Postoperative controls of ventilation tubes in children - by general practitioner or otolaryngologist? Study protocol for a multicenter, randomized, controlled trial (The ConVenTu study)

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Abstract

Background Insertion of ventilation tubes (VTs) in the tympanic membrane is one of the most common ambulatory surgeries performed on children. Postoperative care may continue for two or more years and is today mostly done by otolaryngologists. Controls by general practitioners (GPs) may represent a sufficient level of health care regarding clinical outcome, but there exist no evidence-based guidelines concerning the level of expertise for this task. Aim To evaluate whether postoperative care after surgery with VTs performed by GPs represent a sufficient alternative to otolaryngologists.

Methods/design Randomized controlled trial including patients from seven hospitals in all four Regional Health Authorities in Norway. A total of 400 children aged 3-10 years will be randomized to postoperative care by either otolaryngologist or their regular GP after surgery with VTs in the tympanic membrane. Two years after surgery we will compare hearing thresholds, middle ear function, complication rate, health related quality of life as well as the guardians' evaluations of the postoperative care.

Discussion Results from the ConVenTu study are expected to contribute with knowledge necessary to develop evidence-based guidelines regarding the level of expertise for safe postoperative care for children after surgery with VTs.

Background

Otitis media with effusion, defined as middle-ear effusion without acute signs of infection, is the major cause of acquired hearing problems in children (1). Some of the affected children need surgery to reduce ear complaints and to improve hearing, middle ear function and health-related quality of life (HRQoL) (2). During surgery a small incision is made in the tympanic membrane to drain the fluid from the middle ear. Then a tiny ventilation tube (VT) (also called tympanostomy tube or grommet) is placed in the opening to keep the middle ear ventilated and prevent fluid from accumulating again. Surgery with VTs is one of the most common ambulatory surgeries performed on children (3). In Norway, about 6700 children undergo surgery annually (4).

Postoperative care may continue for two or more years to "assure that the tubes are functional, hearing loss has been corrected, and potential complications are properly diagnosed and managed" (5). A meta-analysis concluded, however, that sequelae after VTs are generally transient (otorrhea) or cosmetic (focal atrophy, tympanosclerosis) (6). Nevertheless, VTs that are not spontaneously rejected within two-three years are recommended to be removed surgically to avoid persistent perforations (7, 8).

Despite the large annual number of surgeries with VTs, there exist no evidence-based consensus regarding frequency and the level of expertise sufficient for the postoperative controls (8–10). A Dutch study found that most postoperative controls did not lead to any clinical interventions and therefore questioned the need for regular follow-ups (11). The Swedish Council on Health Technology Assessment completed a systematic literature review focusing on the documentation of VT treatment, but did not reach a conclusion regarding optimal postoperative care of healthy children with inserted VTs (9). The Norwegian Society of Otorhinolaryngology, Head- and Neck Surgery recommends that postoperative care is performed by otolaryngologists (7). Consequently, otolaryngologists are doing most of the postoperative controls in Norway, but occasionally this is done by GPs (12).

In a previous study we have reported no difference in hearing thresholds and middle-ear function two years after VT surgery between children receiving postoperative care by otolaryngologists and by their regular GPs (13). However, the low sample size and lack of randomization did not allow final conclusions on whether postoperative care performed by GPs represent a safe alternative to otolaryngologists regarding clinical outcome. Moreover, we did not examine complication rate, HRQoL of the children or the guardians' evaluations of the postoperative care.

To confirm or reject previous findings with a higher level of scientific evidence, we decided to carry out a larger, randomized controlled trial. The goal of our new study “Control of Ventilation Tubes” (ConVenTu) is to increase knowledge about which professional level in the healthcare system is sufficient for performing safe postoperative care of otherwise healthy children after surgery with VTs. The primary outcome measure is hearing thresholds measured two years after surgery, and we will compare children that receive postoperative care by otolaryngologists and by their GPs. We will also compare middle ear function, complication rate, HRQoL of the children and guardians’ evaluations of the postoperative care. Results from our study can be utilized for deriving evidence-based clinical practice guidelines, and it is our intention to come up with recommendations for sufficient postoperative care after surgery with VT.

