Curr Allergy Asthma Rep (2012) 12:240–245
DOI 10.1007/s11882-012-0251-x

Migraine and Allergy: A Review and Clinical Update

Mark E. Mehle

Published online: 23 February 2012

Abstract Migraine and allergy are both common diseases. Many patients suffer from both, and the vast majority of patients with "sinus headache" complaints are found to have migraine, making migraine identification important to allergists. This review addresses the possibility that allergy and migraine are comorbid conditions, focusing on epidemiology, shared biochemical pathways, and underlying mechanisms. Therapeutic implications of this possible relationship have been the subject of several recent studies, making a review of this association timely and prudent.

Keywords Allergy · Migraine · Sinus headache · Epidemiology · Mechanisms · Food allergy · Trigger · IgG · Muscle contraction headache

Introduction

In 2011, Martin and coworkers [1••] (see below) published a study on migraine headache in allergy sufferers. Although it was published in the journal *Headache* and may have escaped the notice of many allergists, their conclusions were interesting: in younger allergy patients with migraine, immunotherapy seemed to be correlated with migraine improvement [1••]. This was just the latest contribution to the literature regarding a longstanding question that has fascinated allergists and neurologists for more than a century: are migraine and allergy related?

M. E. Mehle (✉)
Northeast Ohio Medical University,
25761 Lorain Road, 3rd Floor,
North Olmsted, OH 44070, USA
e-mail: dr.m.mehle@att.net

Allergists are often confronted by patients complaining of "sinus headache." It is well-established that well over 50% of these patients satisfy the International Headache Society (IHS) criteria for migraine headache [2–5]. Knowing that 20% of women and 6% of men suffer from migraine [6], familiarity with these diagnostic criteria (Table 1) [7] has been suggested for otolaryngologists and allergists [8]. Schreiber et al. [2], in a neurology and primary care setting, found that 80% of 2,991 "sinus headache" patients satisfied the criteria for migraine. An additional 8% had migranous headache (now termed *probable migraine*) [2]. Eross et al. [3] found that 86% of 100 consecutive self-diagnosed "sinus headache" patients had migraine or probable migraine. Only 3% had rhinosinusitis-attributable headache [3].

Among sinus headache patients referred to otolaryngologists, 50% to 75% are found to have migraine [5]. In a tertiary otolaryngology practice, Perry et al. [4] reported that sinus headache referrals with normal examinations and CT scans had a 58% incidence of migraine. Jackson and Dial [9] found that 49 of 100 patients referred to their otolaryngology office for sinus headache had previously unrecognized migraine. Among these 49 migraineurs, 19 had allergic rhinitis as well, 11 had sinusitis, and 6 had allergic rhinitis and sinusitis [9]. Thus, migraine and allergy are often concomitant, and both are frequently seen in the offices of allergists and otolaryngologists. Whether or not the two diseases are linked remains controversial.

Historical Perspective

The possibility of a migraine/allergy link has been debated for more than a century. In 1927, Vaughn [10] reported that 12 of 33 migraine sufferers in his practice (36.4%) had "definite" allergy triggers, and presented 10 case studies

Table 1 The diagnostic criteria for migraine

Migraine without aura
A. At least 5 attacks fulfilling criteria B–D
B. Headache attacks lasting 4–72 h (untreated or unsuccessfully treated)
C. Headache has at least 2 of the following characteristics:
1. Unilateral location
2. Pulsating quality
3. Moderate or severe pain intensity
4. Aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
D. During headache, at least 1 of the following:
1. Nausea and/or vomiting
2. Photophobia and phonophobia
E. Not attributed to another disorder
Migraine with aura: If aura is present, at least 2 attacks fulfilling criterion B is sufficient for diagnosis

Adapted from Headache Classification Subcommittee of the International Headache Society [13]

with apparent food sensitivity who improved with specific food avoidance. His discussion included literature from the 1800s.

In 1952, Unger and Unger [11] showed that 32 of 55 migraine headache sufferers had a personal history of allergy, and well over 50% had a family history positive for allergic disease. They reported "complete relief" from migraine headaches with diets withholding specific trigger foods, such as milk, chocolate, or wheat. They concluded that "migraine is basically an allergic disease."

"Allergic headache" was reported as a clinical entity by Shapiro and Eisenberg [12] in 1965, based on a series of 100 patients who were diagnosed with allergy and in whom allergy therapy (primarily immunotherapy [94%] or dietary restriction [17%]) was used. They reported that 36% were free of headaches, 40% were greatly improved, and 19% were moderately improved after treatment, based on subsequent patient interviews. No attempt was reported in this series to differentiate migraine and non-migraine sufferers [12].

