Sonotubometry
Measurement of Eustachian tube function

Stijn J.C. van der Avoort

Print: Graficolor
Lay-out: Diny Helsper

ISBN: 90-9021450-X

Sonotubometry, measurement of Eustachian tube function.
Thesis Radboud University Nijmegen Medical Centre, Nijmegen.

Sonotubometry
Measurement of Eustachian tube function

Een wetenschappelijke proeve
op het gebied van de Medische Wetenschappen

PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Radboud Universiteit Nijmegen,
op gezag van de Rector Magnificus prof.dr. C.W.P.M. Blom,
volgens besluit van het College van Decanen
in het openbaar te verdedigen op dinsdag 27 maart 2007
om 13.30 uur precies

door

S.J.C. van der Avoort

geboren op 4 juli 1978

te Breda

Promotores:	Prof. dr. C.W.R.J. Cremers
	Prof. dr. G.A. Zielhuis
Copromotor:	Dr. N. van Heerbeek
Manuscriptcommissie:	Prof. dr. P. Spauwen
	Prof. dr. S. Bergé
	Prof. dr. L. Feenstra

Publication of this thesis was financially supported by:
Altana Pharma, Artu Biologicals, ATZE Spoorfonds, Alk Abelló, Bayer, Beter Horen, EmiD audiologische apparatuur, GlaxoSmithKline, Hal-Allergy, Schering-Plough, Schoonenberg, F. van Lanschot Bankiers.

CONTENTS

1

Introduction

History

The Eustachian Tube is called after Bartolomeo Eustachi, one of the most important anatomists of the Renaissance. He was born between 1498 and 1507 in San Severino in Italy[1]. He studied medicine and philosophy in Rome. During his life he published one work, the Opuscula Anatomica (1564) which was a collection of earlier published smaller books. One of them is Epistola de auditus organi (1562) which contains the first detailed description of the connection between the middle ear and the nasopharyngeal space. Also the cranial nerves, middle ear cavity and cochlea are discussed in this only 17 pages counting book. In addition Eustachius was the first who described the adrenal glands, thoracic duct, thyroglossal duct en the primary and secondary dentition. Antonio Valsalva (1665-1723) proposed in his Tractatus de aure humani (1704) to call the tuba after Eustachi to honour this great anatomist. Bartolomeo Eustachi died in 1574 in Fossatodi Vico. A sculpture (1874) in his city of birth and a memorial in Sapienza in Rome were raised to honour him.[1]

Anatomy of the Eustachian tube

The Eustachian tube (ET) is the connection between the nasopharyngeal space and the middle ear (figure1).

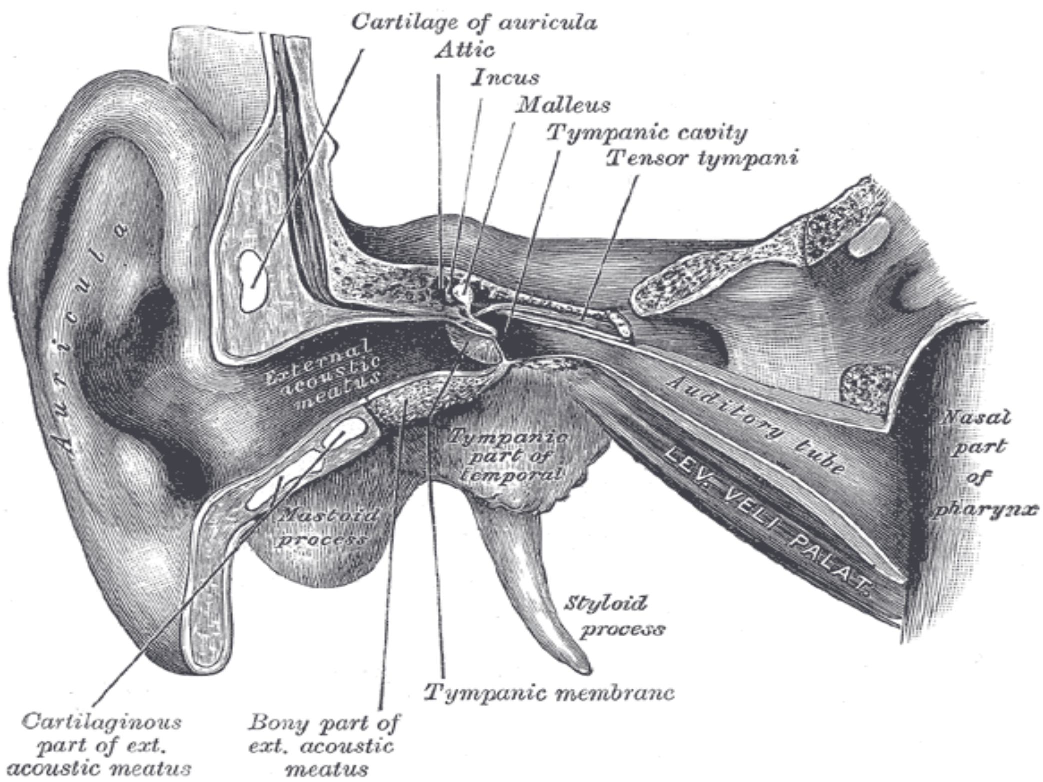

Figure 1. Anatomy of the Eustachian tube

In adults, the length of the tube varies from 31 to 38 mm and lies in an angle of 30 to 40 degrees with the horizontal plane[2,3]. The tube consists of two parts: a fixed osseous posterolateral portion and a mobile fibrocartilaginous anteromedial portion. The osseous part and the fibrocartilaginous part are both shaped like a cone. Their apices meet each other forming the isthmus, which is the narrowest section of the ET with an average diameter of 0.5 to 1.5 mm in adults[4]. At rest, the Eustachian tube is closed because of a collapsing fibrocartilaginous part. The Eustachian tube can be opened by contraction of the paratubal muscles; the tensor veli palatini muscle, the levator veli palatini muscle, the salpingopharyngeus muscle and the tensor tympani muscle. Active opening of the Eustachian tube is accomplished during swallowing, yawning or another movement of the mandible. The tensor veli palatini muscle originates from the superior cartilage and the lateral fibrous wall of the Eustachian tube (ET), bends round the pterygoid process and continues as the palatal aponeurosis. The tensor veli palatini muscle is considered to be the main dilatator of the Eustachian tube (ET). The levator palatini muscle that partially originates from the medial portion of the Eustachian tube (ET) cartilage and inserts into the soft palate is supposed to support the Eustachian tube (ET) opening. The salpingopharyngeus muscle, running from the medial cartilaginous wall to the pharyngeal wall, and the tensor tympany muscle that is continuous with the tensor veli palatini muscle are relatively small and only seem to play a marginal role in the Eustachian tube opening[5,6,7] (figure 2).

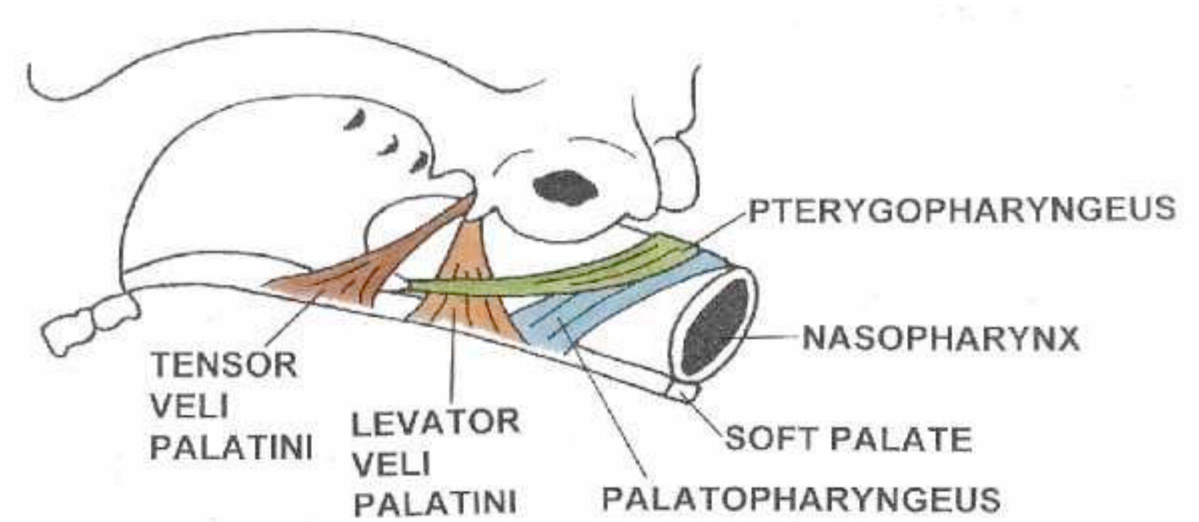

Figure 2. Anatomy of paratubal muscles

The epithelium of the Eustachian tube differs with the localisation within the tube. The posterolateral portion, is lined with epithelium continuous with strands of ciliated epithelium in the middle ear cavity. This epithelium is thin, columnar and ciliated. The epithelium in the lower part of the Eustachian tube is thicker and consists of upper respiratory tract epithelium. This epithelium is continuous with and identically to the the epithelium of the nasopharynx. This epithelium is pseudostratified and is composed of columnar cells with cilia. Contraction of these cilia results in a beating movement. The beating movements of all the cilia together result in a continuous stream of mucus from the middle ear to the nasopharyngeal orofice of the Eustachian tube, carrying with it dead cells from mucosal turnover as well as foreign particles such as bacteria and inflammatory products: the mucociliary transport. The mucus is produced by globet cells and small mucus glands at the orofice of the Eustachian tube[8]. After reaching the nasopharynx, the mucus is swallowed. In the subepithelial layer of the Eustachian tube mucosa there are numerous blood capillaries, lymph capillaries and lymphoid tissue. All these elements play a role in the defending properties of the Eustachian tube wich will be discussed later.

The anatomy of the Eustachian tube during childhood is different from the anatomy of the adult Eustachian tube. To start, the position of the Eustachian tube is more horizontal. The tube lies in an angle of 10 degrees with the horizontal plane whereas this is 30 to 40 degrees in the adult anatomy. Furthermore the tube is shorter and a relatively greater part of the tube has an osseus wall. Besides this, the lumen of the Eustachian tube in children is remarkably smaller than in adults. The Eustachian tube in children also is more rigid because of the larger osseous part and less elastic poperties of the fibrocartilaginous wall[3,9,10].

Functions of the Eustachian tube

The Eustachian tube has three important functions with respect to the middle ear. These three functions are protection, clearance and ventilation.

Protective function

One of the functions of the Eustachian tube is to protect the middle ear cavity. The protective function can be subdivided in mechanical protection and immunological protection. In rest the Eustachian tube is closed and it only opens actively by contraction of the paratubal muscles during acts of swallowing, yawning or movements of the mandible. Due to the closed tube the middle ear is protected against pressure changes that occur in the nasopharynx. It also gives protection against ascending nasopharyngeal secretions and micro-organisms. When during active opening of the Eustachian tube nasopharyngeal secretion enters the lumen

of the Eustachian tube, it will not reach the middle ear because it is not able to pass the narrowest point of the tube, the isthmus. Besides this the continuous stream of mucus, which is produced by the Eustachian tube epithelia, forms a physical barrier to ascending nasopharyngeal secretions.
In addition to the mechanical barrier, the Eustachian tube offers protection to the middle ear against invading pathogens by several local immunological defence mechanisms[11,12]. The presence of viruses or bacteria in the Eustachian tube or middle ear stimulates the production of effector and memory lymphocytes in the mucosa-associated lymphoid tissue of the Eustachian tube[13]. Besides this, the adenoid, near the nasopharyngeal orifice of the Eustachian tube, protects the host against invasion of viruses and pathogens. Also the tubal surfactant has a role in the local defense, because surfactant proteins play a role as opsonins to facilitate phagocytosis and regulates C1q-independent activation of the complement cascade[14].

Clearance function

The ciliated epithelium of the Eustachian tube lumen supplies mucociliary clearance of the middle ear cavity. Together with a thin mucus blanket that covers the epithelium of the Eustachian tube secretions and debris from the middle ear are transported to the nasopharyngeal end of the Eustachian tube by synchronized ciliary movements[15]. Both cilia and mucus are essential for normal functioning of the mucociliary transport and disturbance of either cilia or mucus may immediately affect this[16,17]. A possible second mechanism for clearance is the pumping action of the Eustachian tube, accomplished by alternate contraction and relaxation of the paratubal muscles[18,19]. During acts of swallowing, yawning or movements of the mandible, the paratubal muscles contract and this results in an enlarged lumen of the Eustachian tube. This causes a negative pressure in the lumen of the Eustachian tube, so excess of secretions are sucked into the tube. By relaxation of the paratubal muscles the lumen of the tube narrows and the secretions will be pumped to the nasopharyngeal end of the tube. By repeated contraction and relaxation eventually the secretions will be cleared into the nasopharynx and will be swallowed away.

Ventilatory function

Active opening of the Eustachian tube is accomplished by contraction of the paratubal muscles; the tensor veli palatini muscle, the levator veli palatini muscle, the salpingopharyngeus muscle and the tensor tympani muscle. To facilitate the opening of the Eustachian tube and lower the openings pressure the epithelium of the tube secretes surfactant in the mucus. This surfactant is a mixture of surfactant proteins and surface tension lowering phospholipids[20,21,22,23]. Opening of the Eustachian tube allows ventilation of the middle ear cavity and equillibration of small pressure changes in the middle ear. Besides this there is a continous absorbtion of gas through the middle ear mucosa from the middle ear by surrounding tissues[24,25]. A disturbed absorbtion and a dysfunction of the Eustachian tube, by example in palatoschisis patients, are considered to be causative to a negative middle ear pressure.

Disturbance of Eustachian tube function

A disturbance of the Eustachian tube can affect its protective, clearance and/or ventilatory function. Disturbance of one of the Eustachian tube functions can result from different factors and can lead to different complaints.

Disturbance in protective function

This can occur in cases of a permanently open Eustachian tube, i.e. a patulous Eustachian tube. It can be the consequence of anatomical variation of the Eustachian tube or a extremely short Eustachian tube like for example in very young children, cleft palate children or children with Down’s syndrome. In all these cases nasopharyngeal secretions and pathogens can easily reflux into the middle ear cavity and cause infections. In addition great pressure changes in the nasopharynx are directly transmitted to the middle ear and possibly cause damage to it and one’s own voice and breathing is easily and often unpleasantly heard (autofonia). Another disturbance of the protective function exists when the immunological local defense mechanism of the Eustachian tube is impaired. Viruses and pathogens can enter the middle ear cavity which can again lead to otitis media.

Disturbance in clearance function

Inflammation and impaired motility of the cilia and less mucociliary *clearance* can be the result of viruses or bacteria and their endotoxins[26,27,28] in the Eustachian tube lumen. Mucocilary dysfunction can also be the result of ciliary dyskinesia, cystic fibrosis, allergy or irradiation[16,29,30,31]. Impaired mucociliary clearance can lead to otitis media (with effusion), caused by ascending pathogens from the nasopharyngeal space. The muscular clearance function can be impaired by altered paratubal muscle insertion and inadequate tubal opening for example in children with cleft palate.

Disturbance in ventilatory function

Opening failure of the Eustachian tube also leads to impairment of *ventilatory function*. Failure to open can exist following inefficient paratubal muscle contraction, altered elastic properties of the Eustachian tube or a deficiency of Eustachian tube surfactant. In children, opening failure is very common[3,9,32,33]. The importance of normal anatomy of the Eustachian tube and surrounding structures for efficient tubal opening is once more illustrated by the high incidence of Eustachian tube opening failure in patients with cleft palate[34,35,36]. The opening failure is most likely the result of several anatomical defects of the Eustachian tube and paratubal muscle insertion. Mechanical obstruction of the Eustachian tube can occur due to inflammation of the nasopharyngeal or tubal mucosa secondary to infection or allergic reaction or an enlarged adenoid[37,38]. The tube can also be obstructed by a nasopharyngeal carcinoma or tumors.

Assessment of Eustachian tube function

As pointed out above, there is an important relationship between normal functioning of the Eustachian tube and the health of the middle ear cavity. Measurements of the Eustachian tube function have been subject of many clinical studies because this could be important for clinical practice. In daily outclinic ENT care such a valuable Eustachian tube function test is still not available. Several tests have been and still are used in a research setting to assess protective, clearance and/or ventilatory function of the Eustachian tube. An overview of these methods is given below.

Measurement of protective fuction:

The protection of the middle ear cavity by the Eustachian tube against extreme nasopharyngeal pressure changes can be measured by use of the sniff test [39,40].

During sniffing a negative pressure is generated in the nasopharyngeal space. Passive opening of the Eustachian tube implies poor protective function of the Eustachian tube against this pressure change. Normally the tube should remain closed during the test.

Measurement of clearance function:

In vitro the ciliary beat frequency and beating pattern can be measured using high speed video imaging or by use of the electromicroscope[41,42]. In vivo, contrast can be injected through the tympanic membrane into the middle ear measuring the time needed before the first contrast appears at the nasopharyngeal orifice of the Eustachian tube[41,43].

Measurement of ventilatory function:

Most of the Eustachian tube function tests have been focussing on ventilatory function.

One of the first tests to measure ventilatory Eustachian tube function was described by dr. Josef Grüber in 'Lehrbuch der Ohrenheilkunde' (Vienna 1870). He caused pressure elevation in the nose and measured whether the pressure reached the ear by passing through the Eustachian tube (figure 3).

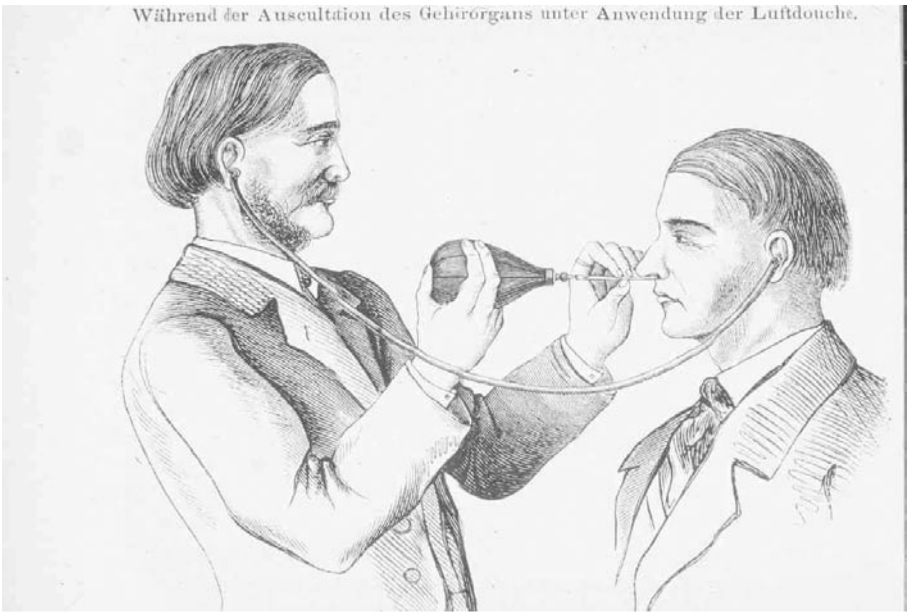

Figure 3. Eustachian tube patency test by Grüber (1870)

Other early manoeuvres to test the ventilatory functioning included Valsalva's manoeuvre and Toynbee's manoeuvre[44,45]. These tests only show whether opening of the Eustachian tube is possible. Later, other more quantitative ventilatory function tests were developed and nowadays several tests are available to measure the ventilatory function of the Eustachian tube. The tests most frequently used are the *forced response test*, *pressure equilibration test*, *nine-step inflation-deflation test* and *sonotubometry*. The first three tests are manometric tests, i.e. tests in which pressure is applied to the middle ear[32,46,47,48,49].

Forced response test and Pressure equillibration test

The *forced response test* measures the pressure at which the Eustachian tube opens passively when the middle ear pressure is increased. The pressure equilibration test measures the ability to equilibrate positive and negative pressures applied to the middle ear and so measures active opening function of the Eustachian tube. In order to apply pressure directly to the middle ear, there must be a perforation or a ventilation tube in the tympanic membrane. The forced response test and the pressure equilibration test therefore cannot be performed on ears with an intact tympanic membrane unless a pressure chamber is used but such equipment is not widely available.

Nine-step inflation-deflation test

In the nine-step inflation-deflation test[49], a tympanometer is used to measure the resting middle ear pressure. A negative pressure (-300 mm H2O) is applied to the external auditory canal to create relative over-pressure in the middle ear. Then the tympanometer measures the ability to normalize this over-pressure.This procedure is repeated with the application of a positive pressure. In a physiologically normal middle ear and Eustachian tube, the pressure normalizes to the resting pressure after swallowing three times.

Sonotubometry

Sonotubometry measures the active ventilatory function of the Eustachian tube using sound (figure 4).

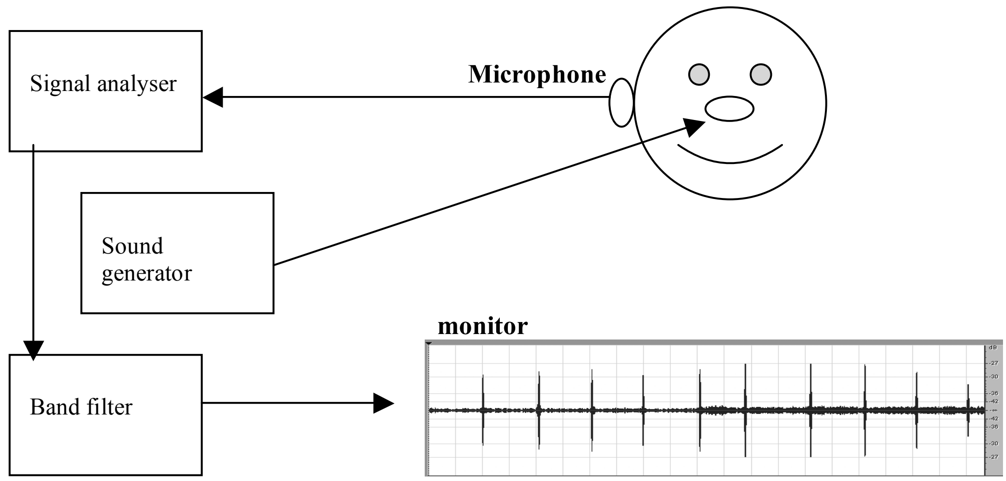

Figure 4. Diagrammatically illustration of equipment

A constant sound source is applied to the nostril, while a microphone in the external auditory canal records the transmitted sound pressure level through the Eustachian tube and middle ear. The subject is asked to swallow and in case of opening of the Eustachian tube, an increase in sound level will be measured in the external auditory canal. Thus, the active ventilatory function of the Eustachian tube can be measured *non-invasively* and the measurements take place *under physiological circumstances*, without the use of extreme pressures and without the need for tympanic membrane perforation. Sonotubometry therefore has advantages compared to other ventilatory function tests. The qualities of sonotubometry have been studied extensively by various investigators in the nineteen seventies, eighties and nineties[50-60] (table 1).

Table 1. Studies on sonotubometry in chronological order

Author	Frequency	dB	Test population	Number of ears	Number of swallowings	% of opening
Naunton & Galluser (1967)	200		Healthy adults	15		53%
Satoh et al. (1970)	2000	Max130	Healthy adults	31		74%
Virtanen (1977)	6000-8000	100-112	Healthy adults	106	6	90%
Holmquist (1981)	6000-8000	100	Healthy adults	187	6	66%
Okubo (1987)	5000-9000	Max125	Healthy females	51	2	89%
Okubo (1987)	5000-9000	Max125	Healthy children	178	2	65%
Palva (1987)	6500-8000	115	Healthy adults	64	5	80%
Jonathan (1989)			Healthy children	50	5	80%
Jonathan (1989)			Glue ear children	126	5	29%
Mondain (1997)	8000	100		240	Variable	63%
Munro et al. (1999)	7000-8000	100	Healthy children	20	6	80%

Despite the fact that the technique of sonotubometry has gradual been improved over the years it is not used routinely to assess Eustachian tube ventilatory function, because its reproducibility, validation and value for clinical practice have not yet been adequately demonstrated

Objectives of this PhD project

Several test methods are available to assess the ventilatory function of the Eustachian tube. Most of these tests have the disadvantage that they can either only be performed on ears with a perforated tympanic membrane or a ventilation tube in situ or they need to be conducted in a pressure room. An even more important disadvantage is that these tests do not measure ventilatory Eustachian tube function under physiological circumstances. Relatively large pressure changes, i.e. non-physiological pressure changes, need to be applied to evaluate the active ventilatory function. Furthermore, these tests can cause an uncomfortable feeling for the test person, wich is a particular disadvantage in children.

