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ORIGINAL ARTICLE

The incidence of atopy in adults with recurrent secretory otitis media: screening with Phadiatop®

Rekürren sekretuar otitis media'lı erişkin hastalarda atopi insidansının Phadiatop® ile araştırılması

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Objectives: This is a preliminary report of a relatively new method: Phadiatop®, in screening atopic adult patients with recurrent secretory otitis media (SOM). The sensitivity and specificity, and its use in atopic adult patients with recurrent SOM are described.

Patients and Methods: Eighty four patients (54 females, 30 males; mean age 36.7; range 19 to 62 years) who were diagnosed as recurrent SOM were included in the study. The patients were evaluated with detailed history, laboratory tests, skin-prick test and total IgE. Patients with at least one positive skin-prick test and/or high total IgE with a positive history were considered to be in atopic status.

Results: According to certain criteria, atopy was detected in 31 of the 84 patients. Negative Phadiatop® values were found on all of 53 non-atopic patients as well as in one atopic patient. Among 31 patients having atopy, 30 of them showed positive Phadiatop® values (Specificity: 1.00, sensitivity: 0.97, predictive value, positive: 1.00, predictive value, negative: 0.98).

Conclusion: These results indicate that Phadiatop® is an effective test to detect atopy in patients with recurrent SOM.

Key Words: Secretory otitis media; atopy; recurrent; Phadiatop®.

Amaç: Rekürren sekretuar otitis mediası (SOM) olan erişkin hastalarda, göreceli yeni bir yöntem olan Phadiatop® ile atopi varlığı araştırıldı; yöntemin duyarlılığı, özgüllüğü ve tarama testi olarak kullanılabilirliği incelendi.

Hastalar ve Yöntemler: Çalışmaya rekürren SOM tanısı alan 84 hasta (54 kadın, 30 erkek; ort. yaş 36.7; dağılım 19-62) alındı. Hastalarda öykü, laboratuvar bulguları, deri testi ve total IgE düzeyi incelendi. En az bir deri testi pozitif ve/veya total IgE sonucu yüksek, öyküsü pozitif olan hastalar atopik olarak kabul edildi.

Bulgular: Belirlenen kriterlere göre rekürren SOM'u olan 84 hastanın 31'inde atopi saptandı. Atopik olmayan 53 hastanın hepsinde ve bir atopik hastada Phadiatop® değerleri negatif bulundu. Otuz bir atopik hastanın 30'unda Phadiatop® değerleri pozitif bulundu (Özgünlük:1.00, duyarlılık: 0.97, pozitif tahmin değeri: 1.00, negatif tahmin değeri: 0.98).

Sonuç: Bu bulgular, rekürren SOM'u olan hastalarda atopinin saptanması için Phadiatop®'un etkin bir tarama testi olduğunu göstermektedir.

Anahtar Sözcükler: Secretuar otitis media; atopi; rekürren; Phadiatop®.

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Secretory otitis media (SOM) is a common disease in children but is less seen in adult population and its etiologic factors are less explained in adults. It is basically an illness of infancy and childhood. SOM is more frequent during childhood related to poor development of Eustachian tube, due to its short and narrow structure with respect to adults or due to physiological causes such as its poor drainage or related to such diseases as adenoid hypertrophy, cleft palate-lip, recurrent upper respiratory tract infections and allergies, of which the incidences of such diseases are less common among adults. It is a chronic inflammatory disease with Eustachian tube obstruction either mechanically or functionally. Prolonged Eustachian tube obstruction leads to decreased middle ear pressures and accumulation of fluid within the middle ear behind the intact tympanic membrane.[1] This disorder is now considered to be a multifunctional disease process with several potential etiologies: Inflammatory, immunologic and biochemical.[2] Allergic etiology has also been suggested to play an important role in SOM. To establish a connection between atopy and recurrent SOM, lots of screening methods like blood eosinophil counts, eosinophilia in nasal smear, serum total IgE values, skin prick tests need to be evaluated, however, a reliable and simple assessment technique to screen recurrent SOM patients for atopy would be an easy way to diagnose and plan the treatment of the atopic patients in otology departments.