Later studies contradicted this early literature. In 1976, Medina and Diamond [13] failed to show an association of serum IgE levels and the presence or absence of migraine. Evaluating 89 migraine and 27 muscle contraction headache (MCH) patients, they found elevated IgE in 5.7% of migraine and 3.7% of MCH patients, similar to a nonatopic general population. They also found no association in the personal and family prevalence of atopic disorders in 504 patients referred to a headache clinic comparing the migraine and MCH groups. Although their evidence did not support the concept that migraine is an IgE-mediated disease [13], this study included only patients with unilateral headache as "migraine," which would exclude more than 40% of migraine sufferers using modern criteria [14].

Are Common Pathways and Mediators a Potential Link?

The currently supported *neurovascular model* describes the migraine process as starting in the brain, with subsequent peripheral trigeminal neuron sensitization, including meningeal branches. This predominantly peripheral early phase may lead to central sensitization at the level of the trigeminal nucleus caudalis in the brainstem, and pain in the distribution of the ophthalmic and/or maxillary divisions of the trigeminal nerve [8]. Secondary parasympathetic nasal symptoms are common [15]. Cady and Schreiber [16] reported nasal congestion and rhinorrhea during a migraine attack based on objective endoscopic evidence. Both allergic rhinitis and migrainous midfacial or nasal pain may be associated with a variety of neuropeptides, such as substance P, calcitonin gene-related peptide (CGRP), vasoactive intestinal peptide (VIP), and others [8, 16]. Migraine and allergic rhinitis share trigeminal and autonomic neural pathways. Is this evidence of a causal relationship?

Gazerani et al. [17] reported in 2003 that serum IgE and histamine levels were significantly higher in a group of 70 non-aura migraineurs as compared with 45 controls. Sixty percent of these migraineurs had a history of allergy. Both levels were significantly higher in patients with both migraine and allergy. All migraine patients in their study had significantly higher histamine levels during headaches than in their non-headache intervals [17].

Kemper et al. [18] found evidence supporting an elevated IgE level in atopic migraineurs, but not in those without allergy (defined as type I hypersensitivity), based on a meta-analysis of the clinical literature up to that point. Higher histamine plasma levels in migraineurs (atopic or otherwise) and increased plasma tumor necrosis factor (TNF)-α levels were also supported. Decreased lymphocyte phagocytic function between migraine attacks was reported as well. They concluded as a whole that there was no support for immune suppression in migraineurs based on the reviewed literature [18].

A study of salivary CGRP and VIP was performed by Bellamy and coworkers [19] in 2006. They analyzed patients with allergic rhinosinusitis, "sinus headache" migraineurs, and controls with neither. They found elevation of VIP and CGRP levels during attacks in the allergic and migraine groups, and found that baseline VIP levels were significantly higher between attacks in the allergic rhinosinusitis and migraine patients as compared with controls. Baseline CGRP was higher in the migraine group than the

allergic group, and both groups were significantly higher than controls. Treatment of migraineurs with sumatriptan and rhinosinusitis patients with pseudoephedrine normalized both VIP and CGRP to baseline levels. In their opinion, they believed that rhinosinusitis and migraine patients share a "physiologically coordinated" regulation of trigeminal and parasympathetic nerve activity [19].

Other authors have cited migraine-related elevation of serum prostaglandin D_2 and F_2 [20], interleukin-1 [21], tryptase [21], histamine [22], and TNF-α [18]. A comparison of migraine- and allergic rhinitis-related mediators [23] is presented in Table 2. Potential mechanisms for these findings may include common neural pathways or the activation of meningeal mast cells, which may be activated even in patients without allergy [21]. Intracranial mast cell degranulation has been shown to induce a prolonged state of excitation of meningeal nociceptors, as well as "downstream" activation of the trigeminal nucleus caudalis, two important components of migraine pain [24]. Subsequent nitric oxide release (eg, triggered by histamine) has been implicated as well [22].

Epidemiology

A 2000 study in Finland showed that allergy and asthma were both comorbid with headache (of any type) development in a prospective sample of 1,205 7-year-olds who were observed for 15 years [25].