In contrast, *sonotubometry* can be performed in patients with or without an intact tympanic membrane and under physiological conditions. Sonotubometry is also inexpensive, painless and easy to perform in both adults and children. Therefore it is thought to have a great potential value as a diagnostic tool for individuals with suspected Eustachian tube pathology.

Since its introduction in the nineteenth century the technique of sonotubometry has undergone valuable improvements. Solutions have been found for some serious problems with the early sound conduction technique, such as susceptibility to background noises, leakage of sound and arbitrarily chosen test frequencies[50-60].

Although this test method has been improved to assess Eustachian tube ventilatory function already, its validity and reproducibility still need additional evaluation which is part of this PhD project. Especially in children there is need for valid assessment of ET ventilatory function in the individual case because they are most affected by recurrent episodes of middle ear effusion or acute otitis media. When validity and reproducibility of this test method can be confirmed, sonotubometry can become of great value in clinical practice and clinical research. One of the applications of sonotubometry may be its value to evaluate the need for surgical insertion of ventilation tubes in case of otitis media with effusion, which by itself eventually is a self-limiting disease. Another application may be the evaluation of Eustachian tube ventilatory function before it is decided to perform myringoplasties. Another application is to use sonotubometry as measuring-instrument in intervention studies with the application of medicaments to evaluate whether an improvement in Eustachian tube ventilatory function may be established.

The *first objective* of this PhD project is to further refine the measurement set-up of a sonotubometer for use in clinical practice and / or research. The *second objective* is to assess validity and reproducibility of this updated sonotubometer in study populations of different age and different middle ear status to conclude whether this Eustachian tube ventilatory function test has the potential to become a standard diagnostic tool in the daily out clinic Ear- Nose-Throat practice.

Outline of this phD project

Chapter 2 describes the principle and development of sonotubometry and provides a review of the studies in the past on sonotubometry. In *chapter 3* the properties of an updated sonotubometer are described. First the outcomes and the reproducibility of the sonotubometric measurements in healthy adults are presented. In chapter 4 the results with this updated sonotubometer in otologically healthy children are given.

In *chapter 5* the outcomes of sonotubometric measurements in children with cleft palate (i.e. children with elevated chance to have a poor Eustachian tube ventilatory function) are presented and compared with outcomes of the test in otologically healthy children to see wether there is a discriminative power with this updated sonotubometry equipment. *Chapter 6* shows the results of sonotubometric measurements in children with otitis media with effusion before and after insertion of ventilation tubes to test the validity and reproducibility of the technique in this group. In *chapter 7* it is questioned whether changes in Eustachian tube function by means of intranasal provocation with histamine can be measured with this sonotubometric equipment. Finally the overall conclusions and answers to the objectives of this thesis will be discussed in *chapter 8*.

References

1. Baarsma EA. Bartolomeo Eustachi. Ned Tijdschr KNO-Heelk 2006;april 12(2):95-99
2. Graves GO, Edwards LF. The Eustachian tube, a review of descriptive, microscopic, topographic and clinical anatomy. Arch Otolaryngol 1944; 39: 359-379
3. Proctor B. Embryology and anatomy of the Eustachian tube. Arch Otolaryngol 1967;68:503-514
4. Poe D, Kujawski O. Endoscopic diagnoses of Eustachian tube dysfunction. Minimally invasive surgery of the ear. Silverstein, Rosenberg, Poe, Eds, 2002
5. Prades JM, Dumollard JM, Calloch F, Merzougui N, Veyret C, Martin C. Descriptive anatomy of the human auditory tube. Surg Radiol Anat 1998;20:335-340
6. Huang MH, Lee ST, Rajendran K. A fresh cadaveric study of the paratubal muscles: implications for eustachian tune function in cleft palates. Plast Reconstr Surg 1997;100:833-842
7. Swarts JD, Rood SR. The morphometry and three-dimensional structure of the adult Eustachian tube: implications for function. Cleft Palate J 1990;27:374-381
8. Sadé J. Ciliary activity and middle ear clearance. Arch otolaryngol 1967;86:128-135

9. Sadler KD, Siegel MI, Todhunter JS. Age-related morphologic difference in the components of the Eustachian tube/middle ear system. Ann otol Rhinol Laryngol 1989;98:854-858
10. Matsune S, Sando I, Takahashi H. Elastin at the hinge portion of the Eustachian tube cartilage in specimens from normal subjects and those with cleft palate. Ann otol rhinol Laryngol 1992;101:163-167
11. Chapel H, Haeney M, Misbah S, Snowden N. Essentials of Clinical Immunology fourth ed. Oxford: Blackwell science; 1999
12. Lim DJ, DeMaria TF. Immunobarriers of the tubotympanum. Acta Otolaryngol 1987;103:355-362
13. Kamimura M, Balaban CD, Sando I, Ganbo T, Suzuki C. Cellular distribution of mucosa-associated lymphoid tissue with otitis media in children. Ann Otol Rhinol Laryngol 2000;109:467-472
14. Haagsman HP, Diemel RV. Surfactant-associated proteins: functions and structural variation. Comp bioch Physiol A Mol Integr Physiol 2001;129:91-108
15. Bluestone CD, Paradise JL, Beery QC. Physiology of the Eustachian tube in the pathogenesis and management of the middle ear effusions. The Laryngoscope 1972; July: 1654-1670
16. Ohashi Y, Nakai Y. Current concepts of mucociliary dysfunctions in otitis media with effusion. Acta Otolaryngol 1991;486(suppl):149-161
17. Houtmeyers E, Gosselink R, Gayan RG, Decramer M. Effects of drugs on the mucus clearance. Eur Respir J 1999;14:452-467
18. Honjo I, Ushiro K, Okazaki N, Kumazawa T. Evaluation of Eustachian tube function by contrast roentgenography. Arch Otolaryngol 1981;107:350-352
19. Honjo I, Hayashi M, Ito S, Takahashi H. Pumping and clearance function of the Eustachian tube. Am J Otolaryngol 1985;6:241-244
20. Paananen R, Sormunen R, Glumoff V. Surfactant proteins A en D in Eustachian tube epithelium. Am J Physiol Lung Cell Mol Physiol 2001;281:L660-L667
21. Paananen R, Glumoff V, Sormunen R, Voorhout W, Hallman M. Expression and localization of lung surfactant protein B in Eustachian tube epithelium. Am J Physiol Lung Cell Mol Physiol 2001;280:L214-L220
22. Mira E, Benazzo M, Tacconi MT, Lligon L, Fumagalli GF, Salmone M. Disaturated phosphatidylcholine in rabbit Eustachian tube surfactant. ORL J Otorhinolaryngol Relat Spec 1990;52:174-179
23. Hills BA. Analysis of Eustachian tube surfactant and its function as a release agent. Arch Otolaryngol 1984;110;3-9
24. Mulder JJS. Morphological and functional aspects of the Eustachian tube of the rat. PhD Thesis. Radboud university Nijmegen Medical Centre, 1999
25. Doyle WJ, Seroky JT. Middle ear gas exchange in rhesus mokeys. Ann Otol Rhinol Laryngol 1994;103:636-645
26. Giebink GS, Ripley ML, Wright PF. Eustachian tube histopathology during experimental influenza A virus infection in the chinchilla. Ann Otol Rhinol 1987;96:199-206
27. Onashi Y, Nakai Y, Esaki Y, Ohno Y, Sugiura Y, Okamo H. Influenza A virus-induced otitis media and mucociliary dysfunction in the guinea pig. Acta Otolaryngol 1991;486(suppl):135-148
28. Park K, Bakaletz LO, Coticchia JM, Lim DJ. Effect of influenza A virus on ciliary activity and dye transport function in the chinchilla Eustachian tube. Ann Otol Rhinol Laryngol 1993;102:551-558
29. Umeki S. Primary mucociliary transport failure. Respiration 1988;54:220-225
30. Downs BW, Butehorn HF, Prazma J, Rose AS, Stamat JC, Pillsbury HC. Action of histamine on Eustachian tube function. Otolaryngol Head Neck Surg 2001;124:141-420
31. Esaki Y, Ohashi Y, Furuya H, Sugiura Y, Ohno Y, Okamota H, Nakai Y. Histamine-induced mucociliary dysfunction and otitis media with effusion. Acta Otolaryngol 1991;486(suppl):116-134
32. Bylander A, Tjernstrom O, Ivarsson A. Pressure opening and closing functions of the Eustachian tube in children and adults with normal ears. Acta Otolaryngol 1983; 95:55-62
33. Cantekin EI, Bluestone CD, Parkin LP. Eustachian tube ventilatory function in children. Ann Otol Rhino Laryngol 1976;85:171-177
34. Bluestone CD, Wittel RA, paradise JL. Roentgenographic evaluation of Eustachian tube function in infants with cleft palate and normal palates. Cleft Palate J 1972;9:93-100

35. Doyle WJ, Cantekin EI, Bluestone CD. Eustachian tube function in cleft paltate children. Ann Otol Rhinol Laryngol 1980;89(suppl)34-40
36. Matsune S, Sando I, Takahashi H. Insertion of the tensor veli palatine muscle into the Eustachian tube cartilage in cleft palate cases. Ann Otol Rhinol Laryngol 1991;100:439-446
37. Friedman RA, Doyle WJ, Casselbrant ML, Bluestone C, Fireman P. Immunologic-mediated Eustachian tube obstruction: A double-blind crossover study. J Allergy Clin Immunol 1983;71:442-447
38. Bluestone CD, Cantekin EI, Beery QC. Certain effects of adenoidectomy of Eustachian tube ventilation function. Laryngoscope 1975;85:113-127
39. Falk B. Sniff-induced negative middle ear pressure: study of consecutive series of children with otitis media with effusion. Am J Otolaryngol 1982;3:155-162
40. Falk B. Negative middle ear pressure induced by sniffing. A tympanometric study in persons with healthy ears. J Otolaryngol 1981;10:299-305
41. Sugiura Y, Ohashi Y, Nakai Y. Roxithromycin stimulates the mucociliary activity of the Eustachian tube and modulates neutrophil activity in the healthy guinea pig. Acta Otolaryngol 1997;531(suppl):34-38
42. Chilvers MA, O'Callaghan C. Analysis of ciliary beat pattern and beat frequency using digital high speed imaging: comparison with the photomultiplier and photodiode methods. Thorax 2000;55:314-317
43. Takahashi H, Hayashi M, Sato H, Honjo I. Primary deficits in Eustachian tube function in patients with otitis media with effusion. Arch Otolaryngol Head Neck Surg 1989;115:581-584
44. Valsalva AM. Tractatus de aura humana. Bologna:1704
45. Toynbee J. The diseases of the ear. London; Churchill; 1860
46. Van Heerbeek N, Ingels KJ, Snik AF, Zielhuis GA. Reliability of manometric Eustachian tube function tests in children. Otol Neurotol 2001; 22:183-7
47. Falk B, Magnuson B. Test-retest variability of the eustachian tube responses in children with persistent middle ear effusion. Arch Otorhinolaryngol 1984;240:145-52
48. Groth P, Ivarsson A, Tjernstrom O. Reliability in tests of the Eustachian tube function. Acta Laryngol 1982; 93:261-7
49. Bluestone CD, Cantekin EI. Current clinical methods, indications and interpretation of eustachian tube function tests. Ann Otol Rhinol Laryngol. 1981 Nov-Dec;90(6 Pt 1):552-62
50. Virtanen H. Sonotubometry, an acoustical method for objective measurement of auditory tubal opening. Acta Otolaryngol 1978; 86:93-103
51. Holmquist J, Björkman G, Olén L. Measurement of Eustachian tube function using sonotubometry. Scand Audiol 1981; 10:33-35
52. Jonathan DA, Chalmers P, Wong K. Comparison of sonotubometry with tympanometry to assess Eustachian tube function in adults. Br J Audiol 1986 aug; 20(3): 231-235
53. Jonathan DA. Sonotubometry: its role in childhood glue ear. Clin Otolaryngol 1989; 14:151-154
54. Okubo J, Watanabe I, Shibusawa M, Ishikawa N, Ishida H, Teramura K. Sonotubometric measurement of the Eustachian tube function by means of band noise; a clinical view of the acoustic measurement of the Eustachian tube. ORL J Otorhinolaryngol Relat Spec 1987; 49(5): 242-245
55. Palva T, Marttila T, Jauhiainen T. Comparison of pure tones and noise stimuli in sonotubometry. Acta Otolaryngol (Stockholm) 1987; 103:212-216
56. Jonathan DA. The predictive value of Eustachian tube function (measured with sonotubometry) in the successful outcome of myringoplasty. Clin Otolaryngol 1990; 15:431-434
57. McBride T, Cunningham M, Derkay C, Doyle W. Evaluation of non-invasive Eustachian tube function tests in normal adults. Laryngoscope 98: June 1988; 655-658
58. Virtanen H. Relation of the body posture to the Eustachian tube function. Acta Otolaryngol 1983 Jan-Feb (1-2): 63-67
59. Leider J, Hamlet S, Schwan S. The effect of swallowing bolus and head position on Eustachian tube function via sonotubometry. Otolaryngol Head Neck Surgery 1993; 109(1): 66-70
60. Iwano T, Ushiro K, Yukawa N, Doi T, Kinoshita T, Hamada E, Kumazawa T. Active opening function of the human Eustachian tube: comparison between sonotubometry and pressure equilibraton test. Acta Otolaryngol 1993; 500:62-65

2

Sonotubometry – Eustachian tube ventilatory function test; a review

Stijn J.C. van der Avoort
Niels van Heerbeek
Gerhard A. Zielhuis
Cor W.R.J. Cremers

Otology & Neurotology 2005 May; 26(3); 538-543

Abstract

Objective:

Disturbance of any of the Eustachian tube functions may contribute to the development of otitis media. Sonotubometry measures the ventilatory function using sound. The qualities of sonotubometry as a test for ET ventilatory function have been studied by various investigators. In this review, we describe the development of the method and provide a summary of the study results to make an estimate of the diagnostic potential of this ET function test.

Data source:

The English language literature on this topic was searched systematically by Medline and Pubmed using the keywords: ventilatory function Eustachian tube, sonotubometry and function test.There were no limits for the year of publication.

Study selection:

Papers that described the method itself (validity, reproducibility, diagnostic value) were studied in more detail**.**

Conclusions:

The technique of sonotubometry has gradual been improved over the years. The results of sonotubometry are at least as good as those of other function tests. However, as the results still tend to be ambiguous in children and otitis media is most common in this population, the reproducibility and application of sonotubometry need further evaluation. Sonotubometry has great advantages over other function tests, but it is not used routinely to assess ET ventilatory function, because its value for clinical practice has not yet been adequately demonstrated. Our review showed that sonotubometry can still be improved further and that efforts to do so seem justified, as it forms a particularly promising method to assess ET function in children with suspected ET pathology.

Introduction

The Eustachian tube (ET) connects the nasopharyngeal space and the middle ear. In adults, the length of the tube varies from 31 to 38 mm[1]. It consists of two parts: an osseus posterolateral portion and a fibrocartilaginous anteromedial portion. Both parts are connected at the isthmus, which is the narrowest section of the ET[2]. The most important functions of the ET are protection, clearance and ventilation of the middle ear[3,4]. Frequent active opening of the Eustachian tube allows ventilation of the middle ear and equilibration of pressure changes. Active opening is accomplished by contraction of the paratubal muscles. The tensor veli palatini muscle plays the most important role. Contraction of the muscles occurs during swallowing, yawning or movement of the mandible. Humans swallow about 1000 times a day, but not every swallowing action leads to ET opening with effective gas transfer into the middle ear[13].

Disturbance of any of the ET functions may contribute to the development of otitis media (OM)[5-13]. This is one reason why it is important to measure the function. Other applications of the ET measurements are to predict the outcome of otological surgery and to establish the need for insertion of ventilation tubes. Research has mainly focused measuring ventilatory function of the ET. One of the first tests to measure ventilatory ET function was described by dr. Josef Grüber in 'Lehrbuch der Ohrenheilkunde' (Vienna 1870). He caused pressure elevation in the nose and measured whether the pressure reached the ear by passing through the Eustachian tube (figure 3, page 15). Other early manoeuvres to test the ventilatory functioning included Valsalva's manoeuvre and Toynbee's manoeuvre[14,15]. Later, other tests were developed.

Nowadays several tests are available to measure the ventilatory function of the Eustachian tube. Tests most frequently used are the forced response test, pressure equilibration test, nine-step inflation-deflation test and sonotubometry. The first three tests are manometric tests[16-20]. The forced response test measures the pressure at which the ET opens passively when the middle ear pressure is increased. The pressure equilibration test measures the ability to equilibrate positive and negative pressures applied to the middle ear.

In order to apply pressure directly to the middle ear, there must be perforation in the tympanic membrane (TM) or a ventilation tube must be present. The forced response test and the pressure equilibration test therefore cannot be performed on ears with an intact TM unless a pressure chamber is used but such equipment is not widely available.

In the nine-step inflation-deflation test[20], a tympanometer is used to measure the resting middle ear pressure. A negative pressure (-300 mm H_2O) is applied to the external auditory canal to create relative over-pressure in the middle ear. Then the tympanometer measures the ability to normalize this over-pressure. This procedure is repeated with the application of a positive pressure. In a physiologically normal middle ear and auditory canal, the pressure normalizes to the resting pressure after swallowing three times.

Sonotubometry measures the function of the Eustachian tube using sound. A constant sound source is applied to the nostril, while a microphone in the external auditory canal records the transmitted sound pressure level. The test is started with a constant sound signal in the nostril. The subject is asked to swallow (drink some water) and when the ET opens, an increase in sound level will be measured as. Thus the active ventilatory function of the Eustachian tube can be measured non-invasively. The measurements take place under physiological circumstances, without the use of extreme pressures and without the need for TM perforation. Sonotubometry therefore has several advantages and can be considered an appropriate method to measure ventilatory ET function.

The qualities of sonotubometry as a test for ET ventilatory function have been studied by various investigators. In this review, we describe the development of the method and provide a summary of the study results to make an estimate of the diagnostic potential of this ET function test.

Methods

The English language literature on this topic was searched systematically by Medline and Pubmed using the keywords: ventilatory function Eustachian tube, sonotubometry and function test. The hits and their related articles were retrieved. There were no limits for the year of publication.

Articles that described sonotubometry as a test for the Eustachian tube function in humans were reviewed and papers that described the method itself (validity, reproducibility, diagnostic value) were studied in more detail.

Results

Development of sonotubometry

Politzer introduced the principle of sonotubometry in 1869. By holding a tuning fork in front of the nostrils of a test person, he found that the sound could be heard more loudly when the test person swallowed[21]. He concluded that the Eustachian tube opened during swallowing and conducted more sound through the ET into the middle ear.

Combining the principle introduced by Politzer and modern electronics, Perlman used low frequency sounds to evaluate ET conductance[22]. Test sounds were transmitted through a rubber tube into the nasal cavity. The sound source was located some distance from the test person. Perlman found that the response was affected by the length of the rubber tube, due to resonance[23]. In 1967, Naunton and Galluser solved this problem by adjusting the length of the tube according to the wavelength of the sound. They also built a wooden box of 38 mm thick around the ear microphone to protect it from direct noise from the sound source[24]. Although testing took place in a soundproof room, there was still the risk that the microphone would pick up unwanted noise. Elpern et al. used a filter set (Brüel & Kjaer, type 1612) with a centre frequency of 200 Hz and 3.7 dB bandwidth[25]. As inadequate sealing of the earplug in the external auditory canal may have been responsible for sound leakage, Satoh et al. designed a tight attachment for the microphone to the ear and taped the speaker hermetically to the nostril[26]. Although these modifications improved the accuracy and precision of the test, sonotubometry was still in need of further improvement.

Until then, only low frequency test sounds had been used. In 1977, Virtanen was the first investigator to suggest the use of frequencies in the range of 1 to 20 kHz to examine ET function. Recording the signals picked up in the external auditory canal revealed that some frequencies were attenuated, while others were amplified, depending on specific physiological changes in the volume and shape of the nasal cavity, the oral cavity and the nasopharynx. Virtanen also found that physiological swallowing produced sounds in the range of 100 - 2000 Hz that interfered with test sounds in the same frequency range (so-called resonance and anti-resonance phenomenon)[27].

Based on these data, Virtanen concluded that frequencies in the range of 6-8 kHz were most suitable to measure opening of the Eustachian tube.

He subsequently used an earphone that could generate a continuous sound of 6, 7 or 8 kHz and be inserted into the nostril of the test person. This sound source was fixed tightly within the nostril to minimise sound leakage. A microphone embedded in a circumaural earmuff was placed in the ipsilateral external auditory canal to protect against ambient noise. The microphone and insert earphone were connected to a heterodyne analyser (type 2010) that consisted of an analyser and a frequency oscillator. A continuous tone generated by the oscillator was transmitted to the earphone inserted into the nose. A filter set (Brüel & Kjaer type 1613) was used to filter out any ambient noise. Test sound that reached the external auditory canal was picked up by a calibrated condenser microphone (Brüel & Kjaer type 4143) connected to a preamplifier (Brüel & Kjaer 2619). A sound level recorder (type 2209) measured the signal. The test subject sat in a quiet room, with his/her mouth closed and without moving the head. Next he or she was asked to swallow some water, while the sound signal in the external ear was being recorded continuously. Opening of the tube was reflected by a sudden increase in signal in he external ear canal (5 dB). The procedure described by Virtanen in 1977 became more or less standard in subsequent studies, with a few minor adaptations[29-34].

Test results in healthy and diseased populations

Several investigators have described sonotubometry properties and results (i.e. either a negative or a positive response) in populations with varying ages and health states. In table 1, these studies are arranged in chronological order and specific characteristics of the study population and test properties are shown. Virtanen tested 106 ears in 60 healthy subjects. The subjects ranged in age from 6 to 73 years; mean age was 32 years. Separate test tones of 6, 7 and 8 kHz were applied to the nostril and the subject was asked to swallow. ET opening was considered to have occurred in 90% of these healthy ears, measured as a minimum increase in amplitude of 5 dB. When the minimum increase was set at 1 dB ET opening was considered to have occurred in 95%.

Table 1. Studies on sonotubometry in chronological order

Author & year of publication	Test Frequency (Hz)	Loudness (dB)	Population	# of Ears	# of Swallows	respons
Naunton & Galluser (1967)	200		Healthy adults	15		53%
Satoh et al. (1970)	2000	max130	Healthy adults	31		74%
Virtanen (1977)	6000-8000	100-112	Healthy adults	106	6	90%
Holmquist (1981)	6000-8000	100	Healthy adults	187	6	66%
Okubo (1987)	5000-9000	max125	Healthy females	51	2	89%
Okubo (1987)	5000-9000	max125	Healthy children	178	2	65%
Palva (1987)	6500-8000	115	Healthy adults	64	5	80%
Jonathan (1989)			Healthy children	50	5	80%
Jonathan (1989)			Glue ear children	126	5	29%
Mondain (1997)	8000	100		240	Variable	63%
Munro et al. (1999)	7000-8000	100	Healthy children	20	6	80%

In 1981, Holmquist[28] performed sonotubometry on 187 ears. Although there was adequate aeration of the middle ear in all the ears at the time of testing, no sound passage was detected after swallowing in 34%. This could not be explained by the medical history, otoscopy, or tympanometry.

Jonathan used sonotubometry on children[30] to compare the test findings in a group of children with Otitis Media with Effusion (OME) to the findings in a group of otologically healthy children. Sonotubometry was feasible and easy to perform in all the children. Test results showed tubal function to be normal in 80% of the control group, compared to only 29% of the OME group. The author concluded that sonotubometry was a valuable tool to establish fluid in the middle ear.

Okubo et al. used slightly modified sonotubometry equipment to test thirty-two women (average age 20 years) without otological diseases (64 ears)[31]. ET opening occurred in 89% of the measurements. In the same experiment, 89 normal children (178 ears), aged 4-12 years, were tested in an identical manner. ET opening occurred in about 65% of these children. These results suggested that the ET does not necessarily open with each swallowing. In a further part of the same experiment, the subjects were asked to swallow in various ways and it turned out that opening of the Eustachian tube depended on the type of swallowing. Therefore during sonotubometry, subjects need to be correctly instructed about how to swallow and the tests have to be performed with appropriate intervals.

Palva et al. (1987) compared the effects of several pure tone frequencies and band noise frequencies[32]. Pure tones of 6, 7 and 8 kHz were used and band noise of between 6.5 and 8 kHz. The latter approach was far less time-consuming.

