Sonotubometry

A Useful Tool to Measure Intra-individual Changes in Eustachian Tube Ventilatory Function

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Objective: To determine whether intra-individual changes in eustachian tube (ET) function induced by local application of a histamine phosphate solution can be detected using an improved sonotubometer.

Design: The function of the ET was measured with a revised sonotubometer before and after histamine was applied to the nasopharyngeal ostium of the ET.

Setting: Tertiary referral hospital.

Patients: Twenty-five otologically healthy adults.

Interventions: A histamine phosphate solution with a concentration of 16 mg/mL was applied to the nasopharyngeal ostium of the ET using a pressure nebulizer.

Main Outcome Measures: The number of openings during 10 acts of swallowing. This outcome value could range from 0 to 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 application of histamine to 2.7 after application. This difference was statistically significant; there was a mean difference of 5.6 (95% confidence interval, 4.4-6.9; \( P < .001 \)).

Conclusion: Sonotubometry is capable of detecting intra-individual changes in ET function and may therefore be a very useful tool in monitoring and/or clinical research of ET dysfunction or function.

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Ever since the importance of the eustachian tube (ET) with respect to the middle ear was first recognized, physicians and investigators have been interested in measuring the ET function. Because ET dysfunction, especially ventilatory dysfunction, is assumed to contribute to the development of otitis media with effusion and other middle ear diseases,1,2 the ability to measure ET function could provide further insight into the etiology of these middle ear diseases and could contribute to the development of new causative therapies and better (surgical) treatment. Several test methods have been used (and still are being used) to study the ventilatory function of the ET. Most of these are qualitative test methods and determine only whether the ET can be forced open (eg, the Valsalva maneuver, Toynbee maneuver, and endoscopy). Other test methods, such as the forced response test,3 the pressure equilibration test,4,5 and sonotubometry,6 have been used to actually measure passive and active ET function. Of these test methods, sonotubometry seems 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.7 Since its introduction in the 19th century, the technique of sonotubometry has undergone radical improvement, and solutions have been found for some serious problems with the early sound conduction technique (eg, susceptibility to background noises, leakage of sound, and arbitrarily chosen test frequencies). Recently, this test method has been further improved with the use of modern and more sensitive microphones and sound sources.8 These technical improvements resulted in a high reproducibility in both adults and children. Moreover, sonotubometry has been shown to be able to discriminate between groups of various states of ET ventilatory function.
(N.H., S.J.C.A., G.A.Z., and C.W.R.J.C., 2007, unpublished data). Despite these improvements, it is still unknown whether intra-individual changes in ET function can be detected with sonotubometry as well.

Our objective was to detect intra-individual changes in ET function induced by local application of a histamine phosphate solution in healthy adults by using sonotubometry to test the discriminative power of our updated sonotubometry setup. Several authors9-12 have already studied the effect of histamine on the ET function in both humans and animals and have indeed found a deterioration of the ET function. In those studies, however, other, less physiologic, ET function tests were used.

**METHODS**

Twenty-five otologically healthy adults were included in this study (mean age, 32.2 years [range, 24-52 years]). Exclusion criteria were abnormal otoscopic findings, previous ear surgery (except insertion of ventilation tubes during childhood), recurrent ear infections 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 (N.H.). The subjects signed an informed consent form agreeing to participate in this study. The study was performed according to the regulations of the local medical ethics 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 that was 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.7 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 make up the probe tube microphone measurements.13 Therefore, we applied high-frequency narrow-band noise. 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 per octave. This test signal was delivered to the nasopharyngeal ostium using an Ear Tone 3A insert earphone (Auditory Systems, Indianapolis, Indiana) that was fixed in one of the nostrils with a foam ear tip. A probe tube microphone (model 7c; Etymotic Research, Elk Grove Village, Illinois) 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 bandpass 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 a sound pressure level of 90 dB, 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 tube 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- to 8-kHz range by 40 dB each. Therefore, the direct airborne stimulation of the microphone was considered to be negligible.

Additional measurements were performed 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 already described in this section. No change in sound pressure level was detected in the nose during swallowing. This means that the present setup was free of artifacts caused by

![Figure 1. Test setting of our revised sonotubometer with an example of the outcome. ET indicates eustachian tube.](image-url)
sounds of swallowing or sound pressure changes caused by acoustic alterations in the nose during swallowing.