Table 2 Immune mediators in allergic rhinitis and migraine

Mediator	Migraine	Allergy
Histamine	↑	↑
IgE	↑	↑
Substance P	↑	↑
Tumor necrosis factor-α	↑	↑
CGRP	↑	↑
IL-1β, lymphocyte D5 receptor expression	↑	
IL-2, IL-4	↓	
IL-3, IL-5, IL-13		↑
Neurokinin A, K		↑
Granulocyte-macrophage colony-stimulating factor		↑
Cysteinyl leukotrienes		↑
Serum monocyte counts, monocyte chemotaxis	↓	
PMN phagocytosis	↓	
Lymphocyte β-endorphin	↓	

CGRP calcitonin gene-related peptide; *IL* interleukin; *PMN* polymorphonuclear neutrophil

Adapted from Kemper et al. [18], Gelfand [23], Mehle [32], and Sarin et al. [49]

The Finnish Migraine Gene Project (2006) evaluated 1,000 migraine family members with at least 3 first-degree relatives affected by migraine. Familial migraine was found to be comorbid with allergy, as well as hypertension and psychiatric disorders [26]. A total of 678 of the 1,000 responders were migraine sufferers themselves.

In the 2006 Spanish National Health Survey, more than 29,000 adults had a 1-year diagnosed migraine prevalence of approximately 11%, and migraine was comorbid with self-reported asthma in this population [27]. Ku et al. [22] evaluated the incidence of migraine in allergy patients. Of 123 rhinitis patients evaluated, 76 were found to have allergic rhinitis. In this group, 26 (34%) were found to have migraine based on IHS criteria, compared with only 2 (4%) of the nonallergic group. They also found that among patients who had no allergy testing (294 cohort patients seen in their clinic for other reasons), those with symptoms of allergic rhinitis (25% of the group) were significantly more likely to satisfy migraine criteria (38% vs 4%) [22].

Aamodt et al. [28] reported 51,383 patients who completed headache and respiratory disease questionnaires as part of a Norwegian health study. Headache (migraine and otherwise) was 1.5 times more likely in patients with asthma, hay fever, and chronic bronchitis. The association was stronger with increasing headache frequency [28].

A study from 2008 looked at more than 51,000 migraineurs in the UK General Practice Research Database and found that the relative risk of developing asthma was 1.3 as compared with non-migraineurs, but a more thorough case–control analysis showed an adjusted OR of only 1.17, showing that the diagnosis of migraine does not seem to be associated with an increased risk of subsequently developing asthma [29]. Among American children, a large recent study showed that 17.1% of 10,198 children 4 to 18 years of age reported frequent or severe headaches (including migraine) and that the children were more likely to have asthma, hay fever, and ear infections [30].

Karlstad et al. [31] studied the comorbidities in young Norwegian patients (8–29 years old) on active asthma treatments. More than 35,000 young asthmatics were found based on national health system records. They showed an increased prevalence of migraine headaches in asthmatics as compared with a nonasthmatic control group [31]. Additional information regarding this topic, including older studies, was made available in recent reviews [32, 33].

Clinical Associations

Eross et al. [3] noted that many migraine or probable migraine patients reported "headache triggers" such as weather changes (83%), seasonal variation (73%), and exposure to allergens (62%). Allergens reported as triggers included

grass, trees, dust, foods, animal dander, and mold [3]. Despite this observation, the number of studies evaluating respiratory allergy and migraine has been few.

In 1985, Lehrer et al. [34] reported headache relief in 31 of 34 allergic patients on immunotherapy, with complete resolution in 9 of them. All patients were described as having "frontal" headaches without further classification, but no typical migraine symptoms (eg, aura, throbbing, nausea) were reported in this patient population [34].

In 2011, Martin and coworkers [1••] presented an evaluation of migraine headache in 536 patients with allergic rhinitis in an established allergy practice. The degree of sensitization (based on the number of positive tests) did not correlate with the prevalence of migraine (32.5% overall), but in patients younger than age 45, the frequency and disability of the migraine headaches were lower in the "low atopic" group (defined as sensitivity to ≤45% of 20 allergens used). These correlations were not seen in the older patients included in the study. Among patients younger than 40, allergy patients on immunotherapy were found to have a lower prevalence of migraine and, when present, lower frequency and disability of migraine headaches as compared with those not on immunotherapy regimens. Younger atopic migraineurs, they concluded, may have a headache benefit from immunotherapy [1••].