Palva et al. also compared normal and diseased ears and the response to swallowing and the response to mandible-down movement. A peak of > 5 dB was counted as a positive response. In normal ears, a positive response was found in 57% using pure tones, while a similar response of 59% was found when using band noise sound. The mandible-down movement produced poorer results than swallowing. Sonotubometry was also tested in correlation with tympanomatoid surgery. Forty-four ears were evaluated preoperatively and then followed for a period of 4 years after surgery. Seventy per cent of the ears with a positive preoperative response had a good surgical outcome and remained well-aerated after surgery. The remaining 30% had a poor preoperative response and preoperative otoscopy detected many adhesive changes in the posterior part of the tympanic membrane, while the tubotympanum seemed to be normal.

Jonathan[33] investigated the predictive value of sonotubometry for successful myringoplasty. Preoperative and postoperative tests were performed on 25

patients undergoing a myringoplasty. There was no significant difference between the success rate of myringoplasty between patients who had good ET function preoperatively and those with function. However, the duration of follow-up was only 4 months. All the patients with poor preoperative ET function in whom surgery was successful, showed normal postoperative ET function.
Mondain et al. used a portable device to record ET opening, which enabled them to make longitudinal evaluations of Eustachian tube ventilatory function. A total of 120 ears were examined and 63% of them showed ET opening. Opening occurred a mean number of 21.7 times in 15 minutes.

Sonotubometry vs other ventilatory function tests
Sonotubometry has been compared to various other ET function tests. Jonathan (1986)[29] compared sonotubometry to tympanometry to assess ET function in otologically healthy adults and found a high degree of correlation between the two methods.
Later, Jonathan[30] studied a group of otologically healthy children and children with OME to compare sonotubometry to several indirect ET function tests: pure tone audiometry, tympanometry and otoscopy. Unlike the other tests, sonotubometry was possible on all the children. It was found that sonotubometry and tympanometry had greater specificity than the other function tests to predict the presence of middle ear effusions and both were superior to pure tone audiometry and otoscopy.
McBride et al. (1988) compared sonotubometry to the nine-step inflation-deflation test. A group of 107 otologically healthy young adults were tested with the two methods[34]. The nine-step inflation-deflation test showed better reproducibility than sonotubometry (52% versus 34%). In 78% of the subjects, there was correlation between the results of the two tests: either both tests were positive or both tests were negative. A combination of the two function tests enabled ET function evaluation in 96% of these healthy subjects, with an overall reproducibility of 34% over three sequential tests.

Conditions that influenced test results
A few studies investigated the influence of body posture or swallowing technique on the outcome of sonotubometry. In 1983, Virtanen[35] performed sonotubometry on subjects who were lying down or sitting up. The incidence and duration of ET opening were not influenced by body posture.
Leider et al. (1993) compared the effect of dry swallowing and bolus (10 cc) swallowing and the effect of the position of the head (straight, turned to the left

and turned to the right). No significant differences in the incidence and duration of ET opening were found between the different bolus types or head positions[36].

Discussion

Several test methods are available to assess the ventilatory function of the Eustachian tube. However, most of these tests have the disadvantage that they can only be performed on ears with a perforated tympanic membrane or a ventilation tube in situ (or they need to be conducted in a pressure room). An even more important disadvantage is that these tests do not measure ventilatory ET function under physiological circumstances. Relatively large pressure changes, i.e. non-physiological pressure changes, need to be applied to evaluate the active ventilatory function. Furthermore, the inflation-deflation test can cause an uncomfortable feeling for the test person, wich is a particular disadvantage in children.

In contrast, sonotubometry can be performed in patients with or without an intact tympanic membrane and under physiological conditions. Sonotubometry is also inexpensive, painless and easy to perform in both adults and children. Therefore it has a great potential value as a diagnostic tool for individuals with suspected ET pathology.

In this review we did not find definite proof of the validity of sonotubometry, but comparisons with other ET function tests suggest that it performs equally well. In addition, the reproducibility of sonotubometry was generally found to be as high as that of the other ET function tests. Only for the 9-step inflation-deflation test there is a report suggesting that this test is more reproducible than sonotubometry.

Since its introduction in the nineteenth century the technique of sonotubometry has undergone radical improvement. Solutions have been found for some serious problems with the early sound conduction technique, such as susceptibility to background noises, leakage of sound and arbitrarily chosen test frequencies.

These problems were solved by ensuring a tight fit between the sound source and the nostril and by mounting the microphone in a circumaural ear muff. Virtanen[27] showed that frequencies of at least 5 kHz did not suffer interference from physiological sounds caused by swallowing. The application of a narrow bandwidth filter ensured that only sounds were recorded that had a frequency of equal to that of the test sound presented in the nostril.

In the studies on sonotubometry reviewed in this article the tests did not involve the subject swallowing more than five times. One recorded opening, or more, was considered to be a positive result. Based on this definition, the test results were positive in about 90% of adults[27,31] and 65% in children[31] with well-aerated middle ears. It is possible that test method has already become sufficiently well-developed to assess ET ventilatory function, but its validity and reproducibility still need further confirmation, especially in children with recurrent episodes of middle ear effusion or acute otitis media. The validity of sonotubometry and its predictive value may be further improved by calibrating the method for these groups, by increasing the number of times the subjects swallow during measurement and by scaling the opening frequency according to whether a group has good or poor ET function.

To evaluate the results of sonotubometry, it has to be taken into account that the ET does not open every time a person swallows. It is still uncertain how many times the ET must open in 24 hours to maintain the correct middle ear pressure.

In conclusion, the technique of sonotubometry has gradual been improved over the years. The results of sonotubometry are at least as good as those of other function tests. However, as the results still tend to be ambiguous in children and otitis media is most common in this population, the reproducibility and application of sonotubometry need further evaluation. Sonotubometry has great advantages over other function tests, but it is not used routinely to assess ET ventilatory function, because its value for clinical practice has not yet been adequately demonstrated. Our review showed that sonotubometry can still be improved further and that efforts to do so seem justified, as it forms a particularly promising method to assess ET function in children with suspected ET pathology.

References

1. Graves GO, Edwards LF. The Eustachian tube, a review of descriptive, microscopic, topographic and clinical anatomy. Arch Otolaryngol 1944;39:359-379.
2. Poe D, Kujawski O. Endoscopic diagnoses of Eustachian tube dysfunction. Minimally invasive surgery of the ear. Silverstein, Rosenberg, Poe, Eds, 2002.
3. Bluestone CD, Paradise JL, Beery QC. Physiology of the Eustachian tube in the pathogenesis and management of the middle ear effusions. The Laryngoscope 1972;July: 1654-1670.
4. Bluestone CD. Pathogenesis of otitis media; role of the Eustachian tube. Pediatr Infect Dis J 1996;15:281-291.
5. Takahaski M, Takahaski H, Sato H, Honjo I. Primary deficits in the Eustachian tube function in patients with otitis media with effusion. Arch Otolaryngol Head Neck Surg 1989; 115:581-584.
6. Stenstrom C, Bylander Groth A, Ingvarsson L. Eustachian tube function in otitis prone and healthy children. Int J Pediatr Otorhinolaryngol 1991;21:127-138.
7. Bylander Groth A, Stenstrom C. Eustachian tube function and otitis media in children. Ear Nose Throat J 1998; 77:762-769.
8. Bluestone CD, Paradise JL, Beery QC. Physiology of the Eustachian tube in the pathogenesis and management of the middle ear effusions. The Laryngoscope 1972; July: 1654-1670.
9. Sadé J. Pathology and pathogenesis of secretory otitis media. Arch Otolaryngol 1966; 84:297-305.

10. Sadé J. The nasopharynx eustachian tube and otitis media. J Laryngol Otol 1994;108:95-100.
11. Maw RA. Glue ear in childhood. Cambridge: Mac Keit Press & Cambridge University Press, 1995.
12. Virtanen H, Palva T. The patulous Eustachian tube and chronic middle ear disease. Acta Otolaryngol 1982;93:49.
13. Sadé J, Ar A. Middle ear and auditory tube: Middle ear clearance, gas exchange and pressure regulation. Otolaryngology Head and Neck Surgery 1997;116:499-524.
14. Valsalva AM. Tractatus de aura humana. Bologna:1704.
15. Toynbee J. The diseases of the ear. London; Churchill; 1860.
16. Van Heerbeek N, Ingels KJ, Snik AF, Zielhuis GA. Reliability of manometric Eustachian tube function tests in children. Otol Neurotol 2001;22:183-187.
17. Bylander A, Tjernstrom O, Ivarsson A. Pressure opening and closing functions of the Eustachian tube in children and adults with normal ears. Acta Otolaryngol 1983; 95:55-62.
18. Falk B, Magnuson B. Test-retest variability of the eustachian tube responses in children with persistent middle ear effusion. Arch Otorhinolaryngol 1984;240:145-152.
19. Groth P, Ivarsson A, Tjernstrom O. Reliability in tests of the Eustachian tube function. Acta Laryngol 1982;93:261-267.
20. Charles D Bluestone MD, E.I. Cantekin PhD. Current clinical methods, indications and interpretation of Eustachian tube function tests. Pittsburgh Pennsylvania. Presented at the meeting of the American Otology Society, Inc, Vancouver Colombia, may 9-10,1981.
21. Politzer A. 1869 cited by Politzer A. 1908. Lehrbuch der Ohrenheilkunde. 5. Auflage, Vol. I. F. Enke, Stuttgart.
22. Perlman HB. The Eustachian tube. Abnormal patency and normal physiological state. Arch Otolaryngol 1939;30:212.
23. Perlman H B 1951. Observations on the Eustachian tube. Arch Otolaryngol; 53:370-385.
24. Naunton RF, Galluser J. Measurement of Eustachian tube function. Ann Otol Rhinol Laryngol 1976; 76:455-471.
25. Elpern BS, Naunton RF, Perlman HB. Objective measurement of middle ear function: the Eustachian tube. Laryngoscope 1964;74:359-371.
26. Satoh I, Watanabe I, Sainoo T. Measurement of Eustachian tube function. Arch Otolaryngol 1970; 92:329-334.
27. Virtanen H. Sonotubometry, an acoustical method for objective measurement of auditory tubal opening. Acta Otolaryngol 1978;86:93-103.
28. Holmquist J, Björkman G, Olén L. Measurement of Eustachian tube function using sonotubometry. Scand Audiol 1981;10:33-35.
29. Jonathan DA, Chalmers P, Wong K. Comparison of sonotubometry with tympanometry to assess Eustachian tube function in adults. Br J Audiol 1986 aug;20(3):231-235.
30. Jonathan DA. Sonotubometry: its role in childhood glue ear. Clin Otolaryngol 1989;14:151-154.
31. Okubo J, Watanabe I, Shibusawa M, Ishikawa N, Ishida H, Teramura K. Sonotubomtric measurement of the Eustachian tube function by means of band noise; a clinical view of the acoustic measurement of the Eustachian tube. ORL J Otorhinolaryngol Relat Spec 1987; 49(5):242-245.
32. Palva T, Marttila T, Jauhiainen T. Comparison of pure tones and noise stimuli in sonotubometry. Acta Otolaryngol (Stockholm) 1987;103:212-216.
33. Jonathan DA. The predictive value of Eustachian tube function (measured with sonotubometry) in the successful outcome of myringoplasty. Clin Otolaryngol 1990;15:431-434.
34. McBride T, Cunningham M, Derkay C, Doyle W. Evaluation of non-invasive Eustachian tube function tests in normal adults. Laryngoscope June 1988;98:655-658.
35. Virtanen H. Relation of the body posture to the Eustachian tube function. Acta Otolaryngol 1983; Jan-Feb (1-2):63-67.
36. Leider J, Hamlet S, Schwan S. The effect of swallowing bolus and head position on Eustachian tube function via sonotubometry. Otolaryngol Head Neck Surgery 1993;109(1): 66-70.
37. Iwano T, Ushiro K, Yukawa N, Doi T, Kinoshita T, Hamada E, Kumazawa T. Active opening function of the human Eustachian tube: comparison between sonotubometry and pressure equilibraton test. Acta Otolaryngol 1993;500:62-65.

3

Reproducibility of sonotubometry in healthy adults

Stijn J.C. van der Avoort
Niels van Heerbeek
Gerhard A. Zielhuis
Cor W.R.J. Cremers

The Journal of Laryngology and Otology 2006 Oct; 120 (10): 853-856.

Abstract

Background:

Frequent active opening of the Eustachian tube allows ventilation of the middle ear and equilibration of pressure changes. Active opening is accomplished by the contraction of the paratubal muscles during swallowing. Because a disturbance of the ventilatory function of the ET may contribute to the development of otitis media with effusion (OME) it is important to investigate the functioning of the ET. Sonotubometry can be used to detect whether the ET can open or not during swallowing acts.

Methods:

We developed a sonotubometer to test ET ventilatory function in 36 healthy adults. The width of the test signal frequency was between 5500 and 8500 Hz (centre frequency of 7000 Hz) and loudness 95 dB. To test the reproducibility the testing took place in two sessions of 10 swallowing acts each.

Results:

Opening of the ET could be registered in 92% in at least one of the two measurements. The 1st and the 2nd measurements were highly correlated, with a Spearman 's coefficient of 0,907.

Conclusion:

We confirmed that there is mostly a good ventilatory ET function in otologically healthy adults, although in a few cases openings were not registered. Further we confirmed that our sonometric test equipment has a great reproducibility. Sonotubometry is a promising method towards assessing ventilatory ET function. Research is ongoing to test the discriminative power of sonotubometry in children of various otological healths.

Introduction

The most important functions of the Eustachian tube (ET) are ventilation, protection and clearance of the middle ear[1,2]. Gases are exchanged continuously between the tympanic cavity and the middle ear mucosa via diffusion. Regular active opening of the Eustachian tube allows ventilation of the middle ear and equilibration of pressure changes. Active opening is accomplished by the contraction of the paratubal muscles. These muscles contract during swallowing, yawning or movement of the mandible. However, the Eustachian tube does not open during each swallow.

Because a disturbance of any of the ET functions may contribute to the development of otitis media with effusion (OME)[3-11] it is important to investigate functioning of the ET. Research mainly has been done to measure ventilatory function of the ET. Beside manometric function tests[12-16] and indirect tubal function tests, like tympanometry, pure tone audiometry and otoscopy, sonotubometry[17-27] can be used to detect whether the ET can open or not. The latter function test has some advantages in comparison to the other function tests[28]. Sonotubometry takes place under physiological circumstances, can be performed on ears having an intact tympanic membrane, in contrast to the manometric tests, and is easy tolerated by the test person. Sonotubometry is based on the principle that sound that is applied to the nasopharyngeal ostium of the ET is conducted through the ET to the middle ear. During active opening of the ET, more sound will be recorded in the external auditory canal. Several investigators have studied sono-tubometry to find out if it is a useful test to assess the ET ventilatory function[17-27]. However, so far it is still not applied in clinical practice. Partly because there is no consensus on the test equipment and test properties in literature and partly because its reproducibility and value for clinical practice still needs to be demonstrated. It is therefore argued that sonotubometry is still liable to further improvement. Although various reports have been published about the performance of sonotubometry in adults, it appears to be difficult to get reliable positive test results in more than 60% of healthy ears. Moreover the question arises about the reproducibility of the test results. The aim of this study was to improve the performance of the technique in adults.

Methods and materials

The equipment of the present investigation is schematically illustrated in Figure 1.

A test signal is produced by a computer using the Cool edit pro 2.0 software (Syntrillium Software Corporation) and delivered to the nasopharyngeal ostium of the ET using an Ear Tone 3A insert phone (Auditory Systems) that is fixed into one of the nostrils of the test person with a foam ear tip. This tip adjusts itself to the shape of the nostril to prevent leakage of sound. In the ipsilateral external auditory canal a probe microphone (Etymotic Research-7c) is placed and also fixed with a foam ear tip to prevent loss of test sound and interference of background noises. The microphone is connected to the computer and the sound is recorded using Cool edit pro 2.0 software.

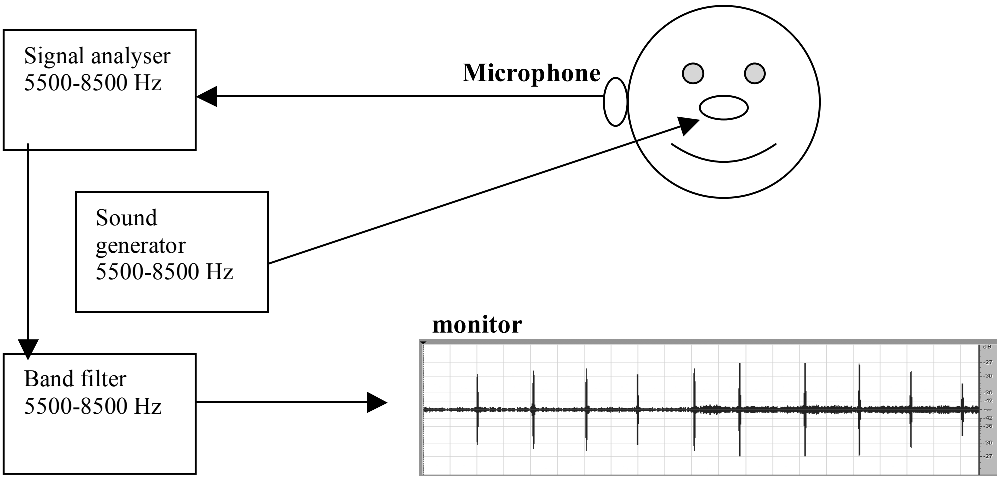

Figure 1. Diagrammatically illustration of equipment

Earlier studies on sonotubometry[27-37] have been considered thoroughly, to choose the optimal test properties. We started with a high frequency test sound following Virtanen. He showed in his study that only frequencies higher than 5000 Hz were appropriate[27]. A pure tone test signal was used with a frequency of 7000 Hz and an initial loudness of 75 dB. By doing so we could register tubal openings in 60 % of a population healthy adults. Because in comparison to the earlier publications this result was disappointing, our equipment or test properties had to be liable to improvement. The loudness was increased to a 95 dB level because the test signal might be too low to be detected by the probe microphone in the external ear canal. The use of a pure tone signal was also considered to be the reason of false negative test responses. In a unilateral closed tube, like the external ear canal, a pure tone sound can cause a standing wave pattern. A standing wave pattern consists of nodes and anti-nodes. Measurement right in a node can be responsible for false negative measurements. To prevent the formation of these standing wave patterns, the test signal was changed from the pure tone signal to a band signal between 5500 Hz and 8500 Hz with a centre frequency of 7000 Hz. We chose to use a sound with a bandwidth between 5500 Hz and 8500 Hz and a fixed loudness of 95 dB. The sound level in the external ear canal is continuously measured and stored. Of line, the recordings are band pass filtered with a central frequency of 7 kHz, with a minimum of 5500 Hz and a maximum of 8500 Hz. Filtering was applied to minimize ambient noise and the sounds that occur during swallowing. Discrimination between a positive and a negative response was done by visual evaluation. Further a measured peak was only counted as a positive response if it occurred simultaneously with a swallow act. To evaluate the patency of the ET normal subjects were instructed to swallow some water 10 times, in sitting position, with intervals of 10 seconds. After a session of 10 swallows, the microphone and the sound source were removed and replaced again after a short break of 5 minutes for the second measurement. The second measurement was performed identically to the first measurement to test its reproducibility. The test population consisted of thirty-six adults, 12 males and 24 females. Their age varied from 18 to 55 years, with a mean age of 33 years. Only otologically healthy subjects were included, individuals with a history of middle ear surgery, recurrent otitis media or complaints of tuba dysfunction were excluded from participation.

Results

Figure 2 shows the results of the sonotubometric measurements. In the first measurement at least one opening of the ET was registered in 31 of the 36 ears and in the second measurement in 32 of the 36 ears. Combining the results of the two measurements per subject, in 33 of the 36 tested ears (91.6 %) openings of the ET could be registered in at least one of the measurements. In the other 3 cases not one single opening was seen. The number of the openings varied from 0 to 10 out of 10 swallowing acts. Figure 3 shows the reproducibility of the test. In 23 of the 36 ears (64 %) there was no difference in number of openings between the first and the second measurement. In 8 cases (22 %) the difference in number of openings between the first and the second test is 1 opening and in 5 cases (14 %) the difference was 2 or more with a maximum difference of 5. The 1st and the 2nd measurement were highly correlated, with Spearman's correlation coefficient 0,91 (with $p < 0{,}001$).

Discussion

The purpose of this study was to develop a sonotubometer and to test whether sonotubometry is a valid and reproducible method to measure the ventilatory function of the Eustachian tube. A non-invasive physiological method to do so is still missing in the ENT-practice. Earlier there have been more studies to investigate the role of sonotubometry in the assessment of Eustachian tube function, but although there have been pretty good results and sonotubometry seemed to be a promising method, there was never reached enough confirmation to use the sonotubometry as a routine tubal test in the ENT-practice[28].

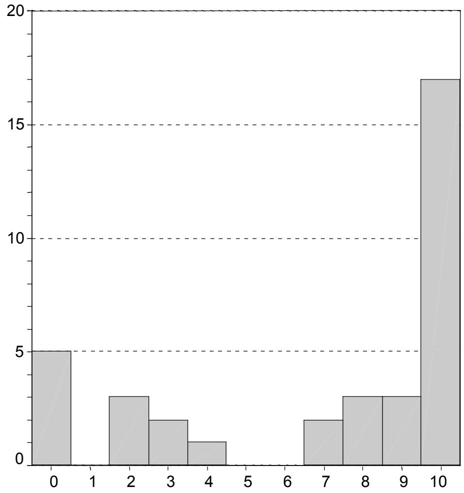

Figure 2a

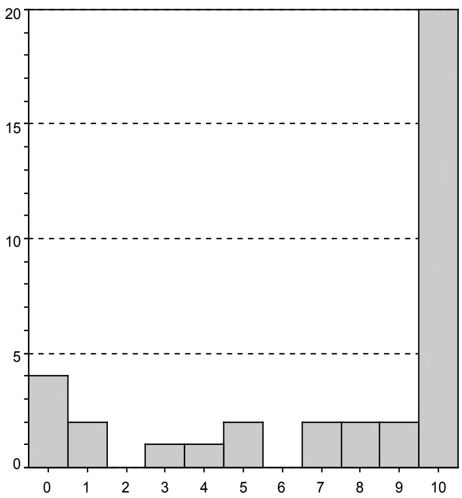

Figure 2b

Figures 2a and 2b represents respectively the first and the second measurement; number of openings are reflected on the X axis, number of test persons (N=36) on the y axis.

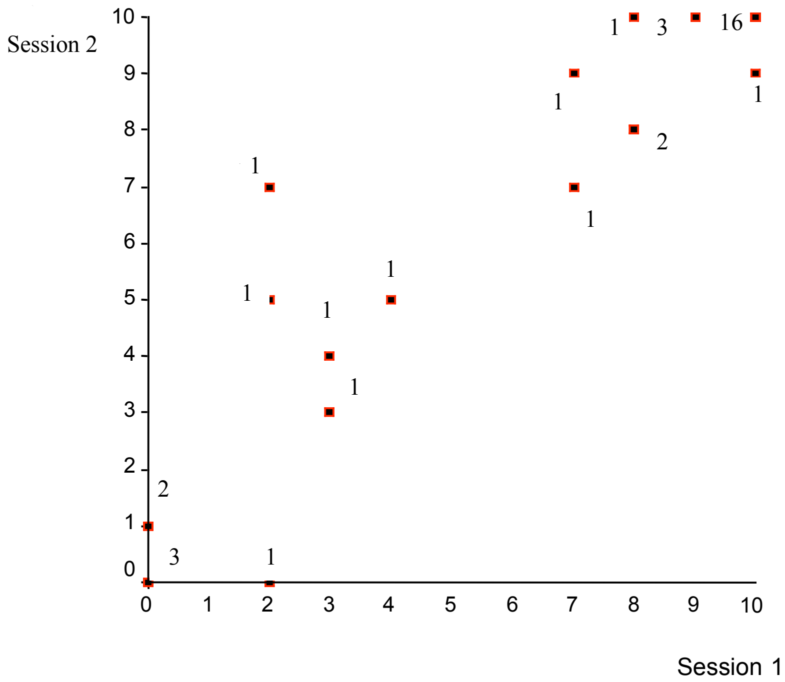

Figure 3. Reproducibility is represented in this figure.
On the x axis the first measurement, on the y axis the second measurement. One dot represents one or more test persons ( ).

