

Audiometric Changes in Chronic Secretory Otitis Media Due to Nasal Allergy

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Purpose: To investigate the possible role of nasal allergy on hearing levels in chronic otitis media with effusion (OME).

Method: In 87 adults who had chronic OME, 185 nasal challenges with allergen were performed using rhinomanometry combined with tympanometry and pure-tone audiometry (PTA).

Results: Of the 87 patients, 71 developed 131 positive nasal responses (NRs; $p < 0.01$), 119 of which were associated with significant changes in middle ear pressure ($p < 0.01$) and 96 with significant changes in PTA ($p < 0.01$). The hearing threshold increased significantly (>30 dB) at tone frequencies of

2,000 Hz during 63 NRs ($p < 0.05$) and at tone frequencies of 4,000 Hz during 93 NRs ($p < 0.01$).

Conclusion: Nasal allergy can affect Eustachian tube function, leading to the changes in the middle ear pressure and resulting in hearing impairment. Nasal challenges with allergen performed using rhinomanometry combined with tympanometry and PTA may be a useful diagnostic supplement in chronic OME patients. **Key Words:** Audiometry—Chronic otitis media with effusion—Chronic secretory otitis media—Nasal allergy—Nasal challenge with allergen—Tympanometry.

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Chronic otitis media with effusion (OME) may have an important clinical impact on hearing level and capacity. This disorder can cause a range of hearing changes at various levels (1–6). Dysfunction of the Eustachian tube (ET) usually plays a pivotal role in the pathogenesis of chronic OME (1,2,7–17). The nasal mucosa is related to the ET in various ways (1,2,7,9,14–19). Pathologic processes taking place in the nasal mucosa, nasal allergy being one of them, can influence ET function (1,2,7,9,10,13–20). Although the association of ET dysfunction and OME with nasal allergy has already been reported, the diagnostic procedures of chronic OME still vary (1–3,7,11,12). The relationship between the nasal allergy on one hand and ET dysfunction and chronic OME on the other hand has been demonstrated by nasal challenges with some selected allergens and histamine (2,7,9,13–17,19,20). However, the exact mechanism(s) underlying this relationship has not yet been fully clarified. There is also a dearth of information concerning audiometric changes due to the nasal allergy.

The purpose of this study, being a continuation of our previous work (19–23), was to investigate 1) the possible

involvement of nasal allergy in ET dysfunction and hence in the chronic OME; 2) the changes in the hearing level and capacity as measured by the pure-tone audiometry (PTA) during particular types of nasal responses (NRs) to allergen of challenge; 3) the possible use of the nasal challenges with allergen, combined with tympanometry and audiometry, in diagnostic procedures of chronic OME.

MATERIAL AND METHODS

Patients

Eighty-seven adults, aged between 15 and 31 years, with a history of bilateral chronic OME since childhood, having been referred to the Department of Allergology and Immunology, Institute of Medical Sciences “De Klokkenberg,” Breda, The Netherlands, in whom nasal allergy had been confirmed, volunteered to participate in this study. They had recurrent rhinitis, otitis media, and hearing loss to various degrees. All patients demonstrated otoscopic changes to various degrees in pneumatic otoscopy. The tympanic membrane (TM) expressed bluish-red color ($n = 13$), erythema ($n = 64$), single cicatrices ($n = 66$), opacification ($n = 77$), an air-fluid level or bubbles ($n = 19$), diminished motility ($n = 87$), and retraction ranging from a slight degree to an atelectasis ($n = 79$). Nasoscopy revealed erythematous and edematous nasal mucosa to various degrees ($n = 87$). All patients demonstrated positive intradermal tests and increased specific immunoglobulin (Ig) E in serum (positive radioallergosorbent test) for various

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inhaled allergens, blood and nasal secretion eosinophilia, slightly altered screening tympanometry, and air-conducted PTA, whereas the screening bone-conducted PTA was not altered (normal range).

In the past, they had been treated with various antibiotics, nasal glucocorticosteroids, H₁-receptor antagonists, and decongestants. All had undergone an adenoidectomy, tonsillectomy, and myringotomy. Many of them (n = 53) had been fitted out with ventilation tubes during their childhood. None had previously received immunotherapy, oral steroids, or nasal cromolyn. In all patients, the nasal histamine threshold had also been determined. A total of 185 nasal challenges with various inhalant allergens were performed in these patients by means of rhinomanometry, combined with simultaneous tympanometry and audiometry. Patients were examined in a period without manifest nasal or ear complaints and without any infections. Topical glucocorticosteroids and long-acting H₁-receptor antagonists were withdrawn 6 weeks before and short-acting H₁-receptor antagonists and nasal decongestants 48 hours before the study. The study was approved by the local ethical committee. Informed consent was obtained from all participants.