For years, food allergy has been suspected as a migraine trigger. In 1979, Grant [35] evaluated the efficacy of elimination diets in 60 migraineurs. The patients were started on a low-risk diet for 5 days, and then progressively assessed added foods as migraine triggers. Avoidance of the apparent "trigger foods" such as coffee, chocolate, or milk was associated with a dramatic reduction in headaches. Eighty-five percent were reported to become headache free, with improvement of any concomitant hypertension as well [35].

Mansfield et al. [36] studied food allergy in 43 adults with recurrent migraine. Sixteen of these had positive skin testing to a battery of 83 food allergens. A 1-month trial of specific food restriction found that 11 of 16 had fewer headaches. Only 2 of 27 skin test–negative patients who restricted milk, egg, corn, and wheat for 1 month showed improvement. A subsequent food challenge in seven of the positive patients (presenting trigger foods such as wheat or cinnamon vs placebo in gelatin capsules) found that in five of seven, at least one food provoked a migraine, but placebo did not [36].

Of course, not all migraine-associated food intolerance is allergic [37]. Mansfield [38] noted that nonallergic mechanisms for food-related migraine may be involved as well. Chemicals such as ethanol, sodium nitrate, caffeine, phenylethylamine, tyramine, monosodium glutamate, sodium metabisulfite, theobromine, and benzoic acid have all been implicated in this regard [38]. Also, despite some contradiction in the literature, the review by Kohlenberg [39] in 1982 concluded that there was some validity in the hypothesis that tyramine-containing foods can potentially trigger migraines. No putative mechanism was suggested [39].

Is IgG-Mediated Food Sensitivity a Potential Migraine Trigger?

A study from Mexico in 2007 found that all 56 patients with frequent migraine had positive IgG for various food allergens, compared with 26% of non-migraine controls. After 1 to 6 months of a specific restriction diet, 43 of the patients reported no further headaches, with another 4 reporting a decrease in intensity and frequency of attacks. Nine patients reported no difference. Interestingly, six of the patients reported migraine and colitis, both of which resolved on restrictive diets [40].

A recent Turkish study also evaluated IgG antibodies against 266 food antigens (detected by enzyme-linked immunosorbent assay [ELISA]) in 30 migraineurs, and then used the information to do food exclusion or inclusion in a crossover study design. The elimination periods were found to provide a statistically significant reduction in the number of headache days and the number of migraine attacks [41]. This article was accompanied by an editorial reviewing the concept of IgG-mediated allergy as a potential mechanism for migraine attacks [42••].

Duodenal biopsy studies, however, have not supported a food allergy/migraine association. Pradalier et al. [43] performed biopsies in 20 migraineurs, 11 with food-induced migraine and 9 without. They reported no difference in immunocyte populations between the two groups when assessing plasmacyte populations with anti-IgG, anti-IgM, or anti-IgE immunohistochemistry. Their findings did not support the existence of an allergic mechanism in food-induced migraine [43].

Allergy/Migraine: Pharmacologic Therapy

Excluding the dietary studies reviewed above, until recently, few clinical trials have been published regarding the efficacy of pharmacologic allergy therapy in the allergic migraine patient.

In 1990, Mansfield [44] proposed a role for antihistamine therapy in migraine but noted no documented benefit from H1 or H2 blockers in preventing migraine headaches. Earlier studies cited in this report suggested that an antihistamine may potentiate pain relief when combined with a narcotic agent [44]. Cinnarizine, an L-type calcium channel blocker with antihistaminic properties, has shown promise in migraine prophylaxis [45].

In 2002, Carvalho et al. [46] reported that 24-week treatment with montelukast, 5 mg, in an open-label study decreased reported asthma attacks and significantly decreased headache frequency in six children and adolescents with asthma and migraine. Despite another small, open-label study showing promise using montelukast in migraine prophylaxis [47], further studies have has failed to show a benefit. Brandes et al. [48] published a randomized, double-blind, placebo-controlled study on the use of montelukast for migraine prophylaxis. They found no evidence that montelukast, 20 mg, performed better than placebo in 148 patients who completed the study. Similarly, secondary end points such as migraine severity or patient satisfaction showed no significant difference [48].

Conclusions

The existing medical literature supports a correlation between allergy and migraine. The majority of epidemiologic studies support the hypothesis that they are comorbid conditions. Recent clinical studies have suggested a benefit from allergy treatment to the allergic migraineur, although the literature as a whole does not allow clear recommendations. The basic science of diseases incorporating trigeminal and facial autonomic pathways is still being elucidated, and the future may hold a better description of any physiologic migraine/allergy association beyond sharing these pathways.