For the development of the test equipment used in this study the earlier studies[17-27] have been considered thoroughly, to choose the optimal test properties. As described in the methods we started with a high frequency test sound following Virtanen[27]. Later the loudness was increased to 95 dB and to prevent the formation of standing wave patterns, the test signal was changed from the pure tone signal to a band signal between 5500 Hz and 8500 Hz with a centre frequency of 7000 Hz. With these properties the testing was performed under the same conditions as the first measurements. Thirty-six healthy adults were tested and openings of the Eustachian tube could be registered in 33 test persons (91,6%). This response agrees with the highest positive response found in earlier studies[17,21]. It indicates that in a otologically healthy adult population mostly there is a good ET ventilatory function but in some cases no openings of the ET were registered during 20 swallowing acts. In these test persons otoscopy did not show any disturbances and they had no complaints of a dysfunctioning Eustachian tube. Probably a much lower incidence of opening of the ET during a swallowing act is needed to have sufficient function by the ET. Secondly dysfunction of the Eustachian tube may not always lead to middle ear problems.

Furthermore we confirmed that our sonotubometry test equipment had a great reproducibility (or negligible test-retest variability).

Because there is lack of a physiological tubal function test applicable to ears having an intact tympanic membrane these results are promising towards assessing ventilatory tubal function in daily ENT-practice. Additional research is needed to evaluate the role of sonotubometry as a tubal function test. The outcomes of these studies in children of various otological health states are needed to substantiate the benefit of sonotubometry for the routine outclinic ENT consultations.

References

1. Bluestone CD, Paradise JL, Beery QC. Physiology of the Eustachian tube in the pathogenesis and management of the middle ear effusions. The Laryngoscope 1972; July: 1654-1670
2. Bluestone CD. Pathogenesis of otitis media; role of the Eustachian tube. Pediatr Infect Dis J 1996; 15: 281-291
3. Takahaski M, Takahaski H, Sato H, Honjo I. Primary deficits in the Eustachian tube function in patients with otitis media with effusion. Arch Otolaryngol Head Neck Surg 1989; 115:581-584
4. Stenstrom C, Bylander Groth A, Ingvarsson L. Eustachian tube function in otitis prone and healthy children. Int J Pediatr Otorhinolaryngol 1991; 21:127-138
5. Bylander Groth A, Stenstrom C. Eustachian tube function and otitis media in children. Ear Nose Throat J 1998; 77:762-769

6. Bluestone CD, Paradise JL, Beery QC. Physiology of the Eustachian tube in the pathogenesis and management of the middle ear effusions. The Laryngoscope 1972; july: 1654-1670
7. Sadé J. Pathology and pathogenesis of secretory otitis media. Arch otolaryngol 1966; 84:297-305
8. Sadé J. The nasopharynx eustachian tube and otitis media. J Laryngol Otol 1994; 108:95-100
9. Maw RA. Glue ear in childhood. Cambridge: Mac Keit Press & Cambridge University Press, 1995
10. Virtanen H, Palva T. The patulous Eustachian tube and chronic middle ear disease. Acta Otolaryngol 1982; 93:49
11. Sadé J, Ar A. Middle ear and auditory tube: Middle ear clearance, gas exchange and pressure regulation. Otolaryngology Head and Neck Surgery 1997; 116:499-524
12. Van Heerbeek N, Ingels KJ, Snik AF, Zielhuis GA. Reliability of manometric Eustachian tube function tests in children. Otol Neurotol 2001; 22:183-7
13. Bylander A, Tjernstrom O, Ivarsson A. Pressure opening and closing functions of the Eustachian tube in children and adults with normal ears. Acta Otolaryngol 1983; 95:55-62
14. Falk B, Magnuson B. Test-retest variability of the eustachian tube responses in children with persistent middle ear effusion. Arch Otorhinolaryngol 1984;240:145-52
15. Groth P, Ivarsson A, Tjernstrom O. Reliability in tests of the Eustachian tube function. Acta Laryngol 1982; 93:261-7
16. Charles D Bluestone MD, E.I. Cantekin PhD. Current clinical methods, indications and interpretation of eustachian tube function tests. Ann Otol Rhinol Laryngol. 1981 Nov-Dec;90(6 Pt 1):552-62.
17. Virtanen H. Sonotubometry, an acoustical method for objective measurement of auditory tubal opening. Acta Otolaryngol 1978; 86:93-103
18. Holmquist J, Björkman G, Olén L. Measurement of Eustachian tube function using sonotubometry. Scand Audiol 1981; 10:33-35
19. Jonathan DA, Chalmers P, Wong K. Comparison of sonotubometry with tympanometry to assess Eustachian tube function in adults. Br J Audiol 1986 aug; 20(3):231-235
20. Jonathan DA. Sonotubometry: its role in childhood glue ear. Clin Otolaryngol 1989; 14:151-154
21. Okubo J, Watanabe I, Shibusawa M, Ishikawa N, Ishida H, Teramura K. Sonotubometric measurement of the Eustachian tube function by means of band noise; a clinical view of the acoustic measurement of the Eustachian tube. ORL J Otorhinolaryngol Relat Spec 1987; 49(5): 242-245
22. T. Palva, T. Marttila, T. Jauhiainen. Comparison of pure tones and noise stimuli in sonotubometry. Acta Otolaryngol (Stockholm) 1987; 103:212-216
23. Jonathan DA. The predictive value of Eustachian tube function (measured with sonotubometry) in the successful outcome of myringoplasty. Clin Otolaryngol 1990; 15:431-434
24. T. McBride, M. Cunningham, C. Derkay, W. Doyle. Evaluation of non-invasive Eustachian tube function tests in normal adults. Laryngoscope 98: June 1988; 655-658
25. Virtanen H. Relation of the body posture to the Eustachian tube function. Acta Otolaryngol 1983 Jan-Feb (1-2): 63-67.
26. Leider J, Hamlet S, Schwan S. The effect of swallowing bolus and head position on Eustachian tube function via sonotubometry. Otolaryngol Head Neck Surgery 1993; 109(1): 66-70
27. Iwano T, Ushiro K, Yukawa N, Doi T, Kinoshita T, Hamada E, Kumazawa T. Active opening function of the human Eustachian tube: comparison between sonotubometry and pressure equilibraton test. Acta Otolaryngol 1993; 500:62-65
28. Van der Avoort S, Van Heerbeek N, Zielhuis G, Cremers C. Sonotubometry –Eustachian tube ventilatory function test; a review. Otol. & Neurot. 2005; 26:538-543

4

Reproducibility of sonotubometry as Eustachian tube ventilatory function test in healthy children

Stijn J.C. van der Avoort
Niels van Heerbeek
Ad F.M. Snik
Gerhard A. Zielhuis
Cor W.R.J. Cremers

International Journal of Pediatric Otorhinolaryngology.2006 In press.

Abstract

Objectives:

To devise a simple and reliable diagnostic procedure to test Eustachian tube function routinely in an ENT outpatient setting. One method to measure ET ventilatory function is sonotubometry. The reproducibility of a recently updated sonotubometry set-up was tested in healthy children.

Methods:

The test population comprised 61 school children aged from 6 to 8 years. Only otologically healthy children were included. Health state was established by means of a 12-item questionnaire. To test reproducibility, sonotubometric testing took place in two sessions of 10 acts of swallowing each. Spearman’s coefficient was used to test the correlation between the two sets of measurements. All testing took place at a primary school in a nearby village.

Results:

Opening of the ET was recorded in at least one of the two measurement sessions in 82% of the children. The first and second sessions were highly correlated, with a Spearman‘s coefficient of 0.89.

Conclusions:

In otologically healthy children, opening of the ET was recorded frequently using the updated sonotubometry set-up. Measurement results had high reproducibility. Therefore, the test forms a useful method to assess ET ventilatory function in otologically healthy children. The performance of this updated version needs to be established in children with otological diseases.

Introduction

The most important functions of the Eustachian tube (ET) are ventilation, protection and clearance of the middle ear[1-3]. Regular active opening of the Eustachian tube allows ventilation of the middle ear and equilibration of pressure differences. Active opening is accomplished by contraction of the paratubal muscles, for example during swallowing, yawning or movement of the mandible, but the Eustachian tube does not open during every act of swallowing.

Disturbance of Eustachian tube (ET) function is assumed to contribute to the development of otitis media with effusion (OME)[4-7]. Therefore, ET function has been studied extensively using manometric function tests[8-12] and sonotubometry[13-21]. The latter has several advantages over the other function tests[18], for example it is performed under physiological circumstances, i.e. without the need to apply non-physiological pressures to the middle ear. In addition, it can be performed on ears with an intact tympanic membrane and it is well-tolerated by adults and children. Sonotubometry is based on the principle that sound applied to the nasopharyngeal ostium of the ET is conducted through the ET to the middle ear. During active opening of the ET, more sound will be conducted, which means that higher levels of sound can be recorded in the external auditory canal. In the nineteen seventies and eighties, several investigators studied whether sonotubometry was a useful means to test ET ventilatory function. As the sensitivity to detect tubal opening was generally low, sonotubometry was not introduced into clinical practice despite the fact that some studies showed promising results. Recently, the subject of sonotubometry has been reopened, using modern and more sensitive microphones and sound sources. In a pilot study that employed a technically improved set-up om an otologically healthy adult population, the sensivity to record tubal opening (92 %) was high compared to other studies and the measurements were highly reproducible. Table 1 provides a survey of comparable studies on sonotubometry in the literature.

In children it is even more worthwhile to obtain reliable ET function test recordings, because of the potential value to predict the natural course of OME and the outcome of otological interventions. The aim of this study was to evaluate the reproducibility of an updated sonotubometry method in children with no history of OME or other ear complaints.

Table 1. Studies on sonotubometry in chronological order

Authof & year of publication	Test frequency (Hz)	Loudness (dB)	# of ears	# of swallows	Respons
ADULTS					
Naunton & Galluser (1967)	200		15		53%
Satoh et al. (1970)	2000	Max 130	31		74%
Virtanen (1977)	6000-8000	100-112	106	6	90%
Holmquist (1981)	6000-8000	100	187	6	66%
Okubo (1987)	5000-9000	Max 125	51	2	89%
Palva (1987)	6500-8000	115	64	5	80%
McBride (1988)	3000-10000		132		78%
Mondain (1997)	8000	100	240	variable	63%
CHILDREN					
Okubo (1987)	5000-9000	Max 125	178	2	65%
Jonathan (1989)			50	5	80%
Munro et al. (1999)	7000-8000	100	20	6	80%

Methods and materials

A large group of children aged 6-8 years who were attending a primary school in a nearby village were approached for this study. Several children had to be excluded, because their parents reported a history of middle ear surgery, recurrent otitis media or complaints related to ET dysfunction in a 12-item questionnaire, or otoscopy showed signs of middle ear disease, retraction of the tympanic membrane or OME. Our study population ultimately comprised 61 otologically healthy children. Their parents signed an informed consent form agreeing with participation in this study. The study was performed according to the regulations of the local Medical Ethical Committee.

All the children were tested with the sonotubometer shown as a diagram in figure 1. The equipment comprised a sound generator with a speaker placed in one of the nostrils and a measurement microphone placed in the occluded ear canal.

After a thorough review of earlier studies on sonotubometry[18] we gave close consideration to our choice of test conditions. To minimize interference with sounds that occur during swallowing, the test tone must be of high frequency, above 5 kHz. However, such high-frequency pure tones might cause standing waves in the occluded external ear canal that comprise probe tube microphone measurements[22]. Therefore, we applied high frequency narrow band noise. The test signal comprised filtered white noise with a centre frequency of 7 kHz, bandwidth of 5.5 to 8.5 kHz and slopes of 48 dB/octave. This test signal was delivered to the nasopharyngeal ostium using an Ear Tone 3A insert phone (Auditory Systems, Indianapolis, USA) that was fixed in one of the nostrils with a foam ear tip. A probe tube microphone (Etymotic Research-7c, Ilinois, USA) was placed in the ipsilateral external auditory canal and fixed with a foam ear tip to minimize interference with the airborne test signal. The microphone output was amplified, digitally band-pass filtered (from 5.5 to 8.5 kHz) and displayed as a function of time (see Figure 1).

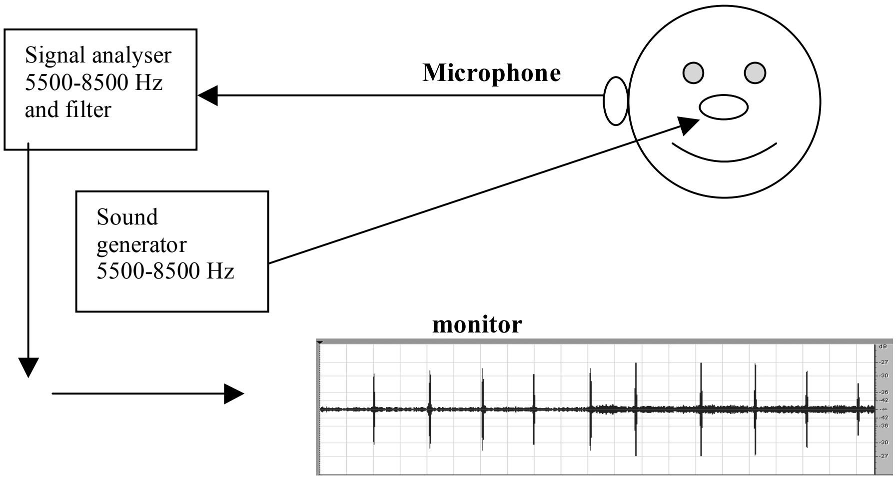

Figure 1. Diagram of the updated sonotubometry set-up

The loudness level of the test signal was fixed at 90 dB SPL, in accordance with the level measured in the nostril with the (calibrated) probe tube microphone during thepilot experiments. This level was chosen because the test signal had to be loud enough to be detected by the probe microphone in the external ear canal during ET opening, but soft enough to prevent direct airborne stimulation of the microphone. According to the specifications, the foam ear tips used to connect the speaker to the nostril and to position the probe tube microphone to the ear canal attenuate sounds in the 6-8 kHz range by 40 dB each. Therefore, the direct airborne stimulation of the microphone was considered to be negligible.
Additional measurements were carried out to study the time course of the intensity of the test signal in the nose during swallowing by placing the probe tube microphone and the sound source in the same nostril. During the act of swallowing, the sound pressure level was measured after bandpass filtering, as described above. No change in sound pressure level was detected in the nose during swallowing. This means that the present set-up was free of artefacts caused by e.g. sounds of swallowing or sound pressure changes due to acoustic alterations in the nose during swallowing.
Positive peaks were firstly identified in the microphone recordings in the ear canal on-line by marking peaks that occurred during the act of swallowing. Then the difference in microphone output between a possible peak and baseline was tested for significance. Based on a characteristic period between two swallows, the noise

level was determined by calculating the standard deviation from the baseline of the noise amplitude. The ET was judged as having opened when the level of the peak excedeed three times the standard deviation of the noise.

To evaluate opening of the ET, the children were instructed to swallow some water at intervals of 10 seconds in the sitting position. After a session of 10 acts of swallowing, the microphone and the sound source were removed to give the children a short break. Then to test reproducibility, the equipment was replaced and the second measurements were taken in an identical manner.

The number of positive recordings from 10 acts of swallowing was the outcome of the test and could range from 0-10. Reproducibility of the number of peaks in the two sessions (test and retest) was tested by means of Spearman's correlation coefficient.

Results

Figure 2 shows the results of the two sonotubometric measurement sessions. The ET opened in at least one of the two measurement sessions in 51 out of the 61 (82%) children. In 10 cases, the ET did not open in either of the sessions. The number of times that the ET opened varied from 0 to 10 in each session. Mean number of times was 3.7 (SD=3.5).

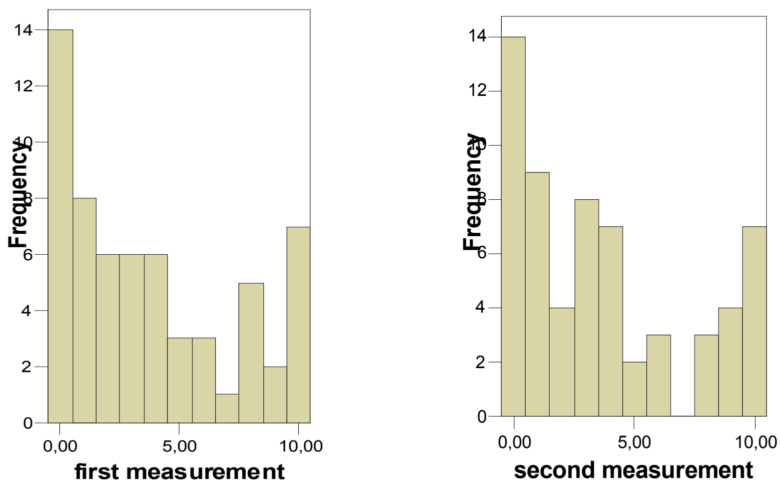

Figure 2. A and B represent the first and the second measurement sessions,respectivily. Number of times the ET opened is shown on the X axis, number of children (N=61) on the Y axis.

Figure 3 shows the reproducibility of the test. Spearman's correlation coefficient was 0.89. In 33 out of the 61 cases (54%) there was no difference in the number of times that the ET opened between the first session and the second session. In

19 cases (30%) there was a difference of only one. In 10 cases (16%) there was a difference of 2 or more, with a maximum of 5.
The test was simple to perform and well-tolerated by all the children.

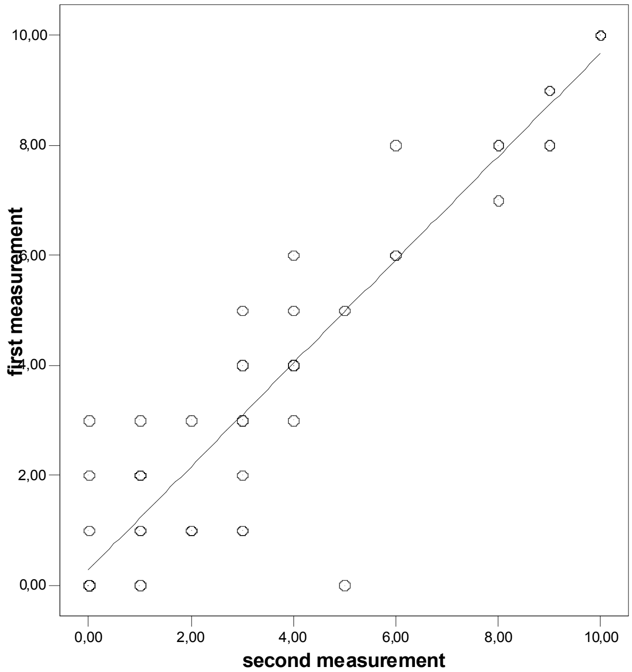

Figure 3. Reproducibility is represented in this figure. On the y-as the first measurement, on the x-as the second measurement. One dot represents one or more test persons. The line represents the mean of all the test persons.

Discussion

The purpose of this study was to test an upgraded sonotubometer in otologically healthy children and to assess the reproducibility of the measurements.
In a previous study, we tested whether the revised set-up was a feasible and reproducible method to measure ET ventilatory function in otologically healthy adults. Recordings showed that the ET opened in 92% of the population and that reproducibility was high (Spearman's coefficient = 0.91).
In the current study, we demonstrated that sonotubometry was also highly feasible in otologically healthy primary school children. In 82% of the children, the recordings showed that the ET opened in at least one of the two measurement sessions. In the remaining 18%, non of the recordings showed tubal openings, which might indicate poorer ventilatory Eustachian tube function, or far less frequent opening than in the other 82%. The responses were comparable with those found by other authors in stusies on children[14,19]. In the vast majority of our otologically healthy children, the ET did open, but the frequency was sometimes low. However, Spearman's coefficient of 0.89 demonstrated that the results

obtained with our sonotubometry set-up were highly reproducible in this study population. This is in accordance with our findings in adults in an earlier study.
It was interesting to note that in 10 children, the ET did not open in either test session despite their negative otological history and normal otoscopy findings. There are several possible explanations for this. First, even a low incidence of measurable opening of the ET during the act of swallowing may be sufficient to ensure normal aeration of the middle ear. Second, ET dysfunction may not necessarily lead to middle ear problems. In other words, although sonotubometry might be a good manner to assess ET ventilatory function, ET functioning might not be a good means to study OME-prone children, because the pathogenesis of OME is considered to be being multifactorial.
To record an even higher incidence of tubal opening in these otologically healthy children, it might be worthwhile to increase the number of acts of swallowing, so that more children show ET opening at least once and fewer children have negative results. However, all the studies listed in the table showed a substantial percentage of otologically healthy subjects with poor outcomes, which suggests that this is a physiological phenomenon.
In clinical practice, forms apotential physiological test to assess ET function in ears with an intact tympanic membrane. Additional research is needed to evaluate the validity of sonotubometry and to determine the clinical applicability of this test method. Further studies should focus on children with various otological health states to substantiate the value of sonotubometry as a routine test in outpatient clinic ENT consultations.

References

1. Bluestone CD, Paradise JL, Beery QC. Physiology of the Eustachian tube in the pathogenesis and management of the middle ear effusions. The Laryngoscope 1972; July: 1654-1670
2. Bluestone CD. Pathogenesis of otitis media; role of the Eustachian tube. Pediatr Infect Dis J 1996; 15: 281-291
3. Bluestone CD, Hebda PA, Alper CM, Sando I, Buchman CA, Stangerup SE, Felding JU, Swarts JD, Ghadiali SN, Takahashi H. Recent advances in otitis media; Eustachian tube, Middle ear, and mastoid anatomy; Physiology, pathofysiology, and pathogenesis. Otol Rhinol Laryngol Suppl. 2005 jan;194:16-30
4. Bluestone CD, Paradise JL, Beery QC. Physiology of the Eustachian tube in the pathogenesis and management of the middle ear effusions. The Laryngoscope 1972; july: 1654-1670
5. Sadé J. The nasopharynx eustachian tube and otitis media. J Laryngol Otol 1994; 108:95-100
6. Straetemans M, van Heerbeek N, Tonnaer E, Ingels K, Rijkers GT, Zielhuis GA. A comprehensive model for the aetiology of otitis media with effusion. Medical Hypotheses. 2001;57:784-791
7. Sadé J, Ar A. Middle ear and auditory tube: Middle ear clearance, gas exchange and pressure regulation. Otolaryngology Head and Neck Surgery 1997; 116:499-524

8. Van Heerbeek N, Ingels KJ, Snik AF, Zielhuis GA. Reliability of manometric Eustachian tube function tests in children. Otol Neurotol 2001; 22:183-7
9. Bylander A, Tjernstrom O, Ivarsson A. Pressure opening and closing functions of the Eustachian tube in children and adults with normal ears. Acta Otolaryngol 1983; 95:55-62
10. Falk B, Magnuson B. Test-retest variability of the Eustachian tube responses in children with persistent middle ear effusion. Arch Otorhinolaryngol 1984;240:145-52
11. Groth P, Ivarsson A, Tjernstrom O. Reliability in tests of the Eustachian tube function. Acta Laryngol 1982; 93:261-7
12. Charles D Bluestone MD, E.I. Cantekin PhD. Current clinical methods, indications and interpretation of Eustachian tube function tests. Ann Otol Rhinol Laryngol. 1981 Nov-Dec; 90(6 Pt 1):552-62
13. Holmquist J, Björkman G, Olén L. Measurement of Eustachian tube function using sonotubometry. Scand Audiol 1981; 10:33-35
14. Okubo J, Watanabe I, Shibusawa M, Ishikawa N, Ishida H, Teramura K. Sonotubometric measurement of the Eustachian tube function by means of band noise; a clinical view of the acoustic measurement of the Eustachian tube. ORL J Otorhinolaryngol Relat Spec 1987; 49(5): 242-245
15. T. Palva, T. Marttila, T. Jauhiainen. Comparison of pure tones and noise stimuli in sonotubometry. Acta Otolaryngol (Stockholm) 1987; 103:212-216
16. Jonathan DA. The predictive value of Eustachian tube function (measured with sonotubometry) in the successful outcome of myringoplasty. Clin Otolaryngol 1990; 15:431-434
17. Virtanen H. Relation of the body posture to the Eustachian tube function. Acta Otolaryngol 1983 Jan-Feb (1-2): 63-67.
18. Van der Avoort S, Van Heerbeek N, Zielhuis G, Cremers C. Sonotubometry Eustachian tube ventilatory function test; a review. Otol Neurotol. 2005 May;26(3):538-43
19. Munro KJ, Benton CL, Marchbanks RJ. Sonotubometry findings in children at high risk from middle ear effusion. Clin Otolaryngol Allied Sci. 1999 Jun;24(3):223-7.
20. Murti KG, Stern RM, Cantekin EI, Bluestone CD. Sonometric evaluation of eustachian tube function using broadband stimuli. Ann Otol Rhinol Laryngol Suppl. 1980 May-Jun;89(3 Pt 2):178-84.
21. McBride TP, Derkay CS, Cunningham MJ, Doyle WJ. Evaluation of noninvasive eustachian tube function tests in normal adults. Laryngoscope. 1988 Jun;98(6 Pt 1):655-8.
22. Tecca JE. Clinical application of real ear probe tube measurement. In Sandlin RE (ed.) Handbook of hearing aid amplification, Vol II. Clinical considerations and fitting practices. Singular Pub Group Inc, San Diego, 1995:225-256

5

Results of sonotubometry in testing Eustachian tube ventilatory function in cleft palate children

Stijn J.C. van der Avoort
Niels van Heerbeek
Ronald J.C. Admiraal
Gerhard A. Zielhuis
Cor W.R.J. Cremers

Submitted

Abstract

Background:

In previous studies an updated sonotubometry set-up was tested in healthy adults and children to test its validity and reproducibility in the assessment of ventilatory function of the Eustachian tube (ET). These results were promising but further investigations were needed to confirm the discriminative potential of this sonotubometry set-up.

