ASTIM ALLERJi iMMÜNOLOJi
ASTHMA ALLERGY IMMUNOLOGY

Asthma Allergy Immunol 2010;8:189-192

OLGU SUNUMU CASE REPORT

Aspirin-sensitive asthma aggrevation after toothpaste use

Diş macunu kullanımı sonrası aspirine duyarlı astım alevlenmesi

Mehmet HOXHA[1], Eriola PİLURİ[1], Eris MESONJËSİ[1], Alfred PRİFTANJİ[1]

[1] **Department of Allergology and Clinical Immunology, University Hospital Center: "Mother Teresa" Tirana, Albania**
Allerji ve Klinik İmmünoloji Bölümü, "Mother Teresa" Üniversite Hastanesi, Tiran, Arnavutluk

ABSTRACT

Hypersensitivity to aspirin is present in 5-10% of asthmatic patients and is associated with chronic rhinosinusitis and nasal polyposis, a syndrome referred to, recently as Aspirin-exacerbated respiratory disease. Menthol (oil of peppermint) is often used as flavoring in toothpastes, in candies and chewing gums. We report a case of a 50 year old woman, with persistent rhinitis, moderate asthma and nasal polyposis. She was a known, well controlled asthmatic patient. She presented to the emergency room with severe rhinorrhoea, sneezing, nasal obstruction, dyspnea and cough, after having a menthol-flavored candy. She experienced similar symptoms when she used a menthos and after brushing her teeth with toothpaste. Skin prick test with culprit toothpaste and menthol were negative. Because of her history, we speculate that the patient was aspirin-sensitive, so we performed an oral provocation test with aspirin in order to confirm the Aspirin-exacerbated respiratory disease diagnosis and it resulted positive at first dose. A challenge was then performed with menthol and another with toothpaste. The mechanism of the hypersensitivity reaction to aspirin is not immunological. Aspirin is known to cause inhibition of the cyclooxygenases, which metabolize arachidonic acid to

ÖZET

Aspirine karşı aşırı duyarlılık astımlı hastaların %5-10 oranında mevcut ve de kronik rinosinüzit ve nazal polipozis ile ilişkili, bir sendromdur, son zamanlarda aspirinin şiddetlendirdiği solunum hastalığı olarak anılmaya başlamıştır. Mentol (nane yağı) genellikle diş macunu ve şekerlerde tadlandırıcı olarak kullanılmaktadır. Bu makalede persistan rinit, orta düzeyde astım ve nazal polipozisi olan, 50 yaşındaki bir kadın olgumuzu sunuyoruz. Hasta bilinen ve astımı kontrol altında olan bir hastadır. Acil servisine şiddetli burun akıntısı, hapşırma, burun tıkanıklığı, nefes darlığı ve öksürük şikayetleri ile başvurdu. Hastada benzeri belirtiler diş macununu kullandıktan sonra ve Menthos gibi şekerleri yedikten sonra da ortaya çıkmıştı. Söz konusu diş macunu ve mentol ile yapılan deri testi negatifti. Hastanın hikayesinden dolayı hastanın aspirine karşı duyarlı olabileceğinden şüphelenildi, doğrulamak amacıyla, aspirin ile oral provokasyon testi yapıldı. Alınan ilk dozla test sonucu pozitif çıktı ve aspirin duyarlı astım tanısı kondu. Daha sonra benzeri denemeler mentol ve diş macunu ile tekrarlandı. Aspirine karşı aşırı duyarlılık reaksiyonun mekanizması immünolojik değildir. Aspirinin, araşidonik asidini prostaglandinlere çevirerek, siklooksijenaz inhibitörü olarak rol aldığı bilinmektedir. Bu inhi-

Yazışma Adresi/Address for Correspondence
Dr. Mehmet HOXHA
Allerji ve Klinik İmmünoloji Bölümü, "Mother Teresa" Üniversite Hastanesi, Tiran, Arnavutluk
e-posta: klevihoxha@yahoo.com

prostaglandins. This inhibition leads to an up-regulation of the alternative pathway, with lipoxygenases metabolizing arachidonic acid to leukotrienes. The menthol, due to the same mechanism, might be considered one of the triggering of Aspirin-exacerbated respiratory disease.

(Asthma Allergy Immunol 2010;8:189-192)

Key words: Menthol, aspirin, asthma

Received: 09/07/2010 • Accepted: 27/09/2010

bisyon alternatif yollarının up-regülasyonuna yol açar ve lipooksijenazlar araşidonik asidini lökotrienlere çevirir. Mentolün de, aynı mekanizma sayesinde, aspirinin şiddetlendirdiği solunum hastalığını tetiklediği düşünülmüştür.