Allergens

Dialyzed and lyophilized allergen extracts (Allergopharma, Reinbek, Germany) were diluted in phosphate-buffered saline (PBS) and used for skin tests in concentrations of 100 to 500 BU/ml and for nasal challenges in concentrations of 1,000 to 5,000 BU/ml. The following allergens were used for nasal challenges: *Dermatophagoides pteronyssinus* and *farinae* (61), animal danders (45), grass pollen (43), flower pollen (6), tree pollen (19), and weed pollen (11).

Skin Tests

Intracutaneous tests were evaluated 20 minutes after the intradermal allergen injection. A skin wheal reaction (>7.0 mm in diameter) appearing within 20 minutes after the injection was considered a positive immediate skin response

(19,20,22). The negative controls were performed with PBS and positive with histamine diphosphate (0.01 mg/ml).

Nasal Provocation Tests

Nasal challenges with allergens were performed by means of rhinomanometry, which has already been described in our previous articles (19–25). The nasal mucosa response (nasal obstruction) was evaluated by means of nasopharynx-nostril pressure gradient (NPG) parameters, being the pressure differences (ΔP) expressed in centimeter of water. The nasal provocation tests (NPTs) were performed using the following schedule: 1) baseline (initial) values recorded at 0, 5, and 10 minutes before the challenge; 2) PBS control values recorded at 0, 5, and 10 minutes after a 3-minute application of PBS to the nasal mucosa of the nonintubated nasal cavity by means of a saturated wad of cotton wool on a nasal probe inserted under the concha media; 3) postchallenge values recorded after a 3-minute challenge with allergen at 0, 5, 10, 20, 30, 45, 60, 90, and 120 minutes, and subsequently every hour up to the 12th hour, and then every second hour in the periods between the 24th to 38th and 48th to 56th hour. The allergens used for the NPTs were chosen on the basis of the patient's history and skin tests (Table 1). The NR was assessed to be positive when the postchallenge mean NPG values increased by at least 2.0 cm H₂O ($1.2 \pm 0.3 = \text{mean} \pm \text{standard error}$) with respect to the prechallenge values, recorded at least at 3 consecutive time intervals. The NPG changes recorded within 60 minutes after the allergen challenge were considered to be a positive immediate NR, those recorded within 4 to 12 hours to be a positive late NR, and the changes recorded later than 24 hours to be a positive delayed NR (Figs. 1A, 2A, 3A) (19–25).

Control Tests With PBS

The control nasal challenge with PBS was performed in each patient studied following the same manner and time schedule as that used for the NPTs with allergens. A time interval of 2 days was consistently interposed between the consecutive tests.

TABLE 1. Survey of the significant MEP and air-conducted PTA changes and distribution of the PTA threshold values in decibels at sound frequencies of 2,000 and 4,000 Hz

NPT, n = 185	Decrease in MEP	Changes in PTA	Frequency of 2,000-Hz threshold, dB						
			0–10	10–20	20–30	30–40	40–50	50–60	>60
131 positive NRs	119	63							
35 isolated immediate	31	17	3	6	5	1	10	4	2
41 isolated late	39	21	1	9	8	3	9	6	3
28 dual late	23	10	0	5	8	3	4	3	0
19 isolated delayed	18	11	0	1	6	2	7	1	1
8 dual delayed	8	4	1	1	2	1	2	1	0
54 negative NRs	9	1	0	2	6	0	1	0	0
87 control PBS	0	0	19	30	38	0	0	0	0
NPT, n = 185	Decrease in MEP	Changes in PTA	Frequency of 4,000-Hz threshold, dB						
			0–10	10–20	20–30	30–40	40–50	50–60	>60
131 positive NRs	119	93							
35 isolated immediate	31	28	0	1	2	3	4	12	9
41 isolated late	39	33	1	3	2	2	10	8	13
28 dual late	23	13	0	3	7	0	5	4	4
19 isolated delayed	18	14	0	1	3	1	3	4	6
8 dual delayed	8	5	1	1	1	0	1	2	2
54 negative NRs	9	5	0	1	3	1	3	1	0
87 control PBS	0	0	20	32	35	0	0	0	0

Bold numbers indicate significant changes in the PTA thresholds; MEP, ME pressure in millimeters of water; PTA, air-conducted pure-tone audiometric threshold in decibels (<30 dB, normal; >30 dB, increased).