Methods

Study design and setting {5d, 8, 9}

The ConVenTu study is a multicenter, randomized controlled trial conducted in clinical settings in seven hospitals located in all four Regional Health Authorities in Norway. The postoperative care is committed by either an otolaryngologist at the hospital where they had VT surgery, or by the patients regular GP. A flowchart of design and timeline in the study is presented in figure 1, and a SPIRIT schedule of enrolment, interventions, and assessments in figure 2.

The Department of Otolaryngology, Head and Neck Surgery at St. Olavs hospital is the main investigator site and coordinator of the study. The study is performed in collaboration with the Norwegian University of Science and Technology (NTNU). The project team leader and main project coordinator have regularly communication and study visits have been performed at all study sites. In addition, meetings with all study sites are held annually or more frequently.

Eligibility criteria {10}

Eligible to participate are children, age 3-10 years, where VTs are placed in one or two ears. Exclusion criteria are cognitive impairment, medical syndromes or other coexisting severe disease, severe neurogenic hearing loss in at least one ear (> 50 dB hearing thresholds in at least one frequency 0.25 - 4.0 KHz), or no comprehension of Norwegian language.

Randomization {11a, 16a, 16c}

After surgery with VTs the study participants are randomized to receive postoperative care by an otolaryngologist or by their regular GP (Figure 1). The allocation ratio is 1:1. Randomization is done by the project coordinator within each study center, using the ‘WebCRF’ software developed at Unit for Applied Clinical Research at The Faculty of Medicine and Health Sciences, NTNU. The design is block randomization with varying size of blocks, stratified on study center.

Procedures for postoperative controls {6b, 11a}

Children randomized to postoperative care by otolaryngologists will get an appointment at 6, 12 and 18 months after surgery, to reflect the existing management of these patients. Postoperative care by GPs will be on the demand of the guardians and latest 18 months after surgery (Figure 1). If needed, as judged by the GP, the children will be referred to an otolaryngologist.

Guardians of children randomized to the GP group will receive written information on when to contact their GP; for instance, if the child has otorrhea, persistent reduced hearing, or otitis media. The GPs have received information about the study and a procedure for postoperative care and how to treat the most common complications. This includes

referral to otolaryngologist if the VTs have not been spontaneously rejected within 18 months. In addition, a procedure for handling of complications is enclosed in the discharge report after surgery, so it is available at point-of-care.

Assessment of clinical and sociodemographic factors {18a}

All participants will be evaluated with audiological tests and questionnaires before and two years after surgery. The audiological tests include audiometry and tympanometry. Results from at least three of the pure tone thresholds in dB at 0.5-1-2-4 kHz form the pure tone average (PTA). Hearing thresholds is measured by pure tone audiometry; play audiometry is used if needed. Two years after surgery all participants will be examined by an otolaryngologist. Complications during the postoperative period will be registered by carefully examining the patient record.

Sociodemographic information is assessed at enrollment. At the end of the follow-up period the guardians evaluate the postoperative care. Both before and two years after surgery the guardians are asked to complete questionnaires regarding their perception of the child's HRQoL (see secondary outcome).

Each study center has a local coordinator responsible for a Case Report Form to ensure complete recording of individual data.

Outcomes {12}

Comparison of PTA in dB between the randomized groups two years after surgery is defined as primary outcome.

The following clinical and sociodemographic factors are considered as secondary outcomes:

1. Middle ear function assessed with tympanometry and otomicroscopy (14)
2. Complication rates
3. Disease specific HRQoL by the otitis media questionnaire for children ('OM8-30') (15)
4. Generic HRQoL by 'PedsQL', based on proxy-report (participants aged 3-8 years) or by adolescent self-report (8-12 years) and 'SDQ-Nor' (16, 17)
5. Guardians evaluation of the postoperative care

The secondary outcome measures no. 1-2 act as surrogate markers for possible reduced hearing in the future. Complications after insertion of VTs include otorrhea, occlusion of tubes, premature extrusion, persistent perforation in the tympanic membrane, retraction pocket and cholesteatoma (5, 6, 18). The secondary outcome measures no. 3-5 is assessing the risks and benefits of postoperative care and important for patient-centered care.