(Asthma Allergy Immunol 2010;8:189-192)

Anahtar kelimeler: Mentol, aspirin, astım

Geliş Tarihi: 09/07/2010 • Kabul Ediliş Tarihi: 27/09/2010

INTRODUCTION

Hypersensitivity to aspirin (acetylsalicylic acid; ASA) presented in 5-10% of asthmatic patients and is associated with chronic rhinosinusitis and nasal polyposis, a syndrome referred to, as the aspirin triad recently as aspirin-exacerbated respiratory disease (AERD)[1,2]. Menthol (oil of peppermint) is often used as flavoring in toothpastes, in candies and chewing gums.

CASE REPORT

We report a case of a 50 year old woman, with persistent rhinitis, moderate asthma and nasal polyposis (NP). She was a known asthmatic for the past 15 years, well controlled with fluticasone, formeterol, and salbutamol (for the asthma's exacerbations) as prescribing in GINA guidelines. She was taking also nasal topical corticosteroids, (cornerstone for treating NP). She doesn't need short term use of oral steroids. The rhinitis was first appearing, than asthma and later NP. She stopped taking aspirin, arbitrary, 10 years ago. She had no history of personal or familiar atopy. She had no history of other systemic illness. During first eight year's she did not require hospital admission for her asthmatic symptoms. She presented to the emergency department seven years ago with severe rhinorrhoeae, sneezing, nasal obstruction, and with a worsening breathlessness and cough, 5-10 minutes after having a menthol-flavored candy. She experienced similar symptoms when she used a menthos some times later. The third episode was with persistent, cough, wheezing, dyspnea and nasal symptoms after brushing her teeth with toothpaste. We assist the patient in her third episode. After 30 minutes of medical treatment, her condition returned to baseline. She had bilateral wheezing on examination of the respiratory system. The hematological and biochemical profile was essentially normal. The chest radiograph and the electrocardiogram were normal too. Skin prick tests were performed with a common panel of inhalant allergens (Stallergenes) including negative and positive controls. The results were negative. Specific IgE antibodies were negative as well. Because of her history, we speculate that the patient was aspirin-sensitive, so we performed an oral provocation test with aspirin in order to confirm the AERD diagnosis and it resulted positive at first dose 10 mg[3]. The skin prick test with culprit toothpaste and menthol were negative. We did not perform the Mint-specific IgE measurement, because it is not available in our country. Two months after last reaction, with the patient in a stable clinical condition with a low dose of inhaled corticosteroids we performed the challenge tests with toothpaste and menthol. Five minutes after she had used her toothpaste under medical supervision, the pulmonary function tests revealed a typical obstructive flow-volume loop, associated with reversibility after the inhalation of Salbutamol. The spirometry demonstrated a FEV_1 62.9% of predicted. The next day, another challenge was performed with menthol, one of

the components of the patient's toothpaste. The patient was instructed to rinse his mouth with 25 mg of menthol diluted in 50 mL of 5% alcohol for 1 minute and then spit it out. Five minutes later, the spirometry show a decrease of FEV_1, 70% of predicted. The patient complained of tightness. The challenge tests were open placebo-controlled, because we must have the consent of the patient.