Tympanometry

Tympanometry was performed before and during all NPTs with allergens and PBS control tests by means of a Micro Tympanometer (Welch Allyn, Skaneateles Falls, NY, USA). The tympanometric parameters, the middle ear (ME) pressure (MEP), expressed in millimeter of water or in daPa units (1 daPa = 1.02 mm H₂O), were recorded at the same time points as the nasal NPG values. The normal range of MEP values is from -150(-200) to +150(+200) mm H₂O (1,8,11, 12,19-23,26).

Audiometry

PTA was performed by means of an AM 232 manual audiometer (Welch Allyn) in an acoustically isolated room. The audiometric parameters, the hearing level values in decibels (dB), were measured at frequencies of 500, 1,000, 2,000, and 4,000 Hz. This measure was recorded during all nasal challenges with allergens and PBS at the baseline and then 30, 60, and 120 minutes, 4, 6, 8, 12, 24, 36, and 48 hours after the challenge. The normal audiometric threshold values for adults vary between 20 and 28 dB (mean $\pm$ SD, 25 $\pm$ 3). The hearing threshold values are contra-values to the hearing capacity (level) (3-6,26).

Control Group

This group consisted of 51 young adults who had allergic rhinitis, confirmed by allergic tests, but without history of ME disease and with normal otoscopic findings. Fifty-one positive nasal challenges with allergen, recorded using rhinomanometry, were repeated and supplemented with tympanometry and PTA.

Statistical Analysis

The nasal (NR), MEP, and the audiometric responses were analyzed and statistically evaluated by means of generalized multivariate analysis of variance model (generalized MANOVA model) (27,28). Postchallenge parameter values (NPG, MEP, PTA thresholds in decibels) were compared with the prechallenge values. The polynomials were fitted, and the hypotheses were tested by the Potthoff and Roy MANOVA computerized system (27) modified by Timm (28). The statistical evaluation of the MEP and audiometric response changes was performed separately for each of the ears, and then the mean from both the *p* values was calculated. A *p* value less than 0.05 was considered to be statistically significant.

RESULTS

Nasal Responses

Of the 87 patients in whom 185 NPTs were performed, 71 developed 131 positive NRs ($p < 0.01$; Table 1); 35 isolated immediate NRs ($p < 0.001$), 41 isolated late NRs ($p < 0.001$), 28 dual late NRs (immediate, $p < 0.01$ + late, $p < 0.05$), 19 isolated delayed NRs ($p < 0.01$), 8 dual delayed NRs (immediate, $p < 0.01$ + delayed, $p < 0.05$), and 25 negative NRs ($p > 0.05$; Table 1, Figs. 1A, 2A, 3A). In the remaining 16 patients, 29 negative NRs ($p > 0.1$) were recorded. The 87 PBS control tests did not display any significant changes in the NPG values ($p > 0.1$). The differences between the positive and negative NRs were statistically highly significant at all time intervals ($p < 0.01$). No differences in the NRs were found with respect to the particular allergens.

Middle Ear Responses

Of the 131 positive NRs, 119 NRs (31 isolated immediate NR, 39 isolated late NR, 23 dual late NR, 18 isolated delayed NR, 8 dual delayed NR) and 9 of the 54 negative NRs were accompanied by a significant increase in the negativity of the MEP values ($p < 0.01$; Table 1; Figs. 1B, 2B, 3B). No significant changes in the MEP values were recorded during the remaining 12 positive NRs ($p > 0.05$) and 45 negative NRs ($p > 0.05$) or during the 87 PBS control tests ($p > 0.1$). No significant differences in the MEP values were recorded between the right and left ear during all tests ($p > 0.05$).

Audiometric Changes

In 61 of the 87 patients, the air-conducted PTA threshold values were already slightly elevated (30-35 dB; $p \leq 0.05$) before the NPTs. Ninety six of the 131 positive NRs (recorded in 71 patients) and 6 of the 54 negative NRs (25 of them recorded in 71 patients and 29 of them in the remaining 16 patients) were accompanied by significant changes in the air-conducted PTA. The significant audiometric changes were recorded during 29 of 35 isolated immediate NRs ($p < 0.01$), 35 of 41 isolated late NRs ($p < 0.01$), 13 of 28 dual late NRs ($p < 0.05$), 14 of 19 isolated delayed NRs ($p < 0.01$), 5 of 8 dual delayed NRs ($p < 0.05$), and 6 of 54 negative NRs ($p < 0.05$; Table 1). No significant differences in PTA values were found between the right and left ear ($p > 0.1$). The changes in PTA recorded at frequencies of 500 and 1,000 Hz were not numerous and only to a slight non-significant degree ($p > 0.05$). The significant PTA changes, as represented by the elevated air-conducted pure-tone threshold values, were recorded at frequencies of 2,000 Hz during 63 NRs ($p < 0.05$) and of 4,000 Hz in 93 NR cases ($p < 0.01$). The distribution of the PTA changes and threshold values with respect to the tone frequencies is summarized in the Table 1. The mean threshold values recorded during the particular isolated NR types are shown in Figures 1C, 2C, and 3C.