Objectives:

To test the discriminative potential of an updated sonotubometry set-up in children with cleft palates.

Methods:

ET ventilatory function was tested in 56 children with cleft palate, i.e. children with impaired ET function, and compared to the outcomes in 61 healthy children who served as a control group. All the children were aged from 5 to 9 years. To test reproducibility, sonotubometric testing took place in two sessions of 10 acts of swallowing each. Spearman's coefficient was used to test the correlation between the two sets of measurements. The results of measurements in the cleft palate group were compared with those in the otologically healthy control group and analyzed by means of Mann Whitney U test.

Results:

Opening of the ET was recorded in at least one of the two measurement sessions in 57% of the cleft palate children, whereas this was 82 % in the control group. The mean number of openings was lower in the cleft palate group than in the control group (respectively 2.3 vs 3.7 out of 10, $p<0.01$). The first and second sessions were highly correlated in both the cleft palate group and the control group, with a Spearman's coefficient of respectivily 0.96 and 0.89.

Conclusions:

The results of this study show that this updated sonotubometry set-up has the potential to discriminate between these groups of children with various states of Eustachian tube (ET) ventilatory function. Furthermore the results of this study once again show that this updated sonotubometry set-up is capable to assess Eustachian tube (ET) ventilatory function in both healthy children and children with cleft palate and that the measurements are highly reproducible. A persistent disadvantage remains that in 18 % of the 61 healthy children there was a negative outcome, which still prohibits a definite assessment at the individual level.

Introduction

The most important functions of Eustachian tube are ventilation, protection and clearance of the middle ear[1,2]. Continuous gas exchange between the tympanic cavity and the middle ear mucosa and regular active opening of the Eustachian tube allows ventilation of the middle ear and equilibration of pressure differences. A disturbance of Eustachian tube (ET) function is assumed to contribute to the developement of otitis media with effusion (OME) and other middle ear diseases[3-11]. The ability to measure Eustachian tube ventilatory function will provide further insight into the etiology of these middle ear diseases and may contribute to the development of new causative therapies. So far all the methods to measure Eustachian tube (ET) function have either been insufficiently specific and/or sensitive or were less physiologic, like the manometric Eustachian tube (ET) function tests. S*onotubometry* has several advantages over the manometric Eustachian tube function tests[12-16].

Sonotubometry[17-28] is based on the principle that sound applied to the naso-pharyngeal ostium of the Eustachian tube (ET) is conducted through the Eustachian tube (ET) to the middle ear during opening of the ET.

The main advantage is that sonotubometry is performed under physiological circumstances, i.e. without applying unphysiological pressures to the middle ear. In addition, it can be performed on ears with an intact tympanic membrane and it is well-tolerated by both adults and children. Earlier studies[17-28] in the nineteensixties and seventies could not confirm sonotubometry to be a clinically usefull means to test Eustachian tube ventilatory function. Recently, the test method has been studied again using modern and more sensitive microphones and sound sources[29,30]. These technical improvements resulted in a high sensivity to record tubal opening in otologically healthy adults and children and more important a great reproducibility, but in spite of these improvements of this test method sonotubometry needs further validation in children of various degrees of ET function. The power to discriminate between groups of various states of Eustachian tube ventilatory function is important in clinical practice because this could possibly help to choose the best therapies with respect to middle ear diseases.

As pointed out above, the Eustachian tube allows ventilation of the middle ear by active opening of the Eustachian tube, which is accomplished during swallowing, yawning or movement of the mandible by the contraction of the paratubal muscles; the tensor veli palatini muscle, the levator veli palatini muscle, the salpingo-pharyngeus muscle and the tensor tympani muscle.

The tensor veli palatini muscle originates from the superior cartilage and the lateral fibrous wall of the ET, bends round the pterygoid process and continues as the palatal aponeurosis. The tensor veli palatini muscle is considered to be the main dilatator of the ET. The levator palatini muscle that partially originates from the medial portion of the ET cartilage and inserts into the soft palate is supposed to support the ET opening. The salpingopharyngeus muscle, running from the medial cartilaginous wall to the pharyngeal wall, and the tensor tympany muscle that is continuous with the tensor veli palatini muscle are relatively small and only seem to play a marginal role in the Eustachian tube opening[31-33].

Cleft palate children have high rates of otitis media with effusion which is considered to be caused by disturbance of ET ventilation function because of the altered position of the paratubal muscles[38,39]. At the same time less velopharyngeal closure during acts of swallowing leads to oronasal reflux, causing mucosal irritation and edema in the nasopharynx leading to disturbance in Eustachian tube opening[34,35]. Surgical intervention is routinely performed between 12 and 18 months and has two targets. First target is physical closure of the cleft to improve velopharyngeal closure and second target is paratubal muscle realignment to improve opening of the Eustachian tube. Despite this surgical intervention, Eustachian tube dysfunction, often leading to OME, remains a problem in patients with cleft palate because of muscle histology and contractility properties[36,37]. About one third of cleft palate children will show in the long run the sequelae of a chronic otitis[40].

The aim of this study is to compare the sonotubometric measurements in children with a (repaired) cleft palate and a control group of otologically healthy children to test the discriminative power of our updated sonotubometry set-up and its reproducibility.

Our first hypothesis is that children with cleft palate have a poorer ET ventilatory function and therefore less children will show openings of the Eustachian tube compared with a control group of children who are apparently healthy. The second hypothesis is that the cleft palate children show a lower mean number of openings compared with the healthy controls.

Methods and materials

The study population consisted of 56 children with cleft palate, aged 5 to 9 years (mean age 6,6 yrs.). The children were recruited from a database of cleft palate patients treated by a multi diciplinar schisis team in the University Medical Centre Nijmegen. Thirty-nine children in the past underwent surgical repair of a

cheilopalatoschisis, 9 patients of a palatoschisis and 2 patients underwent reconstructive surgery because of an isolated cheiloschisis. Six children had a submucosal incomplete palatoschisis at birth without surgical correction. For the analysis of the data of this study, the two children with isolated cheiloschisis were excluded because technically these children do not have a cleft palate so this would interfere with the results of the study. Most of the children had a history of otitis media with effusion in the past with treatment by grommet insertion (average number of times of grommet insertion was 2,1). By use of otoscopy only children with well aerated middle ears at the moment of testing (with or without grommets) were included for this study.
A control group of 61 otologically healthy children aged 6 to 8 years (mean age 6.7 yrs.), was recruited from a primary school in a nearby village. A questionnaire with 12 items on medical history was used to exclude children with an history of OME, grommet insertion or other ear surgery from participation in this study. Children were also excluded when otoscopy showed signs of middle ear disease, retraction of the tympanic membrane or OME. Also children who had a cold at the moment of testing were excluded. The control group was tested as a separate study previous to the cleft palate study population and measurements took place in the same season[30]. The patients' parents signed an informed consent form agreeing to participation in this study.
Adults and children were tested in our previous studies as in this cleft palate children study with an updated sonotubometer as described earlier[29,30]. High frequency narrow band noise; the test signal comprised filtered white noise with a center frequency of 7 kHz, bandwith of 5.5 to 8.5 kHz and slopes of 12 dB/octave, was used. This test signal was delivered to the nasopharyngeal ostium using an Ear Tone 3A insert phone (Auditory Systems, Indianapolis, USA) that was fixed with a foam ear tip in one of the nostrils. A probe tube microphone (Etymotic Research-7c, Ilinois, USA) was placed in the ipsilateral external auditory canal and fixed with a foam ear tip to minimize interference with the air-borne test signal. The microphone output was amplified, digitally band-pass filtered (from 5.5 to 8.5 kHz) and displayed as a function of time. The loudness level of the test signal was fixed at 90 dB SPL, as measured in the nostril with the (calibrated) probe tube microphone during pilot experiments. This level was chozen because the test signal had to be loud enough to be detected by the probe microphone in the external ear canal during ET opening, however, the test signal should not be too loud to prevent direct air-borne stimulation of the microphone. According to the specifications, the foam ear tips used to connect the telphone to the nostril and to position the probe tube microphone to the ear canal attenuate sounds in the 6-8

kHz range by 40 dB each. Therefore, the direct air-borne stimulation of the microphone was negligible.
Additional measurements were carried out to study the time course of the intensity of the test signal in the nose during swallowing. Therefore, the probe tube microphone and the sound source were placed in the same nostril. During swallowing the sound pressure level was measured after bandpass filtering as described above. No change in sound pressure level was detected in the nose during swallowing. This means that the present set-up is free of artefacts that might have occurred by either sounds of swallowing or sound pressure changes that are caused by changes in the acoustical conditions in the nose during swallowing.
Positive peaks in the microphone recordings in the ear canal were identified from the registrations first of all by on-line marking peaks that occurred during the act of swallowing. Secondly, off-line, the difference in microphone output between a possible peak and baseline was tested for significance. Thereto from a characteristic period in between swallowings, the noise level was determined by calculating the standard deviation from the baseline of the sampled noise amplitude. To be counted as an opening of the ET the level of the peak had to exceed three times the standard deviation of the noise.
To evaluate opening of the ET, all the children were instructed to swallow some water at intervals of 10 seconds in sitting position. After a session of 10 acts of swallowing, the microphone and the sound source were removed to give the children a short break of 5 minutes. Than the equipment was replaced and the second session of measurements was taken in an identical manner, to test reproducibility.
The number of positive recordings out of 10 acts of swallowing was the outcome of the test and could range from 0-10. Low values indicated poor ET ventilatory function, whereas high values corresponded with good ventilatory function. Reproducibility of the measurements was tested by means of Spearman's correlation coefficient. The mean number of openings in both groups was compared and analyzed in SPSS 12.0.1. As data were not assumed to be normally distributed, a non parametric equivalent to the t-test was used (Mann Whitney U-test).

Results

Figure 1 shows the results of the measurements in the cleft palate group and the healthy control group (figure 1).

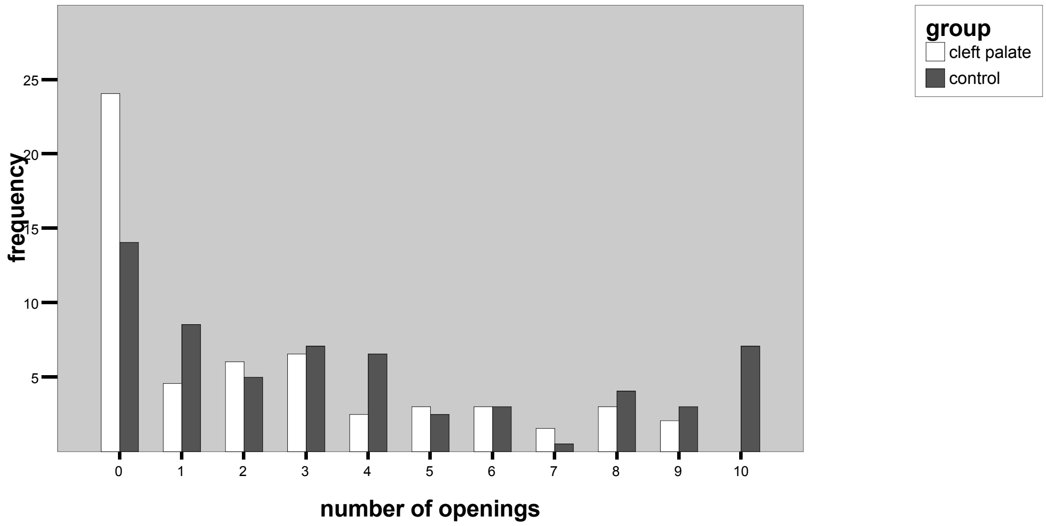

Figure 1. Rrepresents the mean results of first and second measurement sessions in the cleft palate and the controls. Number of times the ET opened is shown on the X axis, number of children on the Y axis.

The ET opened in at least one of the two measurement sessions in 32 out of the 56 (57%) cleft palate children . In the control group the incidence of opening was 51 out of 61 (82%) children[30]. The mean number of times (+SD) that the ET opened out of 10 acts of swallowing was significantly ($p<0.01$) lower in the cleft palate group (mean 2.3; SD 2.8) than in the control group (mean 3.7; 3.5) (table 1). Sensitivity and specificity of the test method was evaluated by means of a ROC Curve (Area Under Curve was 0.65).

Within the cleft palate group the number of openings varied with the type of cleft (table 2). Children with an isolated cheiloschisis (n=2) or a submucosal incomplete palatoschisis (n=6) showed even more openings than the controls. By contrast children with a repaired palatoschisis (n=9) or a cheilognathopalatoschisis (n=39) showed a much lower number of openings: means are 2.7 and 1.4 respectively. Statistical analysis, however, showed no significance. None of the cleft palate cases showed 10 registered openings out of 10 acts of swallowing, while this occurred in 8 out of the 61 healthy controls.

Reproducibility of the measurements both in the cleft palate population and in the control population was very high: Spearman's correlation coefficient 0.96 and 0.89 respectively.

Table 1. Number of openings out of 10 acts of swallowing for sonotubometry in the cleft palate group and in the healthy control group.

Group	N	Mean	Std. deviation	P-value (Mann Whitney Ut-test)
Controls	61	3,7	3,5	<0.01
Cleft palate	54	2,3	2,8	

Table 2. Results of the measurements in the cleft palate group, organized in subgroups of extensiveness of the cleft. Mean number of registered openings out of 10 acts of swallowing are compared with the controls.

Group	N=	Mean number of opening
Cheilognatopalatoschisis	39	1.4
Palatoschisis	9	2.7
Submucosal palatoschisis	6	5.6
Isolated cheiloschisis	2	4.5
Controls	61	3.7

In 30 out of the 56 (54%) cases the number of openings in both measurements was exactly the same. No difference of more than two openings between both measurements was noted.

All measurements were performed quite easily, were well tolerated and never took more time than 15 minutes for both measurement series.

Discussion and conclusions

In previous studies we tested whether a revised set-up for sonotubometry was a feasible and reproducible method to assess Eustachian tube ventilatory function in otologically healthy adults and children[29,30]. Recordings showed that the ET opened respectively in 92% and 82% of otologically healthy adults and children. The measurements were highly reproducible with Spearman's coefficient of 0.91 in adults and 0.89 in children.

The aim of present study was to test discriminative potential of our revised sonotubometry test set-up. For that purpose we have performed sonotubometric tests on children with a cleft palate, because many children with a cleft palate are considered to have a poorer ET ventilatory function[38,39]. As pointed out in the introduction muscle insertion, muscle histology, muscle contraction and oronasal reflux are held responsible for this difference. The results of the measurements in the cleft palate group were compared with the results of measurements in a otologically healthy control group.

Recordings in the cleft palate group showed that approximately half of the children do not have an opening at all when attempted 10 times. In the healthy control group this is less than 20%. This confirmes that there is an important difference in ET openings between both the palatoschizis group and the healthy controls. In addition the mean number of registered openings of the ET out of 10 acts of swallowing is substantially lower in the cleft palate group compared to the control group. This confirms the less good functioning of ET opening in the palatoschisis individuals. Moreover individuals with a more severe cleft palate disorder, i.e. a total cheilognatopalatoschisis or palatoschisis showed poorer ventilatory function of the ET than individuals with less severe schisis (table 2). These results are in accordance with the fact that in the less severe types of the cleft, the paratubal muscles are considered to be less affected and there would be less or no velo-pharyngeal incompetence. Statistical analysis showed no significance probably because these subgroups in the cleft palate population are small.The difference might be due to chance.

In both the study group and the controls the measurements were easy tolerated and highly reproducible. This is in accordance with our earlier findings in previous studies.

The results of this study show that this updated sonotubometry set-up is capable to assess ET ventilatory function in both healthy children and children with cleft palate and that the measurements are reproducible. Besides, this study suggests that this updated sonotubometry set-up indeed has the potential to discriminate between groups of children with various states of ET ventilatory function. The test set-up still needs to be improved to decrease the percentage of negative outcomes, possibly by extending the test series of acts of swallowing too. Evaluation of the results by means of a ROC Curve showed an area under curve of 0.65. Therefore it it is not possible to choose a cutoff value of number of openings with a acceptable sensitivity and specificity to devide a population into two different categories, i.e. children with cleft palate and normal controls, by means of this sonotubometry test set-up. Possibly this is a result of the fact that 18% of the healthy controls do not show openings of the ET measured with sonotubometry and on the other hand there are children with cleft palate that do show openings, so the borderline between these groups is not a sharp line but more vague. Besides, not every child with cleft palate will suffer from otitis media with effusion.

Nevertheless the results of this study suggests that in the near future sonotubometry might be of clinical value. This is particular relevant as still no good functional test for ET ventilatory status exists in daily ENT practice.

Although the present study is a step forwards, the applicability of sonotubometry in daily practice needs further evaluation. Related to the cleft palate group it would be of interest to know whether the non-responders have a much higher risk to develop a chronic otitis media compared to the ones showing Eustachian tube openings. Long term prospective studies in these patient groups are needed to evaluate this. An even more sensitive sonotubometric test setting could be of help in solving this question. Other questions that remain are whether additional changes in sonotubometric test-setting could provide even more valid and valuable measurements of ET function in patients with otitis media with effusion and whether sonotubometry could be of help to predict the outcome of ear surgery like the closure succes rate of myringoplasties. Further research on this Eustachian tube ventilatory function test is ongoing, the results of which will be necessary to further improve this sonotubometric device, necessary to successfully introduce it in ENT clinical practice.

References

1. Bluestone CD, Paradise JL, Beery QC. Physiology of the Eustachian tube in the pathogenesis and management of the middle ear effusions. The Laryngoscope 1972; July: 1654-1670
2. Bluestone CD. Pathogenesis of otitis media; role of the Eustachian tube. Pediatr Infect Dis J 1996; 15: 281-291
3. Takahaski M, Takahaski H, Sato H, Honjo I. Primary deficits in the Eustachian tube function in patients with otitis media with effusion. Arch Otolaryngol Head Neck Surg 1989; 115:581-584
4. Stenstrom C, Bylander Groth A, Ingvarsson L. Eustachian tube function in otitis prone and healthy children. Int J Pediatr Otorhinolaryngol 1991; 21:127-138
5. Bylander Groth A, Stenstrom C. Eustachian tube function and otitis media in children. Ear Nose Throat J 1998; 77:762-769
6. Bluestone CD, Paradise JL, Beery QC. Physiology of the Eustachian tube in the pathogenesis and management of the middle ear effusions. The Laryngoscope 1972; july: 1654-1670
7. Sadé J. Pathology and pathogenesis of secretory otitis media. Arch otolaryngol 1966; 84:297-305
8. Sadé J. The nasopharynx eustachian tube and otitis media. J Laryngol Otol 1994; 108:95-100
9. Maw RA. Glue ear in childhood. Cambridge: Mac Keit Press & Cambridge University Press, 1995
10. Virtanen H, Palva T. The patulous Eustachian tube and chronic middle ear disease. Acta Otolaryngol 1982; 93:49
11. Sadé J, Ar A. Middle ear and auditory tube: Middle ear clearance, gas exchange and pressure regulation. Otolaryngology Head and Neck Surgery 1997; 116:499-524
12. Van Heerbeek N, Ingels KJ, Snik AF, Zielhuis GA. Reliability of manometric Eustachian tube function tests in children. Otol Neurotol 2001; 22:183-7
13. Bylander A, Tjernstrom O, Ivarsson A. Pressure opening and closing functions of the Eustachian tube in children and adults with normal ears. Acta Otolaryngol 1983; 95:55-62
14. Falk B, Magnuson B. Test-retest variability of the eustachian tube responses in children with persistent middle ear effusion. Arch Otorhinolaryngol 1984;240:145-52
15. Groth P, Ivarsson A, Tjernstrom O. Reliability in tests of the Eustachian tube function. Acta Laryngol 1982; 93:261-7

16. Charles D Bluestone MD, E.I. Cantekin PhD. Current clinical methods, indications and interpretation of Eustachian tube function tests. Pittsburgh Pennsylvania. Presented at the meeting of the American Otology Society, Inc, Vancouver Colombia, may 9-10,1981
17. Virtanen H. Sonotubometry, an acoustical method for objective measurement of auditory tubal opening. Acta Otolaryngol 1978; 86:93-103
18. Holmquist J, Björkman G, Olén L. Measurement of Eustachian tube function using sonotubometry. Scand Audiol 1981; 10:33-35
19. Jonathan DA, Chalmers P, Wong K. Comparison of sonotubometry with tympanometry to assess Eustachian tube function in adults. Br J Audiol 1986 aug; 20(3):231-235
20. Jonathan DA. Sonotubometry: its role in childhood glue ear. Clin Otolaryngol 1989; 14:151-154
21. Okubo J, Watanabe I, Shibusawa M, Ishikawa N, Ishida H, Teramura K. Sonotubometric measurement of the Eustachian tube function by means of band noise; a clinical view of the acoustic measurement of the Eustachian tube. ORL J Otorhinolaryngol Relat Spec 1987; 49(5): 242-245
22. Palva T, Marttila T, Jauhiainen T. Comparison of pure tones and noise stimuli in sonotubometry. Acta Otolaryngol (Stockholm) 1987; 103:212-216
23. Jonathan DA. The predictive value of Eustachian tube function (measured with sonotubometry) in the successful outcome of myringoplasty. Clin Otolaryngol 1990; 15:431-434
24. McBride T, Cunningham M, Derkay C, Doyle W. Evaluation of non-invasive Eustachian tube function tests in normal adults. Laryngoscope 98: June 1988; 655-658
25. Virtanen H. Relation of the body posture to the Eustachian tube function. Acta Otolaryngol 1983 Jan-Feb (1-2): 63-67
26. Leider J, Hamlet S, Schwan S. The effect of swallowing bolus and head position on Eustachian tube function via sonotubometry. Otolaryngol Head Neck Surgery 1993; 109(1): 66-70
27. Iwano T, Ushiro K, Yukawa N, Doi T, Kinoshita T, Hamada E, Kumazawa T. Active opening function of the human Eustachian tube: comparison between sonotubometry and pressure equilibraton test. Acta Otolaryngol 1993; 500:62-65
28. Van der Avoort S, Van Heerbeek N, Zielhuis G, Cremers C. Sonotubometry – Eustachian tube ventilatory function test, a review. Otol Neurotol. 2005; 26(3):538-43
29. Van der Avoort S, Van Heerbeek N, Zielhuis G, Cremers C. Reproducibility of sonotubometry in healthy adults. J Otol.Laryngol. 2006; 120(10):853-856.
30. Van der Avoort S, Van Heerbeek N, Zielhuis G, Cremers C. Reproducibility of sonotubometry as Eustachian tube ventilatory function test in healthy children. Int J Ped ORL 2006; in press.
31. Prades JM, Dumollard JM, Calloch F et al. Descriptive anatomy of the human auditory tube. Surg Radiol Anat 1998;20:335-340
32. Huang MH, Lee ST, Rajendran K. A fresh cadaveric study of the paratubal muscles: implications for eustachian tune function in cleft palates. Plast Reconstr Surg 1997;100:833-842
33. Swarts JD, Rood SR. The morphometry and three-dimensional structure of the adult Eustachian tube: implications for function. Cleft Palate J 1990;27:374-381
34. Doyle WJ, Reilly JS, Jardini L, Rovnak S. Effect of palatoplasty on the Eustachian tube in children with cleft palate. Clft palate J. 1986;23:63-
35. Spauwen P, Ritsma R, Huffstadt B, Schutte H, Brown I. The inferiorly based pharyngoplasty: effects on chronic otitis media with effusion. Cleft palte J. 1988;25:26-32
36. Guneren E, Ozsoy Z, Ulay M, Eryilmaz E, Ozkul H, Geary PM. A comparison of the effects of Veau-Wardill-Kilner palatoplasty and furlow double-opposing Z-plasty operations on eustachian tube function. Cleft Palate Craniofac J. 2000 May;37(3):266-70
37. Schendel SA, Cholon A, Delaire J, histochemical analysis of cleft palate muscle. Plast Reconstr Surg. 1994;94:919-923
38. Bluestone CD, Wittel RA, paradise JL. Roentgenographic evaluation of Eustachian tube function in infants with cleft palate and normal palates. Cleft Palate J 1972;9:93-100
39. Doyle WJ, Cantekin EI, Bluestone CD. Eustachian tube function in cleft paltate children. Ann Otol Rhinol Laryngol 1980;89(suppl)34-40
40. Robinson PJ, Lodge S, Jones BM, et al..The effect of palate repair on otitis media with effusion. Plast Reconstr Surg. 1992 Apr;89(4):640-5

6

Results of sonotubometry in children with OME before and after insertion of ventilation tubes

Stijn J.C. van der Avoort
Niels van Heerbeek
Joost A.M. Engel
Gerhard A. Zielhuis
Cor W.R.J. Cremers

Submitted

Abstract

Background:

Frequent active opening of the Eustachian tube is assumed to contribute to equilibration of pressure differences between ambient pressure and middle ear pressure and partly to the ventilation of the middle ear. Malfunction of the Eustachian tube may be instrumental in the development of otitis media with effusion. Sonotubometry is a method to measure Eustachian tube ventilatory function with a closed tympanic membrane. A recently updated sonotubometry set-up has proven to be a reproducible method to measure the Eustachian tube ventilatory function in healthy adults and children.