Phadiatop® is an in vitro test, which detects mixed specific IgE antibody concentrations formed against certain allergens. Patient's sensitivity to any inhalant agent can be figured out with this test by a unique blood sample, as well as, specific causative allergenic antigens can be determined. Eriksson reported the availability of Phadiatop® test for atopy screening in adult population.[3]

In our study group, allergic rhinitis (AR), allergic asthma (AA), atopic eczema/dermatitis syndrome (AEDS) and food related allergy (FRA) were found to be the etiologic factors of atopy in patients with recurrent SOM. The purpose of this study was to evaluate the efficiency of Phadiatop® test as a screening method for the evaluation of atopy in recurrent SOM patients.

MATERIALS AND METHODS

Eighty-four patients (54 females, 30 males; mean age 36.7; range 19 to 62 years) who were diagnosed as recurrent SOM were included in the study. The patients attending to Otolaryngology Department for post-treatment recurrent SOM were enrolled in the study group. The patients had at least 3 serous otitis attacks during the last 6 months or remained unresponsive to two medical treatment.[4] All patients underwent a through otolaryngologic examination and audiologic evaluation with tympanogram.

The following criteria were used during diagnosis of SOM:[1,4-8] 1- The pressure feeling in the ears expressed in patients past history (which lasts for more than 3 months), aural fullness sensation, loss of hearing, existence of tinnitus or dizziness, recovery of hearing through swallowing or yawning. 2- In the otoscopic examination; the colour change of ear drum in the translucent places into opaque, dirty white or yellow colour; the loss of light reflex at the front bottom screen; findings related with the reaction of ear drum; and the existence of intact tympanic membrane and absence of acute otitis media findings. 3- In the tympanogram the middle ear pressures (unilateral or bilateral): to have pressures over -100 mmH2O, to obtain a "B" typed curve or a flat line in Jerger's Classification.

The patient yielding one or more of other etiological factors below were kept out of the study:[9] 1- Nasal septal deviation, 2- nasal poliposis or presence of mass, 3- nasopharynx carcinoma or pathologies, 4- adenoid vegetation, 5- cleft palate or anatomical malformations, 6- insufficient treatment with antibiotics after acute otitis media attack, 7- tubal dysfunction due to radiotherapy or iatrogenic causes after surgery.

Atopy was examined in the patient group with these diagnostic criteria: 1- Family history of atopic illness, 2- history of any allergic illness and existence of such an illness, 3- seasonal recurrences of the symptoms which have not been diagnosed, 4- high sedimentation rates, 5- high total eosinophil count values, 6- increases eosinophil count in nasal smear, 7- high serum total IgE values, 8- positive skin prick tests. Patients with at least one positive SPT and/or high total IgE with a positive history were considered to be in atopic status.[10-17] The study was conducted according to the ethical standards of our hospitals, which require informed consent from each patient.

Family history of allergy was collected by a standardized questionnaire, which was part of the pro-

tocol of the European Community Respiratory Health Survey and was administered by a clinical interview.[18] The presence of history of any allergic disease and seasonal recurrence of the symptoms were based on the patient's statements and previous clinical and laboratory assessment. Following criteria was used for describing atopic disease. Allergic asthma (AA) was described as wheezing and/or dyspnea associated with definitive environmental exposure, and exclusion of other disease for at least 3 months.[19] A patient was described to have allergic rhinitis (AR) if there were symptoms of runny nose, itchy nose, sneezing and stuffed nose after exposure to a particular allergen, and if all of these were unrelated to infection. The diagnosis of Allergic Atopic Eczema/Dermatitis syndrome (AEDS) was based on the description by Hanifin and Rajka.[20] Food related allergy (FRA) was described based on a careful history followed by allergy testing and oral challenge.[21] Concomitant allergic diseases and atopy criteria were determined according to these subgroups.