Control Subjects

The 51 control subjects developed 51 positive NRs to the repeated NPTs; 17 isolated immediate NRs ($p < 0.01$), 21 isolated late NRs ($p < 0.01$), 6 dual late NRs (immediate + late; $p < 0.05$), 5 isolated delayed NRs ($p < 0.05$), and 2 dual delayed NR (immediate + delayed; $p < 0.05$). The MEP and PTA values before the nasal challenges with allergen were within normal ranges in all control subjects. No significant changes in the MEP values ($p > 0.1$) or PTA values ($p > 0.05$) were recorded during the 51 repeated NRs.

DISCUSSION

Secretory otitis media or OME, especially in its acute forms, is a very common disorder in children (1,2). The recurrent and/or chronic OME forms occur more frequently in older children and also in adults (2,7,9).

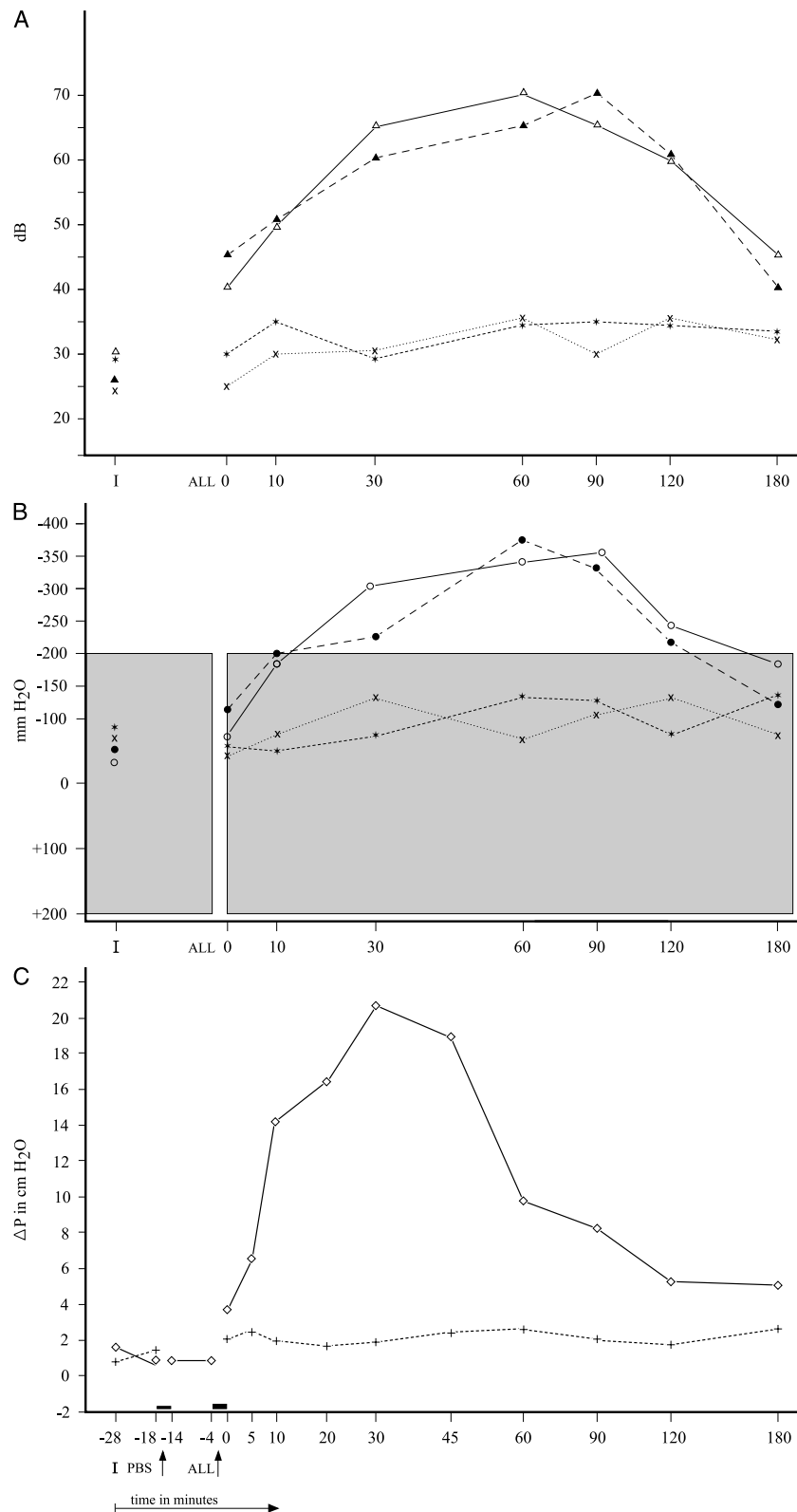


FIG. 1. The ME response accompanying the isolated immediate NR (IINR; $n = 29$) and the control response to PBS ($n = 29$). **A**, The mean PTAs in decibels recorded during IINR (Δ , right ear; $\blacktriangle$, left ear) and PBS (x , right ear; $*$, left ear) at frequency of 4,000 Hz. **B**, The mean values of the MEP recorded during IINR ($\circ$, right ear; $\bullet$, left ear) and PBS (x , right ear; $*$, left ear). **C**, The mean rhinomanometric values (NPG) recorded during IINR ($\diamond$) and PBS ($+$). ALL indicates allergen challenge; I, initial (baseline) values.