DISCUSSION

Menthol (2-isopropyl-5-methyl-cyclohexanol) is a cyclic alcohol, (the main component of peppermint oil), widely appreciated for its ability to produce a cooling sensation, it has been used as a constituent of food and drink, tobacco and cosmetics, or as a flavoring in toothpastes, in candies and chewing gum[4]. Delayed-type contact hypersensitivity to mint oils is well described. A review of the literature revealed a few reported cases of immediate-type hypersensitivity to menthol, leading to urticaria, anaphylaxis, or asthma[5]. Andersson et al. reported a case of rhinitis symptoms caused by products containing menthol. According to them, the hypothesis of a true IgE mediated reaction seems reasonable. The patient also had a history of aspirin intolerance which might have increased his response[6]. Paiva et al. presented a case with an IgE-mediated anaphylaxis to mint (Mentha piperita) and also an IgE mediated anaphylaxis to metamizol, a pyrazolone drug, often associated with IgE-mediated reactions[7]. There is a short report by Tamaoki et al. on the effect of menthol vapor in mild asthmatics[4]. They suggest that, exist a mechanism of efficacy of menthol on airway hyper-responsiveness. However, they did not comment on the effect of menthol in aspirin-induced asthma[8]. And, it seems that menthol vapor does not have a beneficial effect on aspirin-induced asthma[9]. Spurlock and Dailey presented a case of toothpaste-induced asthma[10]. In the meantime Subiza et al. reported on an aspirin-sensitive patient whose asthma was exacerbated by the mint flavor contained in her toothpaste[11]. They performed the challenge test and showed that the mint and menthol contained as flavorings in toothpastes may act as asthma-inducing agents. Hypersensitivity to aspirin (acetylsalicylic acid; ASA), present in 5-10% of asthmatic patients is recently referred as AERD[2]. The mechanism of the hypersensitivity reaction to aspirin is not immunological, but may be related to the inhibition of cyclooxygenase, by aspirin[12]. Aspirin is known to cause inhibition of the cyclooxygenases. This inhibition leads to an up-regulation of the alternative pathway, with lipoxygenases metabolizing arachidonic acid to leukotrienes. Several additional factors have been discussed, like alterations in cyclooxygenase inhibition and in the kinetics of enzymes like leukotriene synthase or an increased sensitivity of respiratory mucosal tissue to leukotrienes in sensitive individuals, or an excessive cysteinyl leucotriene (CysLT) production both in the steady state and for several hours after aspirin challenge[13]. COX-1 inhibition resulting in reduced prostaglandin E2 (PGE2) production has been postulated as one other mechanism for aspirin-induced exacerbations of asthma and rhinitis. Due to the fact that, in our case the skin prick tests were negative, we hypothesize that menthol can induced AERD via the same way. In the literature we find another hypothesis about preservatives or dye (well known to cause broncho-constriction in some persons with asthma who are sensitive to aspirin) present in toothpaste. Kawane have noticed the resemblance between methylsalicylate and methylparaben. There have been no reports that pointed out the similar chemical structures in aspirin, parabens, and artificial flavors. Although the exact pathogenesis of aspirin-induced asthma is unclear, flavor-induced bronchospasm might be in part due to the same mechanism[8]. The menthol might be considered one of the triggering factors of aspirin exacerbated respiratory disease.

REFERENCES

1. *Szczeklik A, Stevenson DD. Aspirin-induced asthma: advances in pathogenesis and management. J Allergy Clin Immunol 1999;104:5-13.*
2. *Bernstein JA, Castells MC, Gawchik SM, Lee TH, Settipane RA, Simon RA, et al. Aspirin challenge and desensitization for aspirin-exacerbated respiratory disease: a practice paper. Ann Allergy Asthma Immunol 2007;98:172-4.*
3. *Nizankowska-Mogilnicka E, Bochenek G, Mastalerz L, Swierczy´nska M, Picado C, Scadding G, et al. EAACI/GA2LEN guideline: aspirin provocation tests for diagnosis of aspirin hypersensitivity. Allergy 2007;62:1111-8.*
4. *Tamaoki J, Chiyotani A, Sakai A, Takemura H, Konno K. Effect of menthol vapour on airway hyperresponsiveness in patients with mild asthma. Respir Med 1995;89:503-4.*
5. *Hennessey L, et al. Toothpaste-induced anaphylaxis due to menthol allergy. J Allergy Clin Immunol 2002; 109, Issue 1, (Suppl 1):S31.*
6. *Andersson M, Hindsen M. Rhinitis because of toothpaste and other menthol-containing products. Allergy 2007:62:336-7.*
7. *Paiva M, Piedade S, Gaspar A. Toothpaste-induced anaphylaxis caused by mint (Mentha) allergy. Allergy 2010:65:1201-2.*
8. *Kawane H. Aspirin-induced asthma and artificial flavors. Chest 1994;106:654-5.*
9. *Kawane H. Menthol and aspirin-induced asthma. Resp Med 1996;90:247-9.*
10. *Spurlock BW, Dailey TM. Shortness of (fresh) breath: toothpaste- induced bronchospasm. N Engl J Med 1990;323:1845-6.*
11. *Subiza J, Subiza JL, Valdivieso R, Escribano PM, Garcia R, Jerez M, et al. Toothpaste flavor-induced asthma. J Allergy Clin Immunol 1992;90(6 Pt 1):1004-6.*
12. *Kowalski ML. Management of aspirin-sensitive rhinosinusitis asthma syndrome: what role for aspirin desensitization? Allergy Proc 1992;13:175-84.*
13. *Sanak M, Simon HU, Szczeklik A. Leukotriene C4 synthase promotor polymorphism and risk of aspirin-induced asthma. Lancet 1997;350:1599-600.*