The complete and differential blood cell counts, erythrocyte sedimentation rate (normal; 0-20 mm/1st hour) were analyzed. Eosinophil count greater than 450/µl. was considered as a "high blood-eosinophil count" according to Lim and Weller's blood eosinophilia determination.[22] Nasal secretions were obtained over the length of the inferior turbinate with a common cotton swab. Smears were stained with Diff-Quik stain to differentiate between eosinophils, neutrophils and epithelial cells and were analyzed by optic microscope (Olympus U-SPT). Samples were examined in a blinded fashion. Nasal eosinophilia was defined by a smear showing an eosinophil count of 10% to 25% of adults'.[23] Serum total IgE concentrations and Phadiatop were determined with the Pharmacia CAP System test (Pharmacia and Upjohn Diagnostics, Uppsala, Sweden) and the results were given in kU/l. Phadiatop® panel were including 10 common aeroallergens, namely D.pteronyssinus; C.herbarum; dander from horse, dog, and cat; and pollen from birch, timothy, mugwort, Olea europaea, and Parietaria. Serum samples with IgE concentrations of 0.35 kU/l or more were regarded as high, as recommended by the manufacturer. The persons performing or recording the in vitro testing did not know the clinical diagnosis. Skin prick tests (SPT) (Soluprick ALK, Denmark) were performed on the flexor aspect of forearm. The tested allergens were D.pteronyssinus, D.farinea, grass mix, tree mix, wool, cow's milk, hen's egg, cacao, dog epithelium, cat pelt and mixed feathers. Reactions were recorded after 15 minutes. SPT results were considered positive if the wheal was larger than 2mm or an area at least 25% that of a reference histamine reaction (1 mg/ml histamine chloride).

TABLE I

CHARACTERISTICS OF RECURRENT SECRETORY OTITIS MEDIA

Patients with recurrent SOM	n	%
Medical treatment		
treated medically before	67	80
non-treated	17	20
High middle-ear pressure*		
unilateral	13	15
bilateral	71	85
SOM attacks in the last 6 months		
2	7	9
3	51	60
4	25	30
unknown	1	1

SOM: Secretory otitis media; *: Middle-ear pressure is above -100 mmH2O.

The physician classified the patients as atopic or non-atopic, depending on the result of case history, laboratory values, positive SPT or high total IgE. Phadiatop® blood sample test was administered to 31 atopic and 53 non-atopic patients. As a consequence, efficiency of Phadiatop® values were considered in the diagnosis of atopy. The following indices were used to characterize the Phadiatop® test:

Sensitivity: proportion of positive tests in atopics.

Specificity: proportion of negative tests in non-atopics.

Positive predictive value (PPV): proportion of true-positive test results among all positive tests.

Negative predictive value (NPV): proportion of true-negative test results among all negative tests.

RESULTS

According to clinical evaluation of 84 patients with recurrent SOM, 31 of them were atopic and 53 non-atopic. The frequency of previous SOM attacks,

TABLE II

DATA FOR CLINIC DIAGNOSIS OF ATOPY IN RECURRENT SECRETORY OTITIS MEDIA PATIENTS

Patients with recurrent SOM	M/F (30/54)	Total (n=84)	Percentages (%)
(+) Family history of allergy	6/16	22	26.2
No family history of allergy	24/38	62	73.8
(+) History of atopic disease	12/19	31	36.9
AR	7/4	11	35.5
AA	0/4	4	12.9
AEDS	1/3	4	12.9
FRA	1/2	3	9.7
AR+AA	3/3	6	19.3
AR+AA+AEDS	0/3	3	9.7
No history of atopic disease	18/35	53	63.1
(+) Seasonal allergic symptoms	4/15	19	22.6
AR	1/5	6	31.6
AA	0/4	4	21.0
AR+AA	3/3	6	31.6
AR+AA+AEDS	0/3	3	15.8
No seasonal allergic symptoms	39/26	65	77.4
Eosinophilia in blood	9/11	20	23.8
AR	6/4	10	50.0
AA	0/2	2	10.0
AR+AA	3/3	6	30.0
AR+AA+AEDS	0/2	2	10.0
Normal eosinophil-count in blood	37/27	64	76.2
Nasal eosinophilia	11/7	18	28.1
AR	6/4	10	55.6
AA	2/2	4	22.2
AR+AA	2/1	3	16.7
AR+AA+AEDS	1/0	1	5.5
Normal nasal smear eosinophil-count	19/47	66	71.9
High total IgE	11/16	27	32.1
AR	7/4	11	40.8
AA	0/3	3	11.1
AEDS	1/3	4	14.8
FRA	1/1	2	7.4
AR+AA	1/2	3	11.1
AR+AA+AEDS	1/3	4	14.8
Normal total IgE	19/38	57	67.9
Positive SPT	9/16	25	29.8
AR	6/4	10	40.0
AA	0/3	3	12.0
AEDS	1/2	3	12.0
FRA	1/1	2	8.0
AR+AA	1/3	4	16.0
AR+AA+AEDS	0/3	3	12.0
Negative SPT	21/38	59	70.2