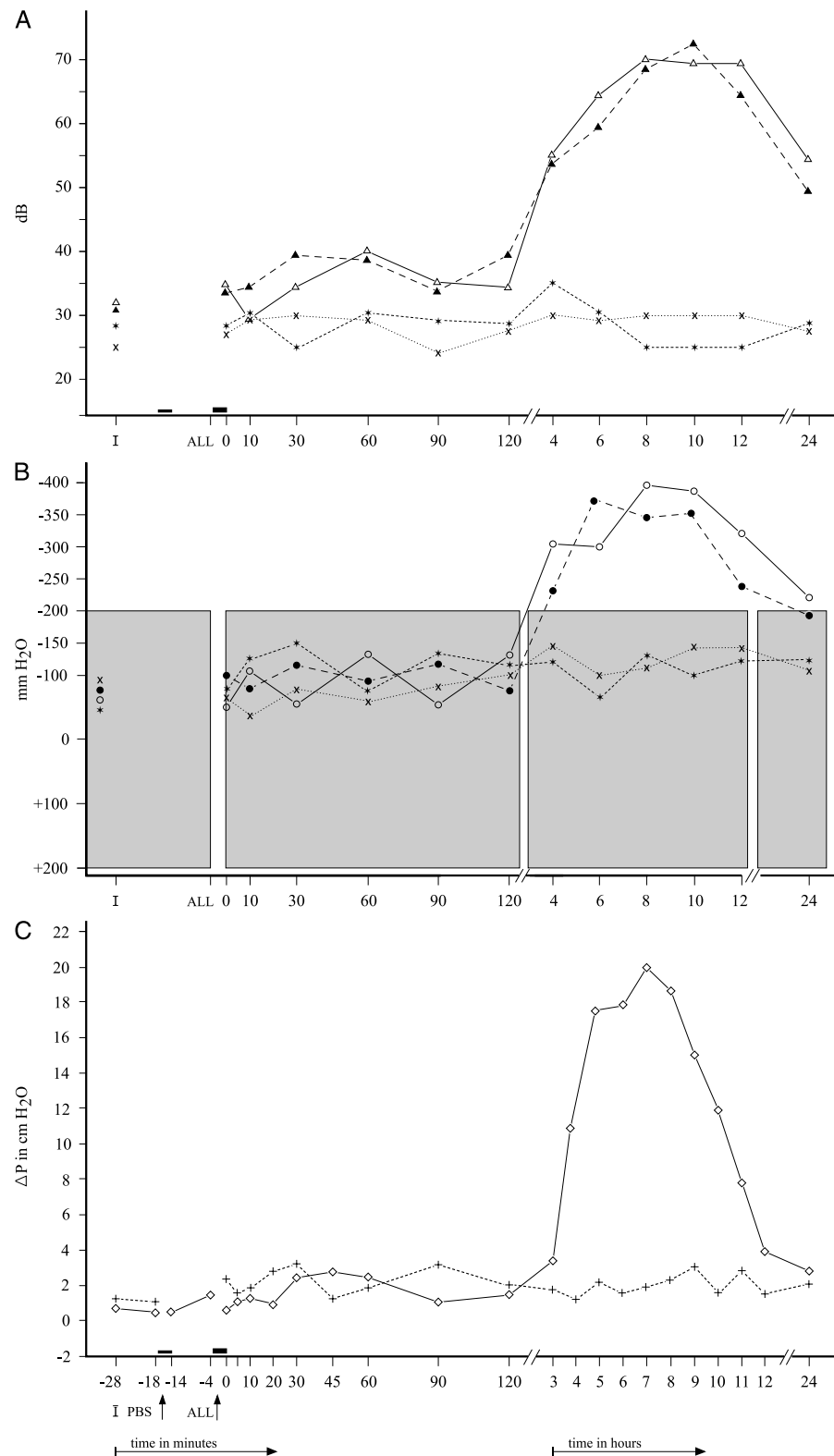


FIG. 2. The ME response accompanying the isolated late NR (ILNR; $n = 35$) and the control response to PBS ($n = 35$). **A**, The mean PTAs in decibels recorded during ILNR (Δ , right ear; $\blacktriangle$, left ear) and PBS ($\times$, right ear; $*$, left ear) at frequency of 4,000 Hz. **B**, The mean values of the MEP recorded during ILNR ($\circ$, right ear; $\bullet$, left ear) and PBS ($\times$, right ear; $*$, left ear). **C**, The mean rhinomanometric values (NPG) recorded during ILNR ($\diamond$) and PBS ($+$). ALL indicates allergen challenge; I, initial (baseline) values.