Seasonal change and stress can increase migraine headache incidence in migraineurs [20], and stressors can include other diseases. Better control of allergies may lead to fewer headaches in patients who have both diseases. It is also known that migraines can trigger autonomic nasal symptoms [2, 3, 15]; perhaps better migraine management will lead to fewer symptomatic days in rhinitis patients with migraine. These are critical questions awaiting further study.

Disclosure Dr. Mehle has served on Speaker's Bureau for GSK and Alcon and has served on rhinitis advisory boards for Merck and Teva.

References

Papers of particular interest, published recently, have been highlighted as:

•• Of major importance

1. •• Martin VT, Taylor F, Gebhardt B, et al. Allergy and immunotherapy: are they related to migraine headache? Headache. 2011;51:8–20. *This article is one of the few to study the headache benefits of allergy therapy in allergic migraineurs.*
2. Schreiber CP, Hutchinson S, Webster CJ, Ames M, Richardson MS, Powers C. Prevalence of migraine in patients with a history of self-reported or physician-diagnosed "sinus" headache. Arch Intern Med. 2004;164:1769–72.
3. Eross E, Dodick D, Eross M. The sinus, allergy and migraine study. Headache. 2007;47:213–24.
4. Perry BF, Login IS, Kountakis SE. Nonrhinologic headache in a tertiary rhinology practice. Otolaryngol Head Neck Surg. 2004;130:449–52.
5. Mehle ME, Kremer PS. Sinus CT scan findings in "sinus headache" migraineurs. Headache. 2008;48:67–71.
6. US Dept of Health and Human Services. Evid Rep Technol Assess. 2002 May;(54):1–198. AHRQ Pub No 02-E024.
7. Headache Classification Subcommittee of the International Headache Society. The international classification of headache disorders, 2nd Ed. Cephalalgia. 2004;24 suppl 1:1–160.
8. Mehle ME, Schreiber CP. Sinus headache, migraine, and the otolaryngologist. Otolaryngol Head Neck Surg. 2005;133:489–96.
9. Jackson A, Dial A. Sinus headache in an ENT setting. Poster presented at the Amer Acad Neurology Annual Meeting. April 9–16, 2004. Miami, Florida.
10. Vaughn WT. Allergic migraine. JAMA. 1927;88(18):1383–6.
11. Unger AH, Unger L. Migraine is an allergic disease. J Allergy. 1952;23(5):429–40.
12. Shapiro RS, Eisenberg BC. Allergic headache. Ann Allergy. 1965;23(3):123–6.
13. Medina JL, Diamond S. Migraine and atopy. Headache. 1976;15 (4):271–3.
14. Tepper S. New thoughts on sinus headache. Allergy Asthma Proc. 2004;25:95–6.
15. Obermann M, Yoon M-S, Dommes P, et al. Prevalence of trigeminal autonomic symptoms in migraine: a population-based study. Cephalgia. 2007;27:504–9.
16. Cady RK, Schreiber CP. Sinus headache: a clinical conundrum. Otolaryngol Clin N Am. 2004;37:267–88.
17. Gazerani P, Pourpak Z, Ahmadiani A, et al. A correlation between migraine, histamine, and immunoglobulin E. Scand J Immunol. 2003;57:286–90.
18. Kemper RHA, Meijler WJ, Korf J, et al. Migraine and function of the immune system: a meta-analysis of clinical literature published between 1966 and 1999. Cephalgia. 2001;21:549–57.
19. Bellamy J, Cady R, Durham P. Salivary levels of CGRP and VIP in rhinosinusitis and migraine patients. Headache. 2006;46:24–33.
20. Schuller DE, Cadman TE, Jeffreys WH. Recurrent headaches: what every allergist should know. Ann Allergy Asthma Immunol. 1996;76:219–30.
21. Levy D, Burstein R, Strassman AM. Mast cell involvement in the pathophysiology of migraine headache: a hypothesis. Headache. 2006;46 suppl 1:S13–8.
22. Ku M, Silverman B, Prifti N, et al. Prevalence of migraine headaches in patients with allergic rhinitis. Ann Allergy Asthma Immunol. 2006;97:226–30.
23. Gelfand EW. Inflammatory mediators in allergic rhinitis. J Allergy Clin Immunol. 2004;114:s135–8.
24. Levy D, Burstein R, Kainz V, et al. Mast cell degranulation activates a pain pathway underlying migraine headache. Pain. 2007;130(1–2):166–76.
25. Sillanpaa M, Aro H. Headache in teenagers: comorbidity and prognosis. Funct Neurol. 2000;15(suppl):116–21.
26. Artto V, Wessman M, Nissila M, et al. Comorbidity in Finnish migraine families. J Headache Pain. 2006;7:324–30.
27. Fernandez-de-las-penas C, Hernandez-Barrera V, Carrasco-Garrido P, et al. Population-based study of migraine in Spanish adults: relation to socio-demographic factors, lifestyle and c-morbidity with other conditions. J Headache Pain. 2010;11:97–104.