Objectives:

To test the outcome of sonotubometry in children with otitis media with effusion before and after insertion of ventilating tubes.

Design:

Eustachian tube ventilatory function was tested in 33 children with otitis media with effusion. To test validity, sonotubometric testing took place before insertion of ventilating tubes (i.e. middle ear filled with glue) and one week and three months after grommet insertion (i.e. aerated middle ear). One set of measurements existed of 10 acts of swallowing. The outcomes of the tests were compared to those in otologically healthy controls (n=61).

Settings:

All testing took place at a outpatient clinic ENT consultation in a city hospital.

Results:

Less openings of the Eustachian tube were recorded in the measurements before insertion of ventilating tubes compared with after insertion. The number of registered openings after insertion of ventilating tubes did not significantly differ from measurements in healthy controls.

Conclusions:

Sonotubometric testing in children with glue ears shows a lower incidence of Eustachian tube opening. Shortly after insertion of ventilating tubes sonotubometry shows no difference in ET ventilatory function compared to measurements in healthy controls. Sonotubometry is not a adequate test method to test Eustachian tube ventilatory function in glue ears.

Introduction

Otitis media with effusion (OME) is a common disease during childhood. Before the age of 4 years, almost every child suffers from at least one period of otitis media with effusion (OME)[1]. As a result of this high incidence of otitis media with effusion (OME) it has become the most frequent indication for surgical intervention, like myringotomy, insertion of ventilation tubes and adenoidectomy, in young children[2-4]. Disturbance of Eustachian tube (ET) function is assumed to play an important role in the development of otitis media with effusion (OME)[5-8]. Other factors involved include viral and bacterial exposure and a deficient or immature immune status. One of the functions of the Eustachian tube (ET) is equillibration of pressure changes in the middle ear[9,10]. In rest, the tube is normally closed but regular active opening due to contraction of the paratubal muscles allows this equillibration of pressure changes and ventilation.

Earlier studies concluded that poor Eustachian tube (ET) function is more a causal factor than a result of otitis media with effusion (OME), because both active and passive opening function of the Eustachian tube (ET), did not improve after grommet insertion, but remained at the same poor level after three months[11]. Apparently, some children like children with palatoschisis have poorer Eustachian tube (ET) ventilatory function, which makes them more susceptible for the development of otitis media with effusion (OME), and maybe to other middle ear diseases, than children with good ET function .

Unfortunately in daily ENT practice there is no valid test available to assess ET ventilatory function. ET function has been studied extensively using manometric function tests[12-16] and sonotubometry[17-22], but neither proved to be satisfactory so far. Sonotubometry has several advantages over the other function tests[22]. The main advantage is that sonotubometry is performed under physiological circumstances, i.e. without applying unphysiological pressures to the middle ear. In addition, it can be performed on ears with an intact tympanic membrane and it is well-tolerated by adults and children. Sonotubometry is based on the principle that sound applied to the nasopharyngeal ostium of the Eustachian tube (ET) is conducted through the Eustachian tube (ET) to the middle ear. During active opening of the ET, more sound will be conducted, which means that higher levels of sound can be recorded in the external auditory canal. Recently, the test method has been studied again using modern and more sensitive microphones and sound sources. These technical improvements resulted in high sensivity to record tubal opening in otologically healthy adults and children with reproducible results. Because decreased ET ventilatory functioning is considered to be one of the

factors contributing to OME, it might be of value to test this method in children with OME before and after insertion of ventilation tubes.
The aim of this study was to evaluate whether ET ventilatory function can be measured in children with OME by means of sonotubometry. The outcomes of sonotubometric measurements before and after insertion of ventilating tubes are compared. The outcomes of these measurements are also compared to results of an earlier sonotubometry study in otologically healthy children[23].

Patients and methods

A group of children (n=33) who were attending an outpatient clinic ENT consultation and were diagnosed with OME were included in the study. OME was confirmed by means of history taking, otoscopic findings, audiometry (30-40 dB conductive hearing loss) and tympanometry (type B). The children were aged between 4 and 9 years with a mean age of 5 years and 8 months at the time of the first measurements. All the children were planned for surgical grommet insertion. Before they underwent this intervention, each child was tested by means of an updated sonotubometer[23] on the side with the worst audiogram. One week after grommet insertion the position of the grommets and aeration of the middle ear were checked, and the measurements with the sonotubometer were repeated in an identical manner as before by the same investigator. The same procedure was also repeated 3 months after grommet insertion.
The sonotubometer used in this study has been described in our earlier studies[23] and has specific properties. To minimize interference with sounds that occurred during swallowing, the test tone should be of high frequency, above 5 kHz. However, such high-frequency pure tones might cause standing waves in the occluded external ear canal, compromizing probe tube microphone measurements. Therefore, we applied high frequency narrow band noise instead; the test signal comprised filtered white noise with a center frequency of 7 kHz, bandwidth of 5.5 to 8.5 kHz and slopes of 48 dB/octave. This test signal was delivered to the nasopharyngeal ostium using an Ear Tone 3A insert phone (Auditory Systems, Indianapolis, USA) that was fixed with a foam ear tip in one of the nostrils. A probe tube microphone (Etymotic Research-7c, Ilinois, USA) was placed in the ipsilateral external auditory canal and fixed with a foam ear tip to minimize interference with the air-borne test signal. The microphone output was amplified, digitally band-pass filtered (from 5.5 to 8.5 kHz) and displayed as a function of time.
The loudness level of the test signal was fixed at 90 dB SPL, as measured in the nostril with the (calibrated) probe tube microphone during pilot experiments. This

level was chozen because the test signal had to be loud enough to be detected by the probe microphone in the external ear canal during ET opening, however, the test signal should not be too loud to prevent direct air-borne stimulation of the microphone. According to the specifications, the foam ear tips used to connect the telphone to the nostril and to position the probe tube microphone to the ear canal attenuate sounds in the 6-8 kHz range by 40 dB each. Therefore, the direct air-borne stimulation of the microphone was considered as negligible.

Additional measurements were carried out to study the time course of the intensity of the test signal in the nose during swallowing. Therefore the microphone and the sound source were placed in the same nostril. During swallowing the sound pressure level was measured after band-pass filtering as described above. No change in sound pressure level was detected in the nose during swallowing. This means that the present set-up is free of artefacts that might have occurred by either sounds of swallowing or sound pressure changes that might have occurred caused by changes in the acoustical conditions in the nose during swallowing.

Positive peaks in the microphone recordings in the ear canal were identified from the registrations first of all by on-line marking peaks that occurred during the act of swallowing. Secondly, off-line, the difference in microphone output between a possible peak and baseline was tested for significance. Thereto from a characteristic period in between swallowings, the noise level was determined by calculating the standard deviation from the baseline of the sampled noise amplitude. To be counted as an opening of the ET the level of the peak had to exceed three times the standard deviation of the noise.

To evaluate opening of the ET, all the children were instructed to swallow some water at intervals of 10 seconds in sitting position. For that purpose the children were given a sign at the moment they were supposed to swallow and these moments were registered carefully.

The number of positive recordings out of 10 acts of swallowing was the outcome of the test and could range from 0-10.

In this study each child was tested three times, one week before, one week after and three months after grommet insertion. The outcomes of the sets of measurements before and after grommet insertion were analyzed in SPSS 12.0.1 and the distributions of differences (mean difference + SD) before and after were compared using T-test for paired samples.

The mean outcomes of the measurements in the group of children with OME were also compared to a control group consisting of 61 otologically healthy children tested in an earlier study[23].

Results

Table 1 shows the characteristics of both study populations.

Figure 1 shows the results of the measurements in the children with OME (n=33) before and one week and three months after grommet insertion and the measurements in the children of the control group (n=61).

Table 1. Characteristics of the study population and the controls.

	N	M:F	Mean age	Previous insertion of ventilation tubes	OME on otoscopy
OME	33	20:13	5 yrs and 8 mnths	18/33	33
Controls	61	29:32	6 yrs and 4 mnths	0/61	0

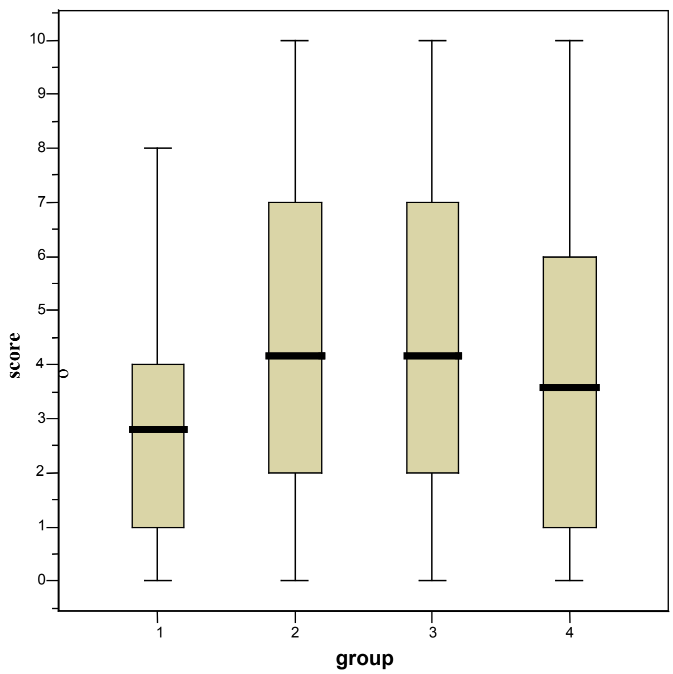

Figure 1. Outcomes of sonotubometric measurement before (1), one week (2) and three months (3) after grommet insertion in children with OME and the outcomes of sonotubometric measurements in an otologically healthy control group (4).

Sonotubometry was performed succesfully in all the children in all sets of measurements.

In the first set of measurements, i.e. sonotubometric measurements before the insertion of grommets, the mean number (+SD) of openings that could be registered was significantly ($p<0.05$) lower (mean 2.7; SD 1.9) than one week and three months after grommet insertion (respectively 4.3; SD 3.2 and 4.4; SD 3.2). Between the measurements one week and three months after grommet insertion there was no significant difference. Mean number of opening in the control group

was 3.7 (SD 3.4) out of 10 acts of swallowing. Compared to the measurements in the OME group before grommet insertion the difference is significant. Compared to the OME children after grommet insertion no significant differences were found.
Also the distribution of differences was tested. Mean difference of measurements one week after grommet insertion and before grommet insertion was 1.67, 95% CI 0.64 – 2.69. Mean difference of measurements three months after grommet insertion and before grommet insertion was 1.85, 95% CI 0.76 – 2.94. Mean difference of measurements three months after grommet insertion and one week after grommet insertion was 0.18, 95% CI 0.53 - 0.89.

Discussion and conclusions

In previous studies we tested whether a revised set-up for sonotubometry was a feasible and reproducible method to assess Eustachian tube ventilatory function in otologically healthy adults and children[23]. These studies showed that sonotubometry is a feasible and reproducible method to assess ET ventilatory function and that more active opening of the Eustachian tube could be registered in otologically healthy adults compared to otologically healthy children between 6 and 8 years of age. Aim of the present study was to test the value of sonotubometry in the assessment of ET ventilatory function in children suffering from OME. Children with OME were tested before and after insertion of ventilating tubes. Insertion of ventilating tubes did result in a significant increase in registered openings of the ET after one week. Three months after intervention the registration of openings of the ET stayed at the same level as after one week. The results of sonotubometry one week and three months after ventilating tube insertion do not differ from sonotubometric results in otologically healthy children, but there is significant difference with the outcomes of the measurements before insertion of ventilating tubes, i.e. when the children had glue ears. This difference seems to be related to the presence of glue in the middle ear cavity at the time of the first measurements. Two explanations can be brought forward. First there is the possibility that in both situations the ET opens with the same frequency without adequate registration of these openings in glue ears. An explanation for this could be that glue in the middle ear partly absorbs or reflects the increase in sound after opening of the ET as a result of the difference in impedance between air and fluids. In this case false negatives would be measured. After removal of glue, these openings would be registered correctly and cause a significant difference of outcome between the two sets of measurements. A second explanation is that indeed there are less openings of the ET tube before the insertion of ventilating tubes. The presence of glue and underpressure in the middle ear could require stronger forces for the ET to be opened. Ventilatory function could be renewed by the removal of glue and underpressure in the middle ear cavity.

Unless the fact that overall less tubal openings could be recorded in cases of glue ears, in some cases some tubal openings could be recorded. Questions are why in some cases tubal openings can be recorded and what might be the meaning of this for the course of otitis media with effusion. Maybe the fluids viscosity or the amount of the middle ear effusion is a factor in the outcome of the measurements. Maybe the children in whom openings of the ET can be recorded are the children that do not need a second or third insertion of ventilating tubes. To answere these questions a study should be designed with a follow up of years and with attention for the properties of the removed middle ear fluid at the time of the surgical intervention, like the volume en the viscosity of the fluid.

In our study no difference of ET ventilatory function between children after insertion of ventilating tubes because of persistent OME and otologically healthy controls was found. This finding leads to two different questions. First it questions if the healthy controls in the past also suffered from OME but without clinical symptoms and are therefore not really otologically healthy. Maybe their hearing loss has been less obvious and this has never been a reason for complaints and ENT consultation. This would mean that eventually both groups do not differ that much from each other, but the overall poorer functioning of the Eustachian tube in children compared to adults makes all children more susceptible to OME. Second, this finding is in favor of the theory that OME is multifactorial and besides negative middle ear pressure[9,8,24], immunological abnormalities[24-26] and the presence of microorganisms and respiratory viruses[27] play an important role in the development of OME. Maybe the role of ET dysfunction is not as big as assumed before. Other studies[28] have also shown that manometric measurements of the Eustachian tube ventilatory function have no value in predicting the recurrence of OME in children.

However, there are significant differences between sonotubometric measurements in children with glue ears before grommet insertion and after grommet insertion or healthy control children. Whether this is only a result of the presence of glue in the middle ear, or whether there is another causal relation could not yet be elucidated.

In summary, the conclusion must be drawn that sonotubometry is not yet capable to assess ET ventilatory in cases of glue ears.

References

1. Zielhuis GA, Rach GH, van den Broek P. The occurrence of otitis media with effusion in Dutch pre-school children. Clin Otolaryngol 1990;15:147-153
2. Black N. Surgery for glue ear. A modern epidemic. Lancet 1984;1:835-7
3. Gates GA, Avery CA, Prihoda TJ, Cooper JC. Effectiveness of adenoidectomy and tympanostomy tubes in the treatment of chronic otitis media with effusion. N Engl J Med 1987;317:1444-1451
4. Paap CM. Management of otitis media with effusion in young children. Ann Pharmacother 1996;30:1291-1297
5. Bluestone CD, Paradise JL, Beery QC. Physiology of the Eustachian tube in the pathogenesis and management of the middle ear effusions. The Laryngoscope 1972; july: 1654-1670
6. Sadé J. The nasopharynx eustachian tube and otitis media. J Laryngol Otol 1994; 108:95-100
7. Maw RA. Glue ear in childhood. Cambridge: Mac Keit Press & Cambridge University Press, 1995
8. Sadé J, Ar A. Middle ear and auditory tube: Middle ear clearance, gas exchange and pressure regulation. Otolaryngology Head and Neck Surgery 1997; 116:499-524
9. Bluestone CD, Paradise JL, Beery QC. Physiology of the Eustachian tube in the pathogenesis and management of the middle ear effusions. The Laryngoscope 1972; July: 1654-1670
10. Bluestone CD. Pathogenesis of otitis media; role of the Eustachian tube. Pediatr Infect Dis J 1996; 15: 281-291
11. Van Heerbeek N, Ingels KJAO, Snik AFM, Zielhuis GA. Eustachian tube function after the insertion of ventilation tubes in children. Ann Otol Laryngol 2001;12:1141-1146
12. Van Heerbeek N, Ingels KJ, Snik AF, Zielhuis GA. Reliability of manometric Eustachian tube function tests in children. Otol Neurotol 2001; 22:183-7
13. Bylander A, Tjernstrom O, Ivarsson A. Pressure opening and closing functions of the Eustachian tube in children and adults with normal ears. Acta Otolaryngol 1983; 95:55-62
14. Falk B, Magnuson B. Test-retest variability of the eustachian tube responses in children with persistent middle ear effusion. Arch Otorhinolaryngol 1984;240:145-52
15. Groth P, Ivarsson A, Tjernstrom O. Reliability in tests of the Eustachian tube function. Acta Laryngol 1982; 93:261-7
16. Charles D Bluestone MD, E.I. Cantekin PhD. Current clinical methods, indications and interpretation of eustachian tube function tests. Ann Otol Rhinol Laryngol. 1981 Nov-Dec;90(6 Pt 1):552-62
17. Holmquist J, Björkman G, Olén L. Measurement of Eustachian tube function using sonotubometry. Scand Audiol 1981; 10:33-35
18. Okubo J, Watanabe I, Shibusawa M, Ishikawa N, Ishida H, Teramura K. Sonotubometric measurement of the Eustachian tube function by means of band noise; a clinical view of the acoustic measurement of the Eustachian tube. ORL J Otorhinolaryngol Relat Spec 1987; 49(5): 242-245
19. T. Palva, T. Marttila, T. Jauhiainen. Comparison of pure tones and noise stimuli in sonotubometry. Acta Otolaryngol (Stockholm) 1987; 103:212-216
20. Jonathan DA. The predictive value of Eustachian tube function (measured with sonotubometry) in the successful outcome of myringoplasty. Clin Otolaryngol 1990; 15:431-434
21. Virtanen H. Relation of the body posture to the Eustachian tube function. Acta Otolaryngol 1983 Jan-Feb (1-2): 63-67
22. Van der Avoort SJC, Van Heerbeek N, Zielhuis GA, Cremers CWRJ. Sonotubometry Eustachian tube ventilatory function test; a review. Otol Neurotol. 2005 May;26(3):538-43
23. Van der Avoort SJC, Van heerbeek N, Zielhuis GA, Cremers CWRJ. Reproducibility of sonotubometry as Eustachian tube ventilatory function test in healthy children. Int J Ped ORL 2006; in press.
24. Falk B, Magnuson B. Evacuation of the middle ear by sniffing: a cause of high negative pressure and developement of middle ear disease. Otolaryngol Head Neck Surg 1984; 92:312-318
25. Straetemans M, van Heerbeek N, Sanders EA, Engel JA, Schilder AG, Rijkers GT, Graamans K, Straatman H, Zielhuis GA. Immune status and eustachian tube function in

recurrence of otitis media with effusion. Arch Otolaryngol Head Neck Surg.2005 Sep;131(9):771-6
26. Takada R, Harabuchi Y, Himi T, Kataura A. Antibodies specific to outer membrane antigens of moraxella catarrhalis in sera and middle ear effusions from children with otitis media with effusion. Int J Pediatr Otorhinolaryngol 1998;46:185-195
27. Park K, Bakaletz LO, Coticchia JM, Lim DJ. Effect of influenza A virus on ciliary activity and dye transport function in the chinchilla Eustachian tube. Ann Otol Rhinol Laryngol 1993;102:551-558
28. Straetemans M, Van Heerbeek N, Schilder AG, Feuth T, Rijkers GT, ZielhuisGA. Eustachian tube function before recurrence of otitis media with effusion. Arch Otolaryngol Head Neck Surg 2005 Feb;131(2):118-23

7

Sonotubometry: a useful tool to measure intra-individual changes in Eustachian tube function

Niels van Heerbeek
Stijn J.C. van der Avoort
Gerhard A. Zielhuis
Cor W.R.J. Cremers

Submitted

Abstract

Introduction:

The Eustachian tube (ET) is known to have three important functions: ventilation, protection and clearance of the middle ear. ET dysfunction is assumed to play a role in the development of several middle ear diseases. Therefore clinicians and investigators have been interested in measuring the ET function. Of all available test methods sonotubometry appears to be the most “physiologic” method. Sonotubometry is based on the principle that sound applied to the nasopharyngeal ostium of the ET is conducted through the ET to the middle ear during active opening of the ET. Recently, the test method has been improved using modern and more sensitive microphones and sound sources. The aim of this study is to determine whether intra-individual changes in ET function induced by local histamine application can be detected using this improved sonotubometer.

Patients and Methods:

ET function was measured with a revised sonotubometer before and after histamine was applied to the nasopharyngeal ostium of the ET in 25 otologically healthy adults.

The number of openings out of 10 acts of swallowing was counted as the outcome of the test. This outcome could range from 0-10. The number of ET openings before and after histamine application was compared.

Results:

The mean number of ET openings dropped dramatically from 8,4 before to 2,7 after application of histamine. This difference was statistically significant: mean difference 5,6 with 95% confidence interval 4,4-6,9.

Conclusion:

Sonotubometry is capable to detect intra-individual changes in ET function and may therefore be a very useful tool in monitoring and/or clinical research of ET (dys)function.

Introduction

Ever since the importance of the ET with respect to the middle ear is recognised, clinicians and investigators have been interested in measuring the ET function. Since ET dysfunction, especially ventilatory dysfunction, is assumed to contribute to the development of otitis media with effusion (OME) and other middle ear diseases,[1-5] the ability to measure ET function will provide further insight into the etiology of these middle ear diseases and may contribute to the development of new causative therapies and better (surgical) management. Several test methods have been and still are being used to study the ventilatory function of the ET. Most of these are qualitative test methods and only determine whether the ET can be forced open or not (e.g. Valsalva's manoeuvre,[6] Toynbee's manoeuvre[7] and endoscopy[8]). Other test methods, such as the forced response test,[9] the pressure equilibration test[10-11]and sonotubometry[12] have been used to actually measure passive and active ET function. Of these test methods sonotubometry appears to be the most "physiologic" method and has the advantage that it can be performed on ears with an intact tympanic membrane and without the use of a pressure chamber.

Sonotubometry is based on the principle that sound applied to the nasopharyngeal ostium of the ET is conducted through the ET to the middle ear during active opening of the ET[13]. Since its introduction in the nineteenth century the technique of sonotubometry has undergone radical improvement and solutions have been found for some serious problems with the early sound conduction technique, such as susceptibility to background noises, leakage of sound and arbitrarily chosen test frequencies. Recently, the test method has been further improved using modern and more sensitive microphones and sound sources[14]. These technical improvements resulted in a high reproducibility in both adults and children. Moreover, sonotubometry showed to be able to discriminate between groups of various states of ET tube ventilatory function. Despite these improvements it is still unknown whether intra-individual changes in ET function can be detected with sonotubometry as well.

The aim of this study is to detect intra-individual changes in ET function induced by local histamine application in healthy adults using sonotubometry in order to test the discriminative power of our updated sonotubometry set-up. Several authors already studied the effect of histamine on the ET function in both humans and animals and found indeed a deterioration of the ET function[15-20]. In these studies, however, other less physiologic ET function tests were used.

