and may have been influenced by the knowledge of what type of VT that was present, obviously revealed by the otomicroscopy examination.

4.5. Persistent perforations

A meta-analysis concluded that VTs intended for prolonged usage (e.g. Goode T-tube) carry an increased risk of persistent perforation [6]. Since the Goode T-tube had significantly longer times to extrusion as well as more persistent perforations, one of our secondary hypotheses was that a difference in time to extrusion would correlate to differences in the incidences of persistent perforations [6,9]. No such differences have previously been presented within the group of VTs not intended for prolonged usage, like the four types of VTs tested in the present study.

In the present study, the pre-study statistical power calculation was based on time to tube extrusion and not persistent perforations. Persistent perforations are relatively uncommon and therefore a larger study population may have revealed statistically significant differences. The present study is however to date by far the largest randomized study of VTs. Well-designed register-data studies would probably be needed to elucidate possible differences between different types of VTs regarding incidence of persistent perforations.

5. Conclusions

Long tubes are significantly less prone to extrude early. Long Armstrong tubes have the least propensity to extrude early. Silicone tubes render significantly longer time to first infection. Short silicone tubes (Donaldson) result in the longest time to first infection. Infection in VT ears does not significantly affect the extrusion rate.

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