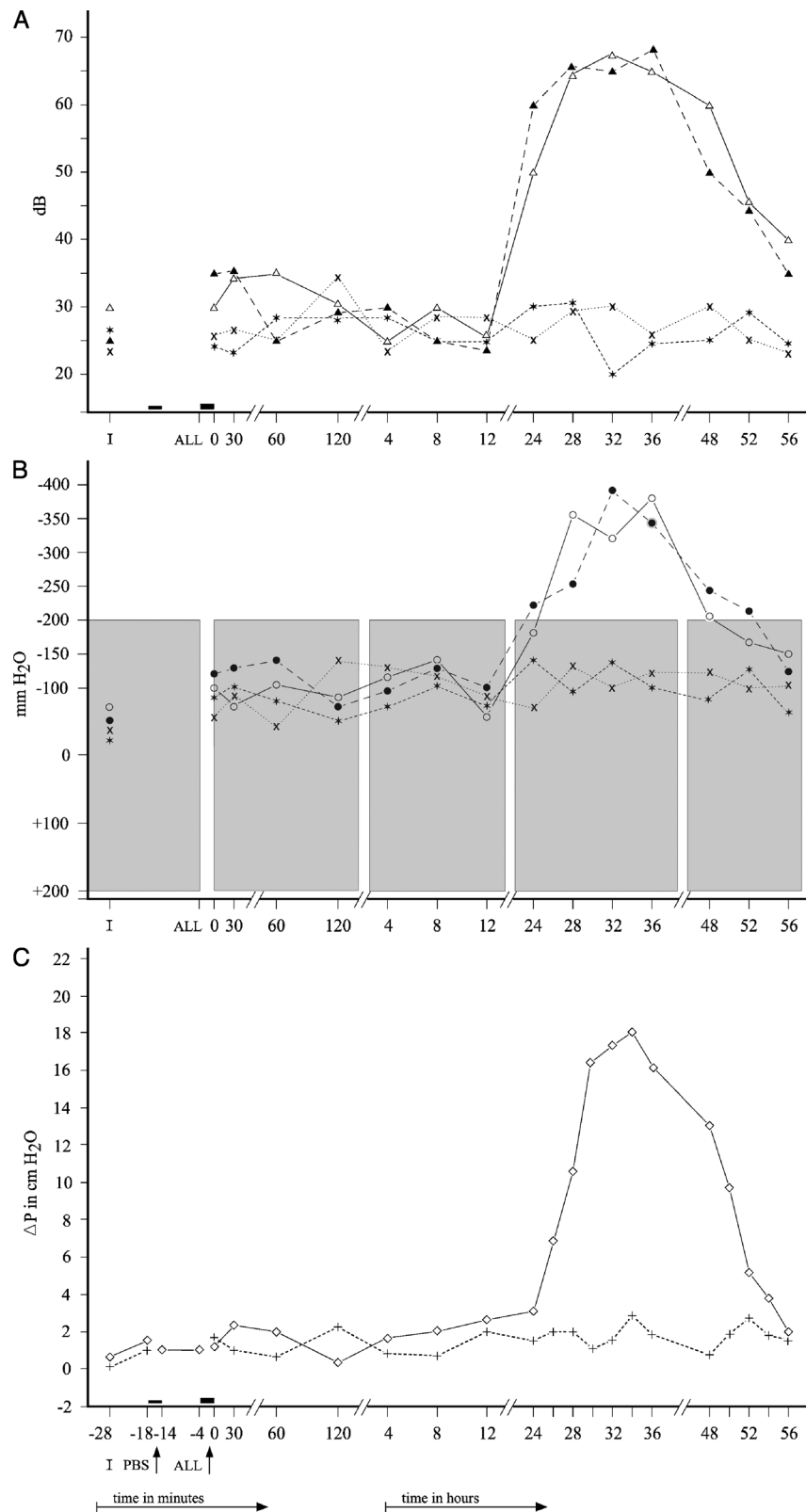


FIG. 3. The ME response accompanying the isolated delayed NR (IDYNR; n = 14) and the control response to PBS (n = 14). **A,** The mean PTAs in decibels recorded during IDYNR (Δ, right ear; ▲, left ear) and PBS (x, right ear; *, left ear) at frequency of 4,000 Hz. **B,** The mean values of the MEP recorded during IDYNR (○, right ear; ●, left ear) and PBS (x, right ear; *, left ear). **C,** The mean rhinomanometric values (NPG) recorded during IDYNR (◇) and PBS (+). ALL indicates allergen challenge; I, initial (baseline) values.

Chronic OME may be caused by a number of factors, nasal allergy being one of them (1,2,8,9,13,18–23).

The pathogenesis of chronic OME is associated with ET dysfunction. The role of the ET is to facilitate the communication of the ME cavity with other organs such as the nasopharynx and nasal cavity (1,2,7,9). Dysfunction of the ET include obstruction, abnormal patency, and nonoptimally functioning ciliated epithelium lining the ET (1,2,7). In this way, the ET plays a pivotal role in ME disorders (1,2,8,9).

Dysfunction of ET may also affect the TM. Abnormally active opening of ET leads to an increased tubal compliance, resulting then not only in the insufflation of the nasopharyngeal secretions into the ME but also increased positive pressure in the ME and a bulging ear drum. Conversely, obstruction of ET can lead to a persistent high negative pressure in ME, resulting in increased absorption of oxygen by the ME epithelium, increased production of secretions with subsequent accumulation in the ME cavity, and in retraction or collapse of the TM, the so-called eardrum atelectasis. These factors and mechanisms may then contribute to the development of OME (1,2,8,9).

Nasal allergy may be involved in chronic OME in various ways (2,7,9,18–21,23). The allergic reaction can take place in the mucosal membrane of the ET and/or the ME cavity, or it can occur in the related tissues such as the nasopharynx, adenoid, or lymphatic tissue. An allergic reaction occurring primarily in the nasal mucosa may affect the ET and ME in 2 ways: 1) the release of mediators, cytokines, and other factors that then migrate into the nasal secretions and are transported to the nasopharyngeal orifice of the ET; 2) a primary NR, characterized by nasal mucosa edema and nasal hypersecretion. The nasal mucosal edema then expands directly to the nasopharyngeal orifice of ET or it leads to nasal obstruction, affecting the ET indirectly through the high fluctuation of the air pressure in the nasopharynx (1,2,13–23).

The diagnostic confirmation of involvement of hypersensitivity mechanism(s) in the nasal mucosa is usually performed by skin tests and/or radioallergosorbent test. However, these tests provide evidence for existence of allergy somewhere in the body but not specifically in a particular organ. Moreover, these tests do not reflect the possible existence and involvement of the local antibodies in a particular tissue. Additionally, these tests usually provide information at a specific time and reveal no information on the dynamic aspects of the hypersensitivity mechanisms (1,2,7,11,18–25).