AA: Allergic asthma; AR: Allergic rhinitis; AEDS: Atopic eczema/dermatitis syndrome; FRA: Food related allergy; SOM: Secretory otitis media; SPT: Skin prick test.

TABLE III

RESULTS OF SKIN PRICK TEST IN 84 PATIENTS WITH RECURRENT SOM

Allergen (≥ 1+)	No. positive test
Dermatophagoides pteronyssinus	20
Dermatophagoides farinea	19
Grass mix	21
Tree mix	22
Wool	21
Cow's milk	12
Hen's egg	11
Cacao	12
Dog epithelium	14
Cat pelt	15
Mixed feathers	6

the presence of negative middle-ear pressure and previous therapy on recurrent SOM patients appear in Table I.

Of the 54 (64%) women and 30 (36%) men, 31 were atopic. 24 (77%) of atopic patients were women. The age distribution of the study group second, third, forth, fifth and sixth decade and older were respectively 20%, 44%, 31%, 4% and 1%. As a consequence, SOM disease was more common in young adult population and in women; also atopic etiology was more common in women in our group.

In the clinic diagnosis of atopy, family history, concomitant atopic disease accompanying to the recurrent SOM, seasonal allergic symptoms were investigated and laboratory values were obtained. After distinguishing patient's history by diagnostic groups, data for atopy criteria are obtained and shown in Table II. The results of SPT in the patients with recurrent SOM are shown in Table III. According to patient's history and age characterization, total IgE results are given in Table IV. In 45 (54%) patient an elevated sedimentation rate was obtained, 29 (35%) of them had atopy history. Majority of patients who have no structural abnormalities or infection are diagnosed as "atopic" and usually have seasonal allergic symptoms. The rest of patients presented with atopy reported longer and perennial symptoms. Patients who had AEDS and food related allergy, presented with SOM symptoms only during the food or allergen contact period. All of the 31 patients with atopy and SOM revealed at least one or more allergic complaints. Most common symptoms of the patients with SOM and atopy were the symptoms of allergic rhinitis (65%). Although 31 patient's history indicated atopy, 25 (81%) of them had positive SPT, and 27 (87%) of them had high total IgE levels.

According to clinic diagnosis, 31 of the 84 adult patients having recurrent SOM also had atopy (37%). Negative Phadiatop® values were found in all of the 53 patients who had recurrent SOM without any evidence of atopic complaints. Positive Phadiatop® values were found in 30 of the 31 patients who had recurrent SOM and atopy (98%). One patient (37y, female) with a falsely negative Phadiatop® test had a positive history of allergic rhinitis, positive SPT to the tree mix and cat pelt, and had symptom-free seasons. Comparison of Phadiatop® results of the atopic and non-atopic patients and statistical analysis are shown in Table V.

TABLE IV

RESULTS OF HIGH TOTAL IgE IN 27 PATIENTS WITH RECURRENT SOM ACCORDING TO THEIR ATOPY HISTORY

Subjects according to	n	Sex (M/F)	Total IgE* atopy history (kU/l)
AR	11	7/4	560 (33-2200)
AA	3	0/3	360 (51-520)
AEDS	4	1/3	250 (30-510)
FRA	2	1/1	350 (55-645)
AR+AA	3	1/2	1140 (33-2100)
AR+AA+AEDS	4	1/3	650 (35-1190)

*: Median and range.