Patients and Methods

Twentyfive otologically healthy adults were included in this study. They were aged 24 to 52 years with a mean age of 32,2. Exclusion criteria were: abnormal otoscopic findings, previous earsurgery (except insertion of ventilation tubes during childhood), recurrent earinfections after the age of 10 years, (allergic) rhinitis at the time of the measurements and complaints of tubal dysfunction. All measurements were performed by the same investigator. The subjects signed an informed consent form agreeing with participation in this study. The study was performed according to the regulations of the local Medical Ethical Committee.
All subjects were tested with an updated sonotubometer with specific properties. The test-setting is shown in Figure 1. The equipment comprised a sound generator with a speaker placed in one of the nostrils and a measurement microphone placed in the ipsilateral ear canal. After a thorough review of earlier studies on sonotubometry we gave close consideration to our choice of test conditions[13].

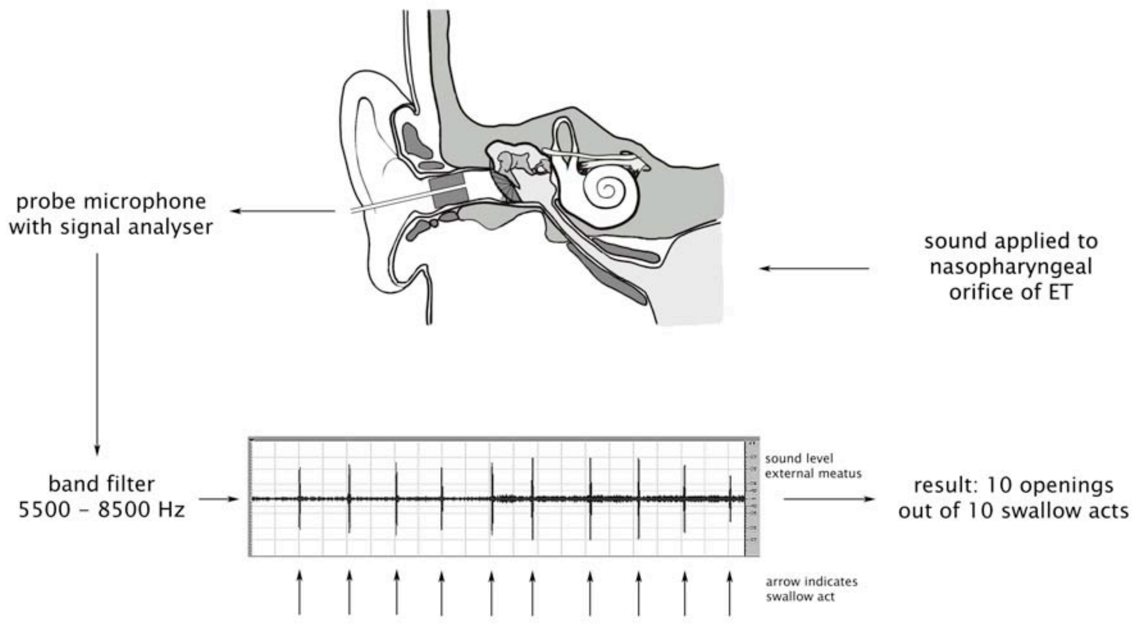

Figure 1. Test setting of our revised sonotubometer with an example of the outcome.

To minimize interference with sounds that occur during swallowing, the test tone must be of high frequency, above 5 kHz. However, such high-frequency pure tones might cause standing waves in the occluded external ear canal that comprise probe tube microphone measurements[21]. Therefore, we applied high frequency narrow band noise. The test signal comprised filtered white noise with a centre frequency of 7 kHz, bandwidth of 5.5 to 8.5 kHz and slopes of 48 dB/octave. This test signal was delivered to the nasopharyngeal ostium using an

Ear Tone 3A insert phone (Auditory Systems, Indianapolis, USA) that was fixed in one of the nostrils with a foam ear tip. A probe tube microphone (Etymotic Research-7c, Ilinois, USA) was placed in the ipsilateral external ear canal and fixed with a foam ear tip to minimize interference with the airborne test signal. The microphone output was amplified, digitally band-pass filtered (from 5.5 to 8.5 kHz) and displayed as a function of time, as shown in Figure 1.

The loudness level of the test signal was fixed at 90 dB SPL, in accordance with the level measured in the nostril with the (calibrated) probe tube microphone during the pilot experiments. This level was chosen because the test signal had to be loud enough to be detected by the probe microphone in the external ear canal during ET opening, but soft enough to prevent direct airborne stimulation of the microphone. According to the specifications, the foam ear tips used to connect the speaker to the nostril and to position the probe tube microphone to the ear canal attenuate sounds in the 6-8 kHz range by 40 dB each. Therefore, the direct airborne stimulation of the microphone was considered to be negligible.

Additional measurements were carried out to study the time course of the intensity of the test signal in the nose during swallowing by placing the probe tube microphone and the sound source in the same nostril. During the act of swallowing, the sound pressure level was measured after bandpass filtering, as described above. No change in sound pressure level was detected in the nose during swallowing. This means that the present set-up was free of artefacts caused by e.g. sounds of swallowing or sound pressure changes due to acoustic alterations in the nose during swallowing.

Positive peaks were firstly identified in the microphone recordings in the ear canal on-line by marking peaks that occurred during the act of swallowing. Then the difference in microphone output between a possible peak and baseline was tested for significance. Based on a characteristic period between two swallows, the noise level was determined by calculating the standard deviation from the baseline of the noise amplitude. The ET was judged as having opened when the level of the peak excedeed three times the standard deviation of the noise.

In all subjects the ear that was tested was randomly chosen. To evaluate opening of the ET, all subjects were instructed to swallow some water at intervals of 10 seconds in sitting position. After a session of 10 acts of swallowing, the microphone and the sound source were removed. A pressure nebulizer was then used to apply histamine-fosfate solution to the nasopharyngeal ostium of the ET in order to induce ET dysfunction[18,20]. In a preceding pilot study several different ways of applying histamine to the nasopharyngeal ostium of the ET were compared, i.e. both transorally as well as transnasally.(unpublished data) With an endoscope the amount of swelling of the tubal mucosa was compared. A pressure nebulizer with an extension piece that was passed trough the nasal cavity until close by the tubal ostium was found to be the most effective way to cause mucosal swelling. A concentration of 16 mg/ml was chosen to maximize the effect[22]. The congestive effect of histamine occurs within a few seconds and reaches a maximum after 5-10 minutes after which the effect lasts for approximately 60-75 minutes[23-25]. Therefore the second session of measurements was performed 10 minutes after administration of the histamine. The equipment was replaced and the second session was performed in an identical manner on the same side by the same investigator.

The number of positive recordings out of 10 acts of swallowing was counted as the outcome of the test. This outcome could range from 0-10. Low values indicate poor ET ventilatory function, whereas high values correspond with good ventilatory function. The results before and after histamine provocation were compared and analysed for significance of differences by use of the paired student's t-test. In previous studies the test results were not normally divided[14], therefore the Wilcoxon Signed Ranks test was performed as well. Statistical analyses were performed with SPSS 12.0.1 (SPSS Inc., Chicago, Illinois).

Results

All measurements were easily performed, well tolerated and succesful. Application of histamine did not cause any adverse effects such as bronchoconstriction, anafylactic reactions or shock. The only reported complaint was a lump in the throat or nasopharynx which lasted for a few hours. Twelve rights ears and 13 left ears were measured. The baseline sound level in the external ear canal, i.e. the sound level that was measured when the subject was not swallowing, before and after histamine application was compared. No significant difference in this baseline sound level was found before and after histamine application. In Figure 2 the ET function before and after histamine application and the mean difference with its distribution are shown. This study population of otologically healthy subjects showed a mean number of ET openings of 8,4 out of 10 acts of swallowing (range: 4-10) before application of histamine. Subsequently, in 22 out of 25 subjects application of histamine resulted in a marked deterioration of the ET function. In the other three subjects histamine was applied again under endoscopic control to optimize application to the tubal ostium. Hereafter the result changed from 6 to 4 openings out of 10 acts of swallowing in one subject, whilst two subjects still scored 10 openings although mucosal swelling of the tubal ostium was seen endoscopically. After histamine application the average number of openings was 2,7 (range: 0-10). The difference between the first and the second measurement was substantial: mean difference 5,6 with 95% confidence interval 4,4-6,9 (Wilcoxon Signed Ranks test: p<0,001).

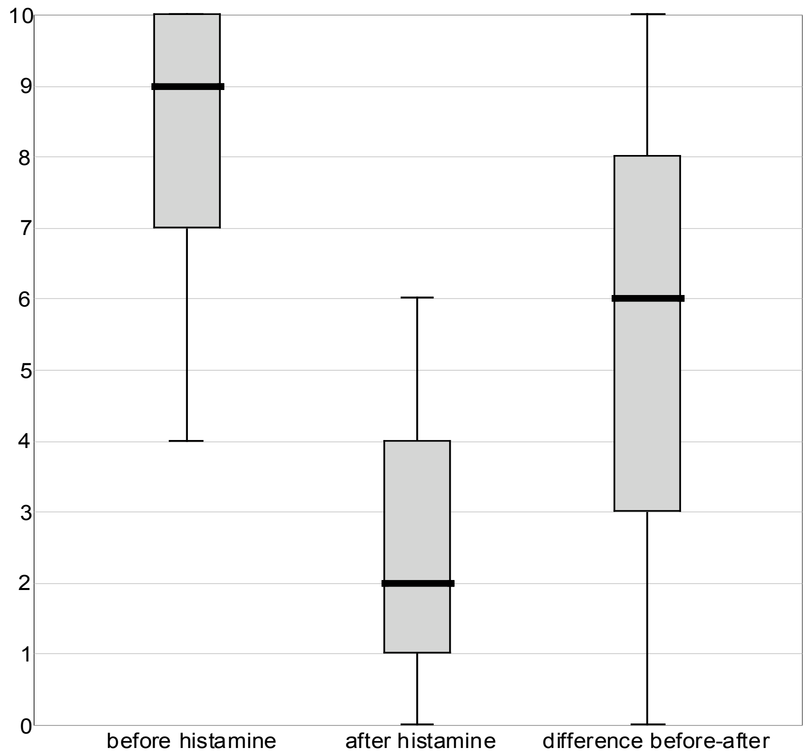

Figure 2. Boxplot showing ET function, i.e. number of openings out of 10 acts of swallowing, before and after histamine application and mean difference with its distribution.

Discussion

Our revised sonotubometry set-up proved to be a reliably instrument to measure ET function and even discriminate between different groups of various states of ET ventilatory function[14]. The aim of this study was to determine whether intra-individual changes in ET function can also be detected with sonotubometry. Therefore, ET function was measured before and after local application of histamine to the of the ET. Histamine is known to cause increased permeability of vessels resulting in oedema and local swelling. We assumed that this local oedema and swelling caused a deterioration of the ET function.

Application of histamine may also cause intranasal swelling and this may result in a reduction of the sound level in the nasopharynx. Since this may theoretically affect the measurement we applied the histamine only posteriorly in the nose and nasopharynx. In addition we compared the baseline sound level in the external ear canal before and after apllication. No significant difference in the baseline sound level was found, indicating that histamine application did not affect the transmission of sound from the nostril through the nasal cavity to the of the ET and in this manner did not affect the measurements.

Measurement of the ET function was succesful in all subjects. The mean number of openings before histamine application was 8,4 with a range from 4 to 10. This is comparable with the findings in a (larger) group of otologically healthy adults[14]. This finding indicates that even in otologically healthy adults, without any complaints of tubal dysfunction, the ET does not open with every act of swallowing. In the first instance no change in ET function was found after histamine application in three subjects. Since a deterioration in ET function was found in all other subjects this was probably due to inappropriate application of the histamine or an insufficient effect. Therefore histamine was aplied again and the measurement was repeated. In one subject the histamine may have missed the nasopharyngeal ostium of the ET during the first application, because a deterioration was found when histamine was applied again under endoscopic control. In the other two subjects the histamine may have only affected the medial part of the ET, because mucosal swelling of the tubal ostium was seen endoscopically but they still scored 10 openings out of 10 acts of swallowing. Mucosal swelling in this medial part may have insufficiently blocked the ET, because this medial part of the funnel-shaped ET is much wider than the more central part of the ET which is the most crucial part during opening of the ET[26]. Especially in subjects with a very good ET function, such as these two subjects (baseline result: 10 out of 10), there may still be opening of the ET with every act of swallowing. Overall an enormous change (mean difference 5,6; 95% confidence interval 4,4-6,9) in ET function was found after histamine application.

We can therefore conclude that sonotubometry is able to detect intra-individual changes in ET function. This finding opens new perspectives for future research and clinical monitoring. Sonotubometry is a reproducible test method and is well tolerated and easily performed. In addition it can be performed on ears with an intact tympanic membrane. Now that is shown that intra-individual changes in ET can be detected with our revised sonotubometer it can for example be used to measure whether the ET function can be improved pharmacologically or whether other factors affect ET function positively or negatively. In addition the course of ET function in children, who are known to overgrow their lessened ET function during childhood, or in selected subgroups can be followed up.

References

1. Bylander Groth A, Stenstrom C. Eustachian tube function and otitis media in children. Ear Nose Throat J 1998;77:762-769
2. Stenstrom C, Bylander Groth A, Ingvarsson L. Eustachian tube function in otitis-prone and healthy children. Int J Pediatr Otorhinolaryngol 1991;21:127-138
3. Takahashi H, Hayashi M, Sato H, Honjo I. Primary deficits in eustachian tube function in patients with otitis media with effusion. Arch Otolaryngol Head Neck Surg 1989;115:581-584
4. Straetemans M, Van Heerbeek N, Tonnaer EL, Ingels K, Rijkers GT, Zielhuis GA. A comprehensive model for the aetiology of otitis media with effusion. Med Hypotheses 2001;57:784-791
5. Van Heerbeek N, Ingels KJ, Snik AF, Zielhuis GA. Eustachian tube function in children after insertion of ventilation tubes. Ann Otol Rhinol Laryngol 2001;110:1141-1146
6. Valsalva AM. Tractatus de aure humana. Bologna: 1704;
7. Toynbee J. The diseases of the ear. Londen: Churchill; 1860;
8. el Guindy A. A correlative manometric and endoscopic study of tubal function in chronic otitis media with effusion. Acta Otolaryngol Stockh 1998;118:692-696
9. Bylander A, Tjernstrom O, Ivarsson A. Pressure opening and closing functions of the eustachian tube in children and adults with normal ears. Acta Otolaryngol Stockh 1983;95:55-62
10. Cantekin EI, Bluestone CD, Parkin LP. Eustachian tube ventilatory function in children. Ann Otol Rhinol Laryngol 1976;85:171-177
11. Holmquist J, Renwall U. Eustachian tube function in secretory otitis media. Arch Otolaryngol 1974;99:59-61
12. Virtanen H. Sonotubometry. An acoustical method for objective measurement of auditory tubal opening. Acta Otolaryngol 1978;86:93-103
13. van der Avoort SJ, van Heerbeek N, Zielhuis GA, Cremers CW. Sonotubometry: eustachian tube ventilatory function test: a state-of-the-art review. Otol Neurotol 2005;26:538-543
14. van der Avoort SJ, Heerbeek N, Zielhuis GA, Cremers CW. Validation of sonotubometry in healthy adults. J Laryngol Otol 2006;120:853-856
15. Minami T, Kubo N, Tomoda K, Kumazawa T. Effects of various inflammatory mediators on eustachian tube patency. Acta Otolaryngol 1992;112:680-685
16. Ebert CS, Jr., Pollock HW, Dubin MG, et al. Effect of intranasal histamine challenge on Eustachian tube function. Int J Pediatr Otorhinolaryngol 2002;63:189-198
17. Downs BW, Butehorn HF, III, Prazma J, Rose AS, Stamat JC, Pillsbury HC, III. Action of histamine on eustachian tube function. Otolaryngol Head Neck Surg 2001;124:414-420
18. Doyle WJ, Ingraham AS, Fireman P. The effects of intranasal histamine challenge on eustachian tube function. J Allergy Clin Immunol 1985;76:551-556
19. Skoner DP, Doyle WJ, Fireman P. Eustachian tube obstruction (ETO) after histamine nasal provocation--a double-blind dose-response study. J Allergy Clin Immunol 1987;79:27-31
20. Walker SB, Shapiro GG, Bierman CW, et al. Induction of eustachian tube dysfunction with histamine nasal provocation. J Allergy Clin Immunol 1985;76:158-162
21. Tecca JE. Clinical application of real ear probe tube measurement. In: Sandlin RE, ed. Handbook of hearing aid amplification, Vol II. Clinical considerations and fitting practices. San Diego: Singular Publishing Group; 1995;225-256
22. Wuestenberg EG, Hauswald B, Huettenbrink KB. Thresholds in nasal histamine challenge in patients with allergic rhinitis, patients with hyperreflectory rhinopathy, and healthy volunteers. Am J Rhinol 2004;18:371-375
23. Birchall MA, Phillips I, Fuller RW, Pride NB. Intranasal histamine challenge in normality and allergic rhinitis. Otolaryngol Head Neck Surg 1993;109:450-456
24. Parvez L, Hilberg O, Vaidya M, Noronha A. Nasal histamine challenge: a reproducible model of induced congestion measured by acoustic rhinometry. Rhinol Suppl 2000;16:45-50
25. Larivee Y, Leon Z, Salas-Prato M, Ganeva E, Desrosiers M. Evaluation of the nasal response to histamine provocation with acoustic rhinometry. J Otolaryngol 2001;30:319-323
26. Djeric D, Savic D. Anatomical variations and relations of the bony portion of the eustachian tube. Acta Otolaryngol 1985;99:543-550

8

General discussion
Summary
Samenvatting

General discussion

The assessment of Eustachian tube ventilatory function has been studied extensively in the past. Although several test methods are available, there is still no golden standard. Reasons for this may be that existing function tests are non-physiological or cannot be performed in ears with an intact tympanic membrane. A test is needed that is painless and easy to perform.

One of the currently available Eustachian tube ventilatory function tests, sonotubometry, has advantages over the others: active ventilatory function can be measured non-invasively and the measurements take place under physiological circumstances, without the use of extreme pressures and without the need for tympanic membrane perforation. Consequently, sonotubometry has been used in many studies. Although the sonotubometry procedure has gradually been improved over the years, it is not used routinely to assess Eustachian tube ventilatory function, because its reproducibility, validation and clinical value have not yet been adequately demonstrated.

The aim of this thesis was to further refine the sonotubometry set-up and to assess the validity and reproducibility of measurements obtained from study populations of different ages and different middle ear status. Based on the outcomes, we assessed whether this updated version of the test has the potential to become a standard diagnostic tool in daily outpatient ENT practice.

Healthy adults and children

After a thorough review of studies on sonotubometry in the English literature *(chapter 2),* a revised sonotubometry set-up was tested in otologically healthy adults and in otologically healthy children (*chapter 3 and 4).* The properties of the test equipment were chosen carefully, such as the frequency and loudness level of the test signal and band-pass filtering of the recorded signal. Additional measurements were carried out to confirm that the present set-up was free of artefacts caused by e.g. sounds of swallowing or sound pressure changes due to acoustic alterations in the nose during swallowing. The measurements in this study were highly reproducible, with Spearman's coefficients of 0.91 in adults and 0.89 in children. Such high reproducibility has not been mentioned in earlier studies. Mean number of registered opening were 4.3 in the adults and 3.7 in the children during 10 acts of swallowing. The measurements obtained with our sonotubometry set-up were highly reproducible in the two study populations and the test was simple to perform and well-tolerated by all the adults and children.

Despite negative otological history and normal otoscopy findings in both healthy study populations, opening of the ET could not be registered in all the cases. Recordings showed that the ET opened in 92% and 82% of otologically healthy adults and children respectively. There could be several explanations for this. First, even a lower incidence of opening of the ET during the act of swallowing may be sufficient to ensure normal aeration of the middle ear. In the literature on Eustachian tube ventilatory function, no answer could be found to the question of how many times the ET must open to maintain normal middle ear physiology. In our test set-up, only two sessions of measurements were performed during 10 acts of swallowing. To help find an answer to this question, it may be worthwhile to increase the measurement time and the number of acts of swallowing, or to repeat the measurements at different times. Future research might focus on continuous sonotubometric measurements over a longer period of the day in otologically healthy test persons. Secondly, the negative otological histories of the test persons might not reflect the true situation, because they may have suffered from OME in the past, but without any clinical symptoms and therefore never had reason to complain or visit an ENT clinic. Thirdly our hypothesis that all the episodes of the ET opening can be registered has to be criticized. It is possible that when the ET is very narrow or opens for a very short time, the sonotubometry test set-up cannot register opening of the ET, despite the fact that it is enough to enable gas exchange or pressure equilibration of the middle ear[1]. All the studies reviewed in chapter 2 showed a substantial percentage of otologically healthy subjects with poor outcomes, which suggests that this might be a physiological phenomenon.

Discriminative power

To answer the question of whether our revised sonotubometry set-up has sufficient discriminative power to assess ET ventilatory function, a study was designed to compare sonotubometric measurements between two groups of children with supposedly different ET function: healthy versus repaired cleft palate. The results of this study are described in *chapter 5*.

A proportion of children with repaired cleft palate are assumed to have impaired ET function. On the long-term two thirds of cleft palate patients develop chronic middle ear diseases, such as COM[2]. Altered muscle insertion and weaker contraction are considered to be responsible for their poorer ET ventilatory function[3,4]. At the same time, less velopharyngeal closure during swallowing gives

rise to oronasal reflux This causes mucosal irritation and oedema in the nasopharynx, which leads to disturbances in Eustachian tube ventilatory function[5,6].
In our discriminative power study we only included cleft palate children who had well-aerated middle ears at the time of sonotubometric testing to prevent other factors for interfering with the outcome of the measurements. Our hypothesis that the updated sonotubometry set-up would show a lower incidence of ET opening in children with a repaired cleft palate than in the healthy control children, was confirmed. The ET in the cleft palate children openened a lower mean number of times (2.3) than in the healthy controls (3.7) during 10 acts of swallowing. Reproducibility was high in the two study populations. Individuals with a more severe cleft palate disorder, i.e. total cheilognatopalatoschisis or palatoschisis, showed poorer ventilatory ET function than individuals with a less severe type of schisis. These results support the notion that in the milder types cleft palate, the paratubal muscles are less affected and there is little or no velopharyngeal incompetence. Unfortunately the subgroups within the cleft palate group were to small to yield significant differences. Statistical analysis led to the conclusion that it was not possible to choose a cut-off point of the number of times the ET opened with an acceptable sensitivity and specificity to divide the population into two distinct categories, i.e. children with repaired cleft palate and healthy controls. This may have been the result of the negative sonotubometry findings in 18% of the healthy controls (i.e. their ET did not open) and the positive measurements in the children with repaired cleft palate. Thus the borderline between these two groups was more vague than sharp. A possible explanation is the (partial) reconstruction of the cleft.

Otitis media with effusion

The study described in *chapter 6* tested the value of sonotubometry to assess ET ventilatory function in children suffering from OME. Comparisons were made of sonotubometric measurements taken before and after the insertion of ventilating tubes. After one week with the ventilating tubes in situ, there were significantly more registrations of ET opening. For two reasons this finding seemed to be related to the presence of glue in the middle ear cavity at the time of the initial measurements. First it is possible that the ET opened with the same frequency in both situations without adequate registrations when the glue was present. In this case, the results would be false negative. Glue in the middle ear might have partly absorbed or reflected the sound stimuli after opening of the ET because of of the differences in impedance between air and fluid. However, in some of the glue

ears, tubal opening was registered before the insertion of ventilation tubes, i.e in the presence of glue. There may be a relation between the positive outcomes of sonotubometric testing and the amount and/or properties of the middle ear fluid. This gives rise to subject matter for future research to find relations between the properties of middle ear glue and hearing loss on audiometry, recurrence of OME and sonotubometric test results. A second possibility is that the ET did indeed open less frequently before the insertion of ventilating tubes, due to the presence of glue and the negative pressure in the middle ear. Ventilatory function may have been restored over the seven days between measurements. However it is not clear whether removal of the glue was the only reason for the better functioning of the ET. Therefore in a future study to learn more of the course of recovery measurements should be taken at an earlier stage, for example one day after the removal of middle ear fluid. Sonotubometric follow-up of ET ventilatory function could also start straight after intervention. We need to find out whether the glue alone was responsible, or wether recovery of the middle mucosa played a contributing role.
The measurements obtained from the children with OME were also compared to the results of sonotubometry in the otologically healthy children. No differences in ET ventilatory function were found between the otologically healthy controls and the persistent OME children. This finding raises two different questions. First, what was the real otological health status of the controls? It is possible that history taking and otoscopic findings at the time of testing were unable to distinguish between moderate and poorer ET functioning in cases with well-aerated middle ears. Second, our finding raises questions about the role of ET dysfunction in the aetiology of OME in children. The results are at least in favour of the notion that mucosal factors and immune status are more important causal factors of OME than ET dysfunction. Other studies showed that manometric measurements of ET ventilatory function did not have any predictive value in the recurrence of OME in children [7]. The main conclusion drawn in chapter 6 nevertheless remains valid: the updated sonotubometry set-up was yet unable to make adequate assessments of ET ventilatory function well in children with glue ears.