Participant timeline {13}

[Figure 1]

[Figure 2]

Sample size and power {14}

We have defined a clinically relevant difference of PTA as 5 dB, and the study is designed to detect a difference in PTA of 5 dB or more. Accordingly, we have set <5 dB as equivalence margin. To avoid an incorrect conclusion about no difference between the groups (Type II error), the power of the tests for detecting a difference of ≥5 dB must be high (≥90 %, error margin <10 %). To detect an absolute difference in PTA between the groups of 5 dB (with standard deviation of 10 dB in each group), with a significance level of 5% (two-sided test), and a power of 90 (95) %, a total of 85 (105) participants in each group is needed. With an additional 15 % added for dealing with potential skewly distributed

variables, and further 20 % for potential dropouts during the follow-up period, we are left with a sample size of 118 (145) participants in each group. To maintain power in analysis stratified for seven study centers (6 additional parameters in model if included as categorical variable), sample size needs to be increased further. We will therefore include 200 participants in each of the two randomization groups (Figure 1).

Statistical analysis {20a, 20c}

The analyses will be performed according to intention-to-treat. A general linear model and/or a linear mixed model (LMM) will be applied to compare PTA and mean change in PTA after two years. Similar methods will be applied for other relevant variables that are measured on a continuous scale (HRQoL). Log-transformation, or non-parametric methods, may need to be considered. Generalized linear mixed model for categorical data, and/or McNemar's test is relevant for analyzing changes in categorical, dichotomous outcome variables. A Chi-square test is relevant for comparing the two study groups with respect to number of complications during postoperative care. Equality between the two treatment groups will be evaluated in terms of the magnitude of observed differences (point and interval estimate).

Discussion

Insertion of VTs is among the most common surgical procedures in childhood (3). The total amount of postoperative controls generated for these patients and the lack of evidence concerning which level in the health care system to handle the postoperative care necessitates the pragmatic design of this study. Possible disadvantages of postoperative care carried out by GPs could be lack of knowledge and equipment, and failure to handle possible complications. On the other hand, possible benefits could be shorter travelling distance and increased flexibility of time point of controls for the patients and guardians. It is therefore important to evaluate whether postoperative care performed by GPs represent a sufficient alternative to otolaryngologists concerning clinical outcome.

One of the major benefits with this multicenter RCT is that it is designed to be comprehensive enough to detect a clinically relevant differences in hearing thresholds (≥ 5dB), middle ear function and complication rates. Another benefit is that the evaluation also includes the guardians' evaluation of the postoperative care and HRQoL of children through standardized questionnaires. The age range of the participants is from 3–10 years. The reason for not including younger children are the difficulties of getting reliable audiological tests prior to surgery.

The ethical concerns in this study are related to whether children that are randomized to postoperative care by GPs may be at risk of poorer clinical outcome. Therefore, all participants are thoroughly examined two years after surgery. There is no summoning to postoperative controls in general practice, so there is a risk that guardians do not book an appointment when needed despite the information given. However, in our previous study with similar design, a lack of attendance in the GP group was not a problem (13). Moreover, children with severe neurogenic hearing loss or other severe coexisting diseases are excluded from the study. If the GP finds that the child needs to see an otolaryngologist, he or she will refer the child. In Norway, nearly every citizen has an appointed regular GP (19) and therefore the guardians will know which GP to contact. The Ethical Committee that reviewed the study did not have any comments on this procedure.

Trial Status

This trial started inclusion of study participants in August 2017 and the recruitment period is estimated to be three years. A challenge in the study has so far been slow recruitment of participants; we are considering prolonging the data recruitment period to reach our target of 400 participants. The follow up period is two years, and the data collection phase are expected to be completed in fall 2022. All personnel who have contributed significantly with the planning and

performance of the study may be included in the list of authors in according with the Vancouver rules (20). The results of this study will be submitted for publications in peer reviewed journals and communicated to the participants and the Ethics Committee according to EU and national regulations. It is our intention to come up with recommendations for sufficient postoperative care after surgery with VTs.

Abbreviations

VT: Ventilation tube

GP: General Practitioner

HRQoL: Health-related quality of life

Declarations

Acknowledgements

The staff of the Departments of Otolaryngology at the study sites are highly acknowledged for participating in the trial.

Authors' contributions {31b}

BA, AHN, ASH, and WMT conceived and designed the study. GA performed the sample size calculation. BA wrote the first draft of the manuscript. BA, AHN, ASH, GA, SN, and WMT

contributed to the writing and review of the manuscript and approved the

final version. All named authors adhered to the authorship guidelines for *Trials* and have agreed to publication. No professional writers were involved in this manuscript.