TABLE V

COMPARISON BETWEEN CLINICAL DIAGNOSIS AND PHADIATOP®

Phadiatop®	Clinical diagnosis	Atopic
Non-atopic		
Positive	30	0
Negative	1	53
Total	31	53

Diagnostic indices for Phadiatop®	
Sensitivity	0.97
Specificity	1.00
PPV	1.00
NPV	0.98

The patients included in the study whose Phadiatop® results were positive have been considered as "atopic recurrent SOM" and their management and follow-ups have been arranged.

DISCUSSION

The study showed the high diagnostic precision of the Phadiatop® in vitro screening method, with a sensitivity of 0.97, a specificity of 1.00. In Eriksson's study, diagnostic indices of Phadiatop® according to former reported studies were listed with a mean sensitivity of 0.91 and a mean specificity of 0.93. Although it is higher than these mean value, Phadiatop® found in this study is in agreement with that found by other authors.[3]

In clinical diagnostics, a patient history is the first step and should always be included in the diagnostic consideration. According to this study, all patients with diagnosis of atopy were exactly accommodating with their history. One patient (37y, female) with a falsely negative Phadiatop® had a positive history of allergic rhinitis revealed positive SPT to the tree mix and cat pelt. These results showed the high sensitivity and specificity of screening questionnaire on the diagnose of atopy.

The presence of high total Ig E in patients with allergic complaints of upper and lower respiratory system, remind us atopy as an etiologic factor. However, Sapan et al[24] reported that during parasite endemies or in childhood, IgE results might be false positive. In those cases, Phadiatop® values should be preferred instead of IgE evaluation for determining atopic status inorder to eliminate over-diagnosis.[24,25]

On the other hand, since allergic diseases have symptoms that can easily be confused with other disorders, even specialists may have difficulty in using only the case history and physical examination to distinguish the different disease etiologies, without using tools to aid in the identification of the atopic etiologies. The majority of allergic patients, may be 80%, are seen by family physicians and primary care physicians or are not seeking medical care for their problems.[26] Also in otolaryngology departments, allergy diagnosis is based on case history and physical examination sometimes accompanied by special tests. If a patient complains about SOM, the basic plan of examination is based on otitis diagnosis and treatment. Therefore we try to figure out a simple and reliable assessment technique to screen recurrent SOM patients for atopy: Phadiatop® test. It should be an easy way to diagnosis of the atopic patients for appropriate treatment, which will aid to decrease the recurrent attacks of SOM.

Phadiatop®, is an in vitro test, which measures the concentrations of the specific IgE antibody, which is formed against the allergens. By the result it is determined whether it is more sensitive to anyone of the mixed allergens and that if it is sensitive to, which antibody is responsible for this. As the allergen causes tubal dysfunction in patients with SOM, this is formed as the result of the nasal inflammation and edema that is caused by allergic rhinitis. According to some researches, the middle ear mucosa is one of the target organs in allergy. In the patients having recurrent SOM, the permanent existence of this allergic stimulation causes the recurrence of the inflammation and increase in the symptoms. The removal of this allergic stimulation shall be the basis of the treatment in atopic patient with recurrent SOM.

This study has been carried out for the determination of the value of Phadiatop® in the diagnosis of atopy of adults having recurrent middle ear inflammation. The results of Phadiatop® measurements and clinical diagnosis of atopy have been examined, and minimal superiority of the clinical diagnosis has been stated, however, this clinical assessment is more time-consuming procedure and need to be performed by allergists. By using Phadiatop® test,

physician doesn't need further testing before referring the patient to allergist, so it could be a sensitive and time-saving measure in atopy diagnosis in otolaryngology department for further evaluation and treatment of the main etiologic factor; atopy, causing recurrent disease. This article describes that adults with recurrent SOM should be investigated for atopy prediction.

In conclusion, Phadiatop® is a rapid and efficient way in diagnosis of atopy with high sensitivity. We suggest that Phadiatop® test is an appropriate method for screening atopy in recurrent SOM patients, which would establish a good communication, network between otolaryngologist and allergist and improve the prognosis on recurrent disease.

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