28. Aamodt AH, Stovner LJ, Langhammer A, et al. Is headache related to asthma, hay fever, and chronic bronchitis? The head-hunt study. Headache. 2007;47:204–12.
29. Becker C, Brobert GP, Almqvist PM, et al. The risk of newly diagnosed asthma in migraineurs with or without previous triptan prescriptions. Headache. 2008;48:606–10.
30. Lateef TM, Merikangas KR, He J, et al. Headache in a national sample of American children: prevalence and comorbidity. J Child Neurol. 2009;24(5):536–43.
31. Karlstad O, Nafstad P, Tverdal A, et al. Comorbidities in an asthma population 8–29 years old: a study from the Norwegian prescription database. Pharmacoepidemiology and Drug Safety 2011. Published online in Wiley Online Library doi:10.1002/pds.2233.
32. Mehle ME. Allergy and migraine: is there a connection? Curr Opin Otolaryngol Head Neck Surg. 2008;16:265–9.
33. Diener HC, Kuper M, Kurth T. Migraine-associated risks and comorbidity. J Neurol. 2008;255:1290–301.
34. Lehrer JF, Silver J, Cordes BG. Headache associated with IgE-mediated allergy: response to immunotherapy. Ear Nose Throat. 1985;64:228–31.
35. Grant ECG. Food allergies and migraine. Lancet. 1979;1:966–8.
36. Mansfield LE, Vaughn TR, Waller SF, et al. Food allergy and adult migraine: double-blind and mediator confirmation of an allergic etiology. Ann Allergy. 1985;55:126–9.
37. Trotsky MB. Neurogenic vascular headaches, food and chemical triggers. Ear Nose Throat J. 1994;73(4):228–30.
38. Mansfield LE. The role of food allergy in migraine: a review. Ann Allergy. 1987;58(5):313–8.
39. Kohlenberg RJ. Tyramine sensitivity in dietary migraine: a critical review. Headache. 1982;22(1):30–4.
40. Arroyave Hernandez CM, Echevarria Pinto M, Hernandez Montiel HL. Food allergy mediated by IgG antibodies associated with migraine in adults. Rev Alerg Mex. 2007;54 (5):162–8.
41. Alpay K, Ertas M, Orhan EK, et al. Diet restriction in migraine, based on IgG against foods: a clinical double-blind, randomized, cross-over trial. Cephalgia. 2010;30(7):829–37.
42. •• Pascual J, Oterino A. IgG-mediated allergy: a new mechanism for migraine attacks? Cephalgia. 2010;30(7):777–9. *This is a review of the controversial concept of IgG-mediated food allergy and migraine.*
43. Pradalier A, DeSaintMaur P, Lamy F, et al. Immunocyte enumeration in duodenal biopsies of migraine without aura patients with or without food-induced migraine. Cephalgia. 1994;14(5):365–7.
44. Mansfield LE. The role of antihistamine therapy in vascular headaches. J Allergy Clin Immunol. 1990;86:673–6.
45. Togha M, Ashrafian H, Tajik P. Open-label trial of cinnarizine in migraine prophylaxis. Headache. 2006;46:498–502.
46. Carvalho DS, Fragoso YD, Coelho FMS, et al. Asthma plus migraine in childhood and adolescence: prophylactic benefits with leukotriene receptor antagonist. Headache. 2002;42:1044–7.
47. Sheftell F, Rapoport A, Weeks R, et al. Montelukast in the prophylaxis of migraine: a potential role for leukotriene modifiers. Headache. 2000;40:158–63.
48. Brandes JL, Visser H, Farmer MV, et al. Montelukast for migraine prophylaxis: a randomized, double-blind, placebo-controlled study. Headache. 2004;44:581–6.
49. Sarin S, Undem B, Sanico A, et al. The role of the nervous system in rhinitis. J Allergy Clin Immunol. 2006;118:999–1014.