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The funding body has no role or ultimate authority in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Availability of data and material {29, 31c}

The datasets generated during and/or analysed during the current study are not publicly available due Norwegian regulations concerning sensitive data but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate {19, 24, 26a, 27}

This study was reviewed and approved by the Regional Committee for Medical and Health Research Ethics (REC) in Mid-Norway (2015/902). The study will be conducted according to the Declaration of Helsinki and ICH-Good Clinical Practice guidelines and follow the CONSORT rules (21, 22). Protocol modifications will be reviewed by REC and Clinical Trials. Processing of personal study data will be done according to procedures approved by the data protection official at each study center.

Guardians must give written informed consent on behalf of themselves and their children in order to participate. In addition, children 8 years and older will by informed of the study.

Consent for publication {32}

Not applicable

Competing interest {28}

The authors declare that they have no competing interests.

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Figures

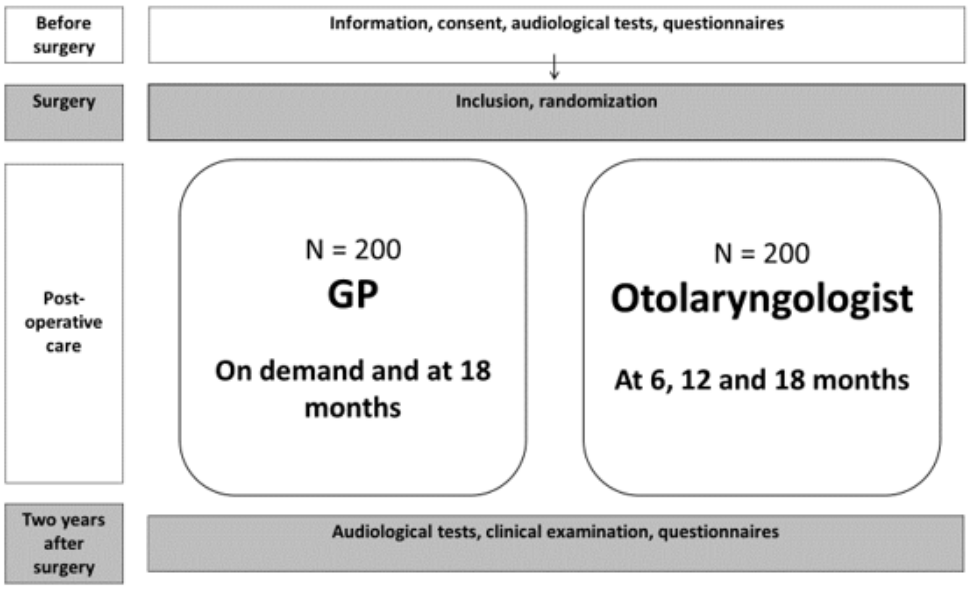

Figure 1

Flowchart

	STUDY PERIOD					
	Enrolment	Allocation	Post-allocation			Close-out
TIMEPOINT	Before surgery	Surgery	6 months	12 months	18 months	24 months
ENROLMENT:						
Eligibility screen	x					
Informed consent	x					
Allocation		x				
INTERVENTION S:						
Postoperative care by GP			←	→	x	
Postoperative care by otolaryngologist			x	x	x	
ASSESSMENTS:						
Baseline variables: ✣ PTA in dB ✣ Tympanometry ✣ Sociodemographic information ✣ HRQoL: 'OM 8-30', 'PedsQL', 'SDQ-Nor'	x					
Outcome variables ✣ PTA in dB ✣ Middle ear function (tympanometry and otoendoscopy) ✣ Complication rates,						x
List other data variables ✣ HRQoL: 'OM 8-30', 'PedsQL', 'SDQ-Nor' ✣ Guardians evaluation of the postoperative care						x

Figure 2

Schedule of enrolment, interventions, and assessments. *PTA=Pure Tone Average, dB=decibel, HRQoL=Health Related Quality of Life, OM8-30, PedsQL, SDQ-Nor: see manuscript

Supplementary Files

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- DemografiogaudiologiBaseline.doc
- PedsQL812aar.BarnerapportPRE.doc
- PedsQL57aar.Foreldrerapport2AARPOST.doc
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