Intraindividual changes

Chapter 7 describes a study that tested the power of our updated sonotubometry set-up to detect intra-individual changes in ET ventilatory function. Measurements were obtained from otologically healthy adults before and after challenging of their nasopharyngeal tubal ostium with histamine. Our hypothesis was confirmed that after histamine, ET ventilatory function decreased. Overall, significantly fewer episodes of tubal opening were registered by our sonotubometry set-up after the application of histamine. This shows that our sonotubometry set-up was capable of detecting intra-individual changes in ET ventilatory function. Therefore it forms a suitable means to measure whether ET function can be improved pharmacologically, for example, or whether other factors have a positive or negative effect on ET function.

Study limitations

Considering the design and the outcomes of the sonotubometric studies, first of all we have to conclude that there are still shortcomings. First there is no golden standard to make physiological assessments of ET ventilatory function, so the outcomes of our studies could not be confirmed by other tests. The study populations were selected by means of a questionnaire to predict ventilatory function of the Eustachian tube. However, this selection method by means of history taking and physical examination may have induced errors. In addition, we studied only a few small and selected study populations. The measurements were interpreted using a cut-off point in the sound peak recordings and were not always carried out in the same environment, which may have introduced some inaccuracy. No imaging techniques, such as endoscopy or X-rays, were employed to investigate the anatomy of the test persons, so false-negatives may have had anatomical causes.

Conclusions and recommendations for further research

Although tubal opening could not be registered in 100% of the healthy adults and children, the further refinements we made to the sonotubometer tested in this thesis increased the power to detect opening of the ET. We found that our sonotubometry set-up produced highly reproducible measurements and formed a valid method to assess ET ventilatory function in a physiological and non-invasive manner in adults and children. Therefore it is a more suitable assessment tool than other function tests, such as the manometric ET function tests.

Regarding earlier studies and the results in this thesis it seems to be a physiological phenomenon that opening of the ET will not be registered in 100% of otologically healthy test persons in measurements of short duration. In the children, fewer episodes of tubal opening were registered than in the adults. This can be explained by difference in the anatomy of the Eustachian tube between adults and children. Our revised sonotubometry set-upwas able to discriminate between groups with different states of ET ventilatory function, as shown by the measurements in the children with cleft palate. However, in children with glue ears, the results were indistinct. Therefore the set-up is not yet capable for the assessment of Eustachian tube ventilatory function in case of OME. Future research to increase the power of sonotubometry in children with OME should be focussed on different degrees of severity and recurrence to elucidate the natural course of Eustachian tube function in this group. It would also be worthwhile to study the relation between the sonotubometric findings and the amount of the middle ear fluid and/or its properties. Extended follow-up of these children should enable us to learn more about the natural course of OME. Introduction of sonotubometry into clinical practice should be postponed until measurements in cases of OME have led to valid and reliable results.

Sonotubometry is a promising tool for the follow-up of ET ventilatory function in a research setting and/or clinical practice, e.g. to determine the effect of interventions to increase ET ventilatory function, such as nasal corticosteroids or decongestives. Also the effect of surfactant, which is assumed to lower the surface tension and therefore the openings pressure of the Eustachian tube[8], on the ventilatory function of the ET could be studied in populations with various states of Eustachian tube function. Sonotubometry could also be used to predict the result of tympanoplasty or to measure the effect of other surgical interventions, such as pharyngoplasties in cases of a cleft palate.

References

1. Gas inflow into and within the middle ear. Sade J, Cinamon U, AR,A, Seifert A. Otol Neurotol. 2004 sep; 25(5):649-52
2. Kemaloglu YK, Kobayashi T, Nakajima T. Analysis of the craniofacial skeleton in cleft children with otitis media with effusion.Int J Pediatr Otorhinolaryngol. 1999 Jan 25;47(1):57-69
3. Bluestone CD, Wittel RA, paradise JL. Roentgenographic evaluation of Eustachian tube function in infants with cleft palate and normal palates. Cleft Palate J 1972;9:93-100
4. Doyle WJ, Cantekin EI, Bluestone CD. Eustachian tube function in cleft paltate children. Ann Otol Rhinol Laryngol 1980;89(suppl)34-40
5. Doyle WJ, Reilly JS, Jardini L, Rovnak S. Effect of palatoplasty on the Eustachian tube in children with cleft palate. Clft palate J. 1986;23:63-68
6. Spauwen P, Ritsma R, Huffstadt B, Schutte H, Brown I. The inferiorly based pharyngoplasty: effects on chronic otitis media with effusion. Cleft palte J. 1988;25:26-32
7. Straetemans M, van Heerbeek N, Schilder AG, Feuth T, Rijkers GT, Zielhuis GA. Eustachian tube function before recurrence of otitis media with effusion. Arch Otolaryngol Head Neck Surg. 2005 Feb;131(2):118-23
8. Chandrasekhar SS, Mautone AJ. Otitis media: treatment with intranasal aerosolized surfactant.Laryngoscope. 2004 Mar;114(3):472-85

Summary

Chapter 1 describes the current concept of the Eustachian tube (ET) and its functional involvement in the middle ear. The ET connects the nasopharyngeal space with the middle ear and has three important functions with respect to the middle ear: protection, clearance and ventilation. Frequent active opening of the ET allows pressure equilibration between the middle ear and ambient air (ventilatory function). At rest, the ET is closed to protect the middle ear from ascending secretions, micro-organisms and pressure variations in the nasopharynx (protective function). The mucociliary epithelium of the ET is involved in the local defence against pathogens and is concerned with the clearance of secretions and debris from the middle ear towards the nasopharyngeal space (clearance function).

Measurements of Eustachian tube function have been the subject of many clinical studies, because the outcomes could be important to clinical practice. Although the majority of Eustachian tube function studies focussed on ventilatory function, there is still no simple and reliable function test to evaluate ET ventilatory function in daily outpatient ENT care. One currently available ET ventilatory function test, sonotubometry, has advantages over the others: active ET ventilatory function can be measured non-invasively and the measurements take place under physiological circumstances, without the use of extreme pressures and without the need for tympanic membrane perforation. Therefore, sonotubometry has received close attention in the past. Despite gradual improvement of the sonotubometry over the years, the test is not used routinely to assess Eustachian tube ventilatory function, because its reproducibility, validity and value for clinical practice have not yet been adequately demonstrated.
The objectives of this thesis were to further refine the sonotubometry measurement set-up for use in clinical practice and / or research settings and to assess the subsequent validity and reproducibility in study populations of different ages and with different middle ear status.

After a thorough review of studies on sonotubometry in the English literature (*chapter 2)*, a revised set-up for sonotubometry was tested in otologically healthy adults and otologically healthy children in *chapter 3 and 4.* The measurements obtained with our sonotubometry set-up were highly reproducible in these two study populations and the test was simple to perform and well-tolerated. Recordings showed that the ET opened in 92% and 82% of otologically healthy adults and children respectively. Despite the negative otological history and

normal otoscopy findings in the both healthy study populations, opening of the ET could not be registered in all the cases. The question arose as to how many times the ET must open to allow normal middle ear physiology? Extending the duration of the measurements and increasing the number of acts of swallowing, or repeating the measurements at different times might yield to the requiered answer.
To addres the question of whether our revised sonotubometry set-up has sufficient discriminative power to assess ET ventilatory function, a study was designed in which the outcomes of sonotubometric measurements in a study population of children with cleft palate were compared to those in a healthy control group of the same age (*chapter 5)*. Altered muscle insertion and less contraction are considered to be responsible for the poorer ET ventilatory function in children with cleft palate. Our hypothesis was confirmed that a lower incidence of ET opening would be registered in the children with cleft palate than in the healthy control children. Reproducibility of the sonotubometry measurements was high in both study populations.
Aim of the study described in *chapter 6* was to test the value of sonotubometry in children suffering from OME. The outcomes of sonotubometric measurements before and after the insertion of ventilating tubes were compared. After one week with the ventilating tubes in situ, there was a significant increase in registered openings of the ET. This difference seemed to be related to the presence of glue in the middle ear at the time of the pretreatment measurements. The outcomes of the children with OME were also compared to the results of sonotubometry in the otologically healthy children. No difference in ET ventilatory function was found between the otologically healthy control children and the persistent OME children after the insertion of ventilating tubes. These findings prompt a new set of questions, especially for example about the role of ET dysfunction in the aetiology of OME in children. Our results are at least in favor of the notion that mucosal factors and immune status are more important causal factors of OME than ET dysfunction.
Chapter 7 describes a study that tested test the power of our sonotubometry set-up to detect intra-individual changes in ET ventilatory function. Measurements of ET ventilatory function were obtained from otologically healthy adults before and after challenging their nasopharyngeal tubal ostium with histamine. The hypothesis in this study was confirmed that histamine would lead to poorer ET ventilatory function. This showed that our sonotubometry set-up was capable of detecting intra-individual changes in ET ventilatory function.
In *chapter 8*, we present and discuss the overall conclusions of this thesis. Although tubal openings could not be registered in 100% of our healthy adults and

children, the further refinements made to the sonotubometer in this thesis increased the power to record opening of the ET. In addition, our sonotubometry set-up proved to be a highly reproducible and valid method to assess ET ventilatory function in a physiological and non-invasive manner in adults and children. Therefore it is more suitable than other function tests, such as the manometric ET function tests.
In the children a lower incidence of tubal opening was recorded than in the adults. This can be explained by differences in the anatomy of the Eustachian tube between adults and children. We also found out that our test method had the power to discriminate between study groups with different ET ventilatory function status, as shown by the measurements in children with cleft palate. In contrast, sonotubometry produced indistinct results in children with glue ears and therefore cannot yet be used to assess Eustachian tube ventilatory function in the case of OME. Future research should focus on expanding the power of sonotubometry to include OME. Sonotubometry is a promising tool in the follow-up of ET ventilatory function in research settings and/or clinical practice for example to determine the effect of interventions to increase ET ventilatory function, such as nasal corticosteroids, decongestives or surfactant.

Samenvatting

De buis van Eustachius is de verbinding tussen de neus-keelholte en het middenoor. Deze verbinding werd voor het eerst in detail beschreven door Bartolomeo Eustachi in zijn Epistola de auditus organi (1562) en werd daarom later naar deze Italiaanse anatoom vernoemd. Sinds de eerste beschrijving van de buis van Eustachius is er veel onderzoek verricht naar de belangrijkste functies ervan, te weten ventilatie, bescherming en klaring van het midden oor.

In *hoofdstuk 1* worden deze functies nader uitgelegd. In rust is de buis van Eustachius gesloten, maar tijdens slikken, gapen of bewegen van de onderkaak gaat hij open. Deze actieve opening van de buis van Eustachius zorgt voor beluchting van het middenoor, zodat de luchtdruk in het middenoor gelijk is aan de buitendruk (ventilatiefunctie). Met uitzondering van deze kortdurende actieve opening is de buis van Eustachius echter gesloten om het middenoor te beschermen tegen secreties en micro-organismen uit de keelholte. Tevens beschermt de gesloten buis van Eustachius het middenoor tegen drukschommeling in de keelholte (beschermingsfunctie). Het mucociliaire epitheel van de buis van Eustachius zorgt voor het afvoeren van secreties en debris uit het middenoor naar de keelholte en speelt een belangrijke rol bij de lokale afweer tegen pathogenen (klaringsfunctie).

Er is in het verleden al veel onderzoek gedaan naar het meten van het functioneren van de buis van Eustachius. Deze onderzoeken waren in de eerste plaats gericht op het meten van de ventilatiefunctie. Ondanks dat er veel studies verricht zijn, is het tot op heden nog steeds niet gelukt om een valide meetmethode te ontwikkelen die als standaard kan worden gebruikt in de Keel-, Neus-, en Oorheelkunde praktijk. Eén van de onderzochte meetmethoden voor de ventilatiefuctie van de buis van Eustachius, sonotubometrie, heeft een aantal voordelen boven de andere methoden. Met een sonotubometer kan op een fysiologische, niet-invasieve en patientvriendelijke manier de actieve openingsfunctie van de buis van Eustachius gemeten worden. Bovendien is er voor het verrichten van deze meting geen trommelvliesperforatie nodig. In het verleden werd er om deze reden al vaak onderzoek gedaan met sonotubometrie. Ondanks het feit dat de meetmethode door de jaren heen sterk verbeterd werd, kan hij nog steeds niet gebruikt worden in de KNO-praktijk omdat de reproduceerbaarheid en de validiteit van de meetmethode nog niet voldoende werden bewezen.

Het doel van de studies beschreven in dit proefschrift is om een nieuwe sonotubometer te bouwen en om de reproduceerbaarheid, validiteit en bruikbaarheid in de KNO-praktijk ervan te onderzoeken.

Na een literatuurstudie (*hoofdstuk 2*) van onderzoeken met sonotubometrie als onderwerp werd een nieuwe sonotubometer gebouwd. Hierbij werd met name rekening gehouden met het juiste frequentiespectrum en luidheid van het test-signaal en werd er gebruik gemaakt van moderne elektronica. De vervaardigde sonotubometer werd als eerste getest in otologisch gezonde volwassenen en kinderen zoals beschreven in *hoofdstukken 3 en 4*. Bij volwassenen konden in 92% van de testpersonen openingen van de buis van Eustachius worden geregistreerd. Bij de kinderen was dit in 82% van de gevallen. In beide groepen waren de resultaten zeer goed reproduceerbaar. Ondanks dat het hier mensen betreft met een blanco otologische voorgeschiedenis konden dus niet in 100% van de gevallen openingen worden gemeten. Dit kan komen omdat er minder openingen nodig zijn om een middenoor gezond te houden dan eerder gedacht werd. Het verlengen van de meetperiode zou hier een antwoord op kunnen geven. Het verschil tussen volwassenen en kinderen is waarschijnlijk mede te verklaren aan de hand van een verschil in anatomie tussen de twee groepen.
Om te onderzoek of de meetmethode onderscheid kan maken tussen groepen met verschillend functioneren van de buis van Eustachius werden in hoofdstuk 5 meetresultaten vergeleken van een groep kinderen met een palatoschizis met de resultaten bij gezonde kinderen van dezelfde leeftijd. Inderdaad konden over het algemeen minder openingen gemeten worden in de schizis groep dan in de controlegroep. Dit kan worden verklaard door het feit dat de paratubale spieren anders zijn aangelegd en verminderd functioneren in de eerste groep.
In *hoofdstuk 6* werd de waarde onderzocht van sonotubometrie in gevallen van otitis media met effusie. Vóór het plaatsen van trommelvliesbuisjes werden er significant minder openingen gemeten vergeleken met een gezonde controle groep. Dit kan het gevolg zijn van de absorptie of terugkaatsing van het geluid als gevolg van het impedantieverschil tussen lucht en vloeistoffen. Een andere verklaring kan zijn dat de buis minder frequent opent. Na het plaatsen van trommelvliesbuisjes en het verwijderen van de middenooreffusie kon echter geen verschil meer worden aangetoond tussen beide groepen. Deze resultaten leveren vragen op wat betreft de rol van de buis van Eustachius in de ontwikkeling van otitis media met effusie.
Om te onderzoeken of de sonotubometer intra-individuele verschillen kan registreren werd een studie ontworpen waarbij met behulp van histamine oplossing de ventilatiefunctie van de buis van Eustachius functie werd verminderd *(hoofdstuk 7)*. Histamine werd aangebracht aan het nasopharyngeale ostium van de buis van Eustachius. De resultaten van metingen voor en na toediening van histamine werden vergeleken. In 23 van de 25 proefpersonen kon een significante

vermindering van het aantal openingen van de buis van Eustachius worden gemeten. Dit biedt perspectieven voor deze meetmethode in de follow–up van buis van Eustachius functie in geval van interventies om deze te verbeteren, zoals bijvoorbeeld de toediening van corticosteroiden, decongestiva of surfactant.

In *hoofdstuk 8* worden de conclusies van dit proefschrift besproken. Ondanks dat openingen van de buis van Eustachius niet konden worden geregistreerd in 100% van de gevallen werd een zeer hoge sensitiviteit gehaald. Daarnaast zijn de test resultaten in alle populaties zeer goed reproduceerbaar. Gezien deze resultaten en de voordelen die sonotubometrie heeft boven andere functietesten lijkt deze testmethode het meest geschikt voor functiemetingen van de buis van Eustachius. Het is mogelijk gebleken met deze meetmethode te discrimineren tussen groepen met verschillend functioneren van de buis van Eustachius. Daarnaast kunnen er veranderingen in buis van Eustachiusfunctie worden geregistreerd binnen één individu. De testresultaten bij kinderen met OME roepen vragen op met betrekking tot de betekenis van positieve testresultaten in geval van otitis media met effusie. Deze resultaten suggereren dat immuunstatus en mucosale factoren van het middenoor wel eens belangrijker in de ontwikkeling van otitis media met effusie kunnen zijn dan de buis van Eustachius.

Toekomstig onderzoek zou gericht moeten zijn op buis van Eustachius functiemetingen gedurende een langer tijdsinterval. Daarnaast zou nader onderzoek moeten leiden tot een duidelijke interpretatie van de testresulaten in geval van otitis media met effusie. Sonotubometrie zou in toekomstig onderzoek van waarde kunnen zijn in studies van buis van Eustachiusfunctie voor en na interventies.

Dankwoord

Voor velen die dit dankwoord lezen zijn dit de eerste en misschien ook wel de laatste woorden die zij van dit proefschrift zullen zien. Voor hen: het gaat over functiemetingen van de buis van Eustachius en ik heb er een aantal jaren best wel hard aan gewerkt. En als je dan bedenkt wie er met mij ook nog aan gewerkt hebben, dan is de totstandkoming van dit proefschrift niet alleen een bijdrage geweest voor de wetenschap rondom de buis van Eustachius maar ook voor de werkgelegenheid in Nijmegen. Echter van de meeste mensen die met mij hieraan werkten, had ik de indruk dat zij dit gewoon uit enthousiasme en behulpzaamheid deden. Tot hen wil ik graag persoonlijk het woord richten.

Professor Cremers, het begon met een wetenschapstage die ik vanuit Antwerpen bij u kwam lopen. Dat was het moment dat we een onderwerp kozen om drie maanden aan te werken. Het mondde uit in dit proefschrift. Door het parcours heen is het u gelukt om, met afwisselend aantrekken en laten vieren van de teugels, mij zo vlot mogelijk over de finish te loodsen. Graag gebruikte u metaforen om uw boodschap kracht bij te zetten. Als u paardenmenner was geworden zou u het beest goed observeren om daarna een dressuurpaard te kunnen laten springen en een springpaard te laten deelnemen in een polowedstrijd. U bezit eigenschappen die met eender welke promovendus tot succes zouden leiden. Bedankt voor uw begeleiding!

Professor Zielhuis, beste Gerhard, naast de epidemiologische en statistieke begeleiding die ik van jou kreeg, zorgde je telkens ook voor een heldere voorstelling van zaken. Daarnaast heb ik je leren kennen als een zeer vriendelijke en laagdrempelige promotor en dit is de efficiëntie van mijn werk zeker ten goede gekomen. Ik dank je graag voor je tijd, inzet, maar zeker voor je persoonlijke betrokkenheid gedurende de afgelopen jaren.

Niels van Heerbeek, eigenlijk wel mijn steun en toeverlaat op weg naar de promotie. Mijn onderzoek was een logisch vervolg op jouw proefschrift. Met jouw kennis op gebied van de buis van Eustachius en jouw ervaring in de onderzoekswereld, maar vooral met het gemak waarmee je dingen op anderen kunt overbrengen ben ik enorm geholpen. Jouw aandeel in dit proefschrift is van grote waarde, zowel op wetenschappelijk als op collegiaal en vriendschappelijk vlak. Bedankt!

Vanaf de zijlijn heb jij, professor Ad Snik, dit project gecoacht. Wanneer ik met een audiologisch of natuurkundig vraagstuk jouw kamer binnenliep, ging ik er altijd met een antwoord buiten, ondanks je (te) drukke agenda.

Van grote waarde voor de totstandkoming van dit proefschrift: Chris-Jan Beerendonk. Dankzij jouw hulp was het mogelijk om met twee linker handen de technische kant van dit promotieonderzoek aan te kunnen. Daarnaast is gebleken dat wij de moeilijkheden van het onderzoek een stuk konden vereenvoudigen door ze te bespreken in Brabants dialect onder het genot van een 'bakske koffie'. Bedankt voor je behulpzaamheid!

Graag bedank ik het bestuur van basisschool 'Het Talent' in Lent voor de gelegenheid om proefpersonen te werven in groepen 3 en 4 en de maatschap van KNO-artsen van het CWZ te Nijmegen voor het aanleveren van kinderen met OME voor het onderzoek. Personeel van polikliniek KNO en het KAC in het Radboud en poli KNO in het CWZ dank ik vanwege de organisatorische hulp en de gezelligheid die ik heb ervaren. De meeste van hen zijn ooit proefpersoon geweest voor mijn het onderzoek waarvoor dank!

Dames van het secretariaat Gonny, Sylvia, Thea en Loes, hartelijke dank voor de hulp die jullie boden met de voorbereidingen van dit proefschrift. Talloze keren werden jullie belast met 'hand in hand' post van mijn promotor naar mij en vice versa. Verder was het vooral gezellig om af en toe bij jullie uit te rusten!
Als je zelf niet zo'n sterke talenknobbel hebt en nauwelijks kunt typen, laat staan lay-outen, heb je mensen nodig die dit soort dingen goed kunnen. Judith Abma-Hill, bedankt voor de snelheid en de geïnteresseerdheid waarmee jij mijn stukken controleerde op 'datgene wat echt niet kon'. Diny Helper-Peters, jij begreep hoe snel ik vooruit wilde en hebt jouw vaart daar op aangepast. Grote klasse voor de snelheid waarmee jij de lay-out in orde gemaakt hebt, bedankt!
Natuurlijk ben ik alle proefpersonen, in leeftijd variërend van 3 tot 60 jaar, die meewerkten aan de onderzoeken zeer dankbaar. Jullie bereidwilligheid om mee te toen, ook al moest je er een keer voor terugkomen, was top!

Collega's arts-assistenten van de KNO: Dirk, Capi, Bom, Bas, Wijffels, Martijn, Ritoe, Erik, Niels, Beertje, Pennings, Hol, Bischoffs, Rottevelia from Julii – princess of thieves, Plant, Bar-dancing, Wibi, Oli4, Gootje - bedankt voor de statistiek, Sylvia's, Binkie en Jan-Willem, bedankt voor de gezelligheid en de geweldige assistententijd die we samen delen, ondanks het feit dat de meeste van jullie te schijterig waren om aan het onderzoek mee te doen.

Lieve Papa en Mama, Koen en Dirk-Jan, eigenlijk hoef ik het jullie niet te zeggen want we weten wat we voor elkaar betekenen. Het is fijn om uit een gezin te komen met zoveel warmte, emotie, nuchterheid, humor, bescherming, vrijheid, steun en liefde. Bedankt voor alles!

Lieve Kathleen, wij kennen elkaar even lang als de tijd dat ik aan mijn proefschrift heb gewerkt. Het proefschrift is nu klaar, maar voor ons begint het pas. Vanaf het eerste moment wist ik dat jij mijn vrouw zou worden en toch ben ik nog altijd verbaasd. Ik hou van je.

Curriculum Vitae

Stijn Johannes Cornelis van der Avoort werd op 4 juli 1978 geboren in Breda. In 1996 behaalde hij het diploma gymnasium β aan het Onze Lieve Vrouwe lyceum te Breda. In 1996 startte hij met de studie geneeskunde aan de Universiteit van Antwerpen in België. In de afrondende fase werd een wetenschappelijke stage gelopen op de afdeling Keel-, Neus- en Oorheelkunde van het UMC st Radboud waar hij onderzoek deed met betrekking tot functiemetingen van de buis van Eustachius. Na het behalen van het artsexamen in juni 2003 werd hij aangesteld als arts-onderzoeker op eerder genoemde afdeling en zette daar het onderzoek voort. In 2004 startte hij met de opleiding tot Keel-, Neus- en Oorarts in het UMC st Radboud welke vermoedelijk op 1 mei 2009 wordt afgerond.