Positive peaks were first identified in the microphone recordings in the ear canal online 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 2 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 exceeded 3 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 10-second intervals while in a 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 to the nasopharyngeal ostium of the ET to induce ET dysfunction. In a previous pilot study (N.H. and S.J.C.A., unpublished data, 2007), several different ways of applying histamine to the nasopharyngeal ostium of the ET were compared (ie, both transorally as well as transnasally). With an endoscope, the amount of swelling of the tubal mucosa was compared for each method. Using a pressure nebulizer with an extension piece that was passed through the nasal cavity until it was close to the tubal ostium was found to be the most effective way to cause mucosal swelling. A histamine phosphate solution with a concentration of 16 mg/mL was chosen to maximize the effect. The congestive effect of histamine occurs within a few seconds and reaches a maximum effect after 5 to 10 minutes, after which the effect lasts for approximately 60 to 75 minutes. 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 (N.H.).

The number of positive recordings of 10 acts of swallowing was counted as the outcome of the test. This outcome value could range from 0 to 10. Low values indicate poor ET ventilatory function. The results before and after histamine provocation were compared and analyzed for significance of differences by use of the paired $t$ test. In previous studies, the test results were not normally divided; therefore, the Wilcoxon signed rank test was performed as well. Statistical analyses were performed with SPSS statistical software (version 12.0.1; SPSS Inc, Chicago, Illinois).

### RESULTS

All measurements were easily performed, well tolerated, and successfully obtained. Application of histamine did not cause any adverse effects such as bronchoconstriction, anaphylactic reactions, or shock. The only reported complaint was a lump in the throat or nasopharynx, which lasted for a few hours. Twelve right ears and 13 left ears were measured. The baseline sound levels in the external ear canal (ie, the sound level that was measured when the subject was not swallowing) before and after histamine application were compared. No appreciable difference in this baseline sound level was found before and after histamine application. Figure 2 shows the ET function before and after histamine application and the mean difference with its distribution. Our study population of otologically healthy subjects showed a mean number of ET openings of 8.4 during 10 acts of swallowing (range, 4-10 openings) before application of histamine. Subsequently, in 22 of 25 subjects, application of histamine resulted in a marked deterioration of the ET function. In the other 3 subjects, histamine was applied again under endoscopic control to optimize application to the tubal ostium. Thereafter, the result changed from 6 to 4 openings during 10 acts of swallowing in 1 subject, whereas 2 subjects achieved 10 openings even though mucosal swelling of the tubal ostium was seen endoscopically. After histamine application, the mean number of openings was 2.7 (range, 0-10 openings). The difference between the first and the second measurements was substantial (mean difference, 5.6 [95% confidence interval, 4.4-6.9]; Wilcoxon signed rank test; $P < .001$).

Our revised sonotubometry setup proved to be a reliable instrument to measure ET function and even discriminate between different groups of various states of ET ventilatory function. 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 ET. Histamine is known to cause increased permeability of vessels and thus result in edema and local swelling. We assumed that this local edema 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. Because this may theoretically affect the measurement, we applied the histamine only
posteriorly in the nose and nasopharynx. In addition, we compared the baseline sound pressure level in the external ear canal before and after application. No important difference in the baseline sound pressure level was found, indicating that histamine application did not affect the transmission of sound from the nostril through the nasal cavity to the ET and in this manner did not affect the measurements.

Measurement of the ET function was successful in all subjects. The mean number of openings before histamine solution application was 8.4 (range, 4-10 openings). This is comparable with the findings in a larger group of otologically healthy adults. This finding indicates that even in otologically healthy adults who have no complaints of tubal dysfunction, the ET does not open with every act of swallowing. In the first test session, no change in ET function was found after histamine application in 3 subjects. Because deterioration in ET function was found in all other subjects, this was probably caused by inappropriate application of the histamine or an insufficient effect. Therefore, histamine was reapplied, and the measurement was repeated. In 1 subject the histamine may have missed the nasopharyngeal ostium of the ET during the first application because deterioration was found when histamine was reapplied under endoscopic control. In the other 2 subjects, the histamine may have affected only the medial part of the ET because mucosal swelling of the tubal ostium was seen endoscopically. However, these subjects still achieved a baseline value of 10 openings during 10 acts of swallowing. Mucosal swelling in the medial part may have insufficiently blocked the ET because that part of the funnel-shaped ET is much wider than its more central part (which is the most crucial part during the opening of the ET)17. Especially in subjects with very good ET function, such as these 2 individuals, the ET may open during every act of swallowing. Overall, an enormous change (mean difference, 5.6; 95% confidence interval, 4.4-6.9; P < .001) 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 offers 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, as shown by the findings described herein, intra-individual changes in the ET can be detected with our revised sonotubometer. For example, this method could be used to determine whether the ET function can be improved pharmacologically or whether other factors affect ET function positively or negatively. In addition, the course of decreased ET function in children (who are known to outgrow their lessened ET function) in selected subgroups can be followed up.

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REFERENCES