The NPTs combined with tympanometry and audiometry are able to demonstrate the causal role of a certain allergen in the nasal mucosa and subsequently in ET and ME and to record quantitatively their response in its dynamic course. In this way, the causal involvement of nasal allergy in OME can be confirmed unequivocally (19–23,25). Our results demonstrating the causal relationship between nasal allergy and chronic OME in some patients are in agreement with other investigators' findings (1,2,7,9,13–16), whereas they disagree with other

authors' observations (29). Yeo et al. (29) did not find any association between allergic rhinitis and OME. However, the lack of such association described in their study may probably be caused by an inadequate choice of a number of diagnostic parameters in their method. They did not indicate if they measured total or allergen-specific IgE antibody in the serum and in the ME effusion. Moreover, even the serum concentration of allergen-specific IgE antibody did not demonstrate significant correlation with positive immediate NR to allergen challenge in NPTs (19,30). A single recording of the eosinophil count in the blood and in the nasal secretions showed insufficient correlation with positive immediate NR to allergen challenge in NPT (19,22,31). Finally, the method of nasal provocation used by these authors was in some ways incomplete. The NR to allergen challenge was evaluated by means of symptom score only and not by recording of relevant objective parameters such as nasal resistance or nasal air-passage/conductance (19,25). No adequate controls such as with discs only and with discs impregnated with allergen diluting means were performed. This may be a very important aspect because the discs themselves may cause a nonspecific irritation of the nasal mucosa. In addition, the postchallenge recording of symptoms up to 20 minutes only seems insufficient with respect to the existence of various NR types (19–25).

One of the most important clinical consequences of chronic OME is its influence on hearing. Changes in hearing due to chronic OME can be of various degrees, from very mild hearing impairment to distinct loss of hearing, reversible or irreversible, and of other various kinds such as decrease in hearing intensity (contravalue of which is elevation of the hearing threshold), and changes at a single or multiple frequencies (1–7,11,12). Hearing can principally be influenced by 2 basic mechanisms, sensorineural and mechanical. In the patients with chronic OME such as those included in our study, the mechanical mechanism was predominantly involved in the ET dysfunction (1–6,26). Audiometry is the exclusive clinical procedure for the evaluation of the hearing quality and capacity. Various kinds of audiometry are used in praxis such as air-conducting PTA, bone-conducting audiometry, speech audiometry, and all 3 methods with or without masking. In addition, impedance audiometry, otoacoustic emissions tests, and auditory brain stem evoked potentials (ABEP) may be used. Nevertheless, PTA continues to be one of the most widely used audiometric tests. Pure-tone audiometry can be performed in 2 forms, either as a determination of the air-conducted or the bone-conducted threshold (5,6,26). We used the air-conducted PTA method, estimating the threshold values at different pure-tone frequencies, because this method is the most suitable for the evaluation of the hearing changes in chronic OME related to ET dysfunction (4–6,26). However, in view of our experiences, we have partly adapted the evaluation criteria for this procedure (19). In the literature, the normal values of the air-conducting hearing threshold for adults vary from 15 to 25 dB for the pure-tone

frequencies from 500 to 8,000 Hz (4–6,26). In our patient population, adults with various allergic disorders with the exception of nasal allergy and otitis media, we found the range of the pure-tone intensity of 20 to 30 dB without any significant differences with respect to particular frequencies. Therefore, we have considered the hearing threshold values up to 30 dB to be normal values for the frequencies of 500, 1,000, 2,000, and 4,000 Hz. The comparison of the prechallenge and postchallenge air-conducted PTA threshold values may lead to a very important conclusion. The prechallenge PTA threshold values were only very slightly elevated (30–35 dB; $p \leq 0.05$), whereas the postchallenge PTA threshold values demonstrated significant changes (elevation) in most patients during many of the positive NPTs (96 from 131; $p < 0.05$ to $p < 0.01$). Hearing losses observed in our patients, exceeding sometimes those expected for negative MEP values, cannot be explained satisfactorily. A possible irregular or partly diminished elasticity of the ear drum or a transient secondary reaction of cochlea cannot be therefore fully excluded, at least in some of these patients. However, this conclusion is only a hypothesis because no bone-conducted PTA thresholds have been recorded simultaneously with the air-conducted PTA thresholds in this actual study. We are aware of this disadvantage in our study. Nevertheless, this aspect was for us the reason to conduct another supplementary study including the simultaneous recording of the air-conducted and bone-conducted PTA thresholds, together with the tympanometry and rhinomanometry, in a smaller group of patients who have chronic OME and demonstrating an isolated late NR to allergen challenge. The data of this supplementary study will be presented, after the final analysis and statistical evaluation, in our next article.

These results emphasize the usefulness of the repeated measurement of the audiometric parameters (e.g. threshold values) related to the nasal allergen challenge, and of following these parameter changes in their dynamic course. These data also confirm the diagnostic value of the NPTs with allergens performed with rhinomanometry and in combination with tympanometry and pure-tone air-conducting audiometry in patients with chronic OME. The confirmation of the role of nasal allergy in chronic OME and consequential hearing impairment would indicate the need of an additional treatment of the nasal allergy in these patients, which may result in an improvement of hearing complaints.

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