

Vasomotor Rhinitis

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Abstract Vasomotor rhinitis is a common disorder that is seen routinely in allergy practice. It affects millions of Americans and results in significant morbidity. The pathophysiology of this complex heterogeneous disorder is unknown, but we are making advances in this regard. Symptoms and signs can closely resemble those of allergic rhinitis and can be difficult to differentiate from those resulting from allergy. A careful history, physical examination, and diagnostic testing help clinicians arrive at a definitive diagnosis, but treatment can be challenging. Therapy should be based on the presenting symptoms of vasomotor rhinitis. Combination therapy with topical corticosteroids and azelastine is useful. However, in patients whose predominant symptom is rhinorrhea, use of atypical anticholinergic agents can be quite useful. Up-to-date pathogenesis, epidemiology, diagnosis, and treatment approaches are discussed in this review.

Keywords Rhinitis · Vasomotor rhinitis · Non allergic rhinitis · Rhinitis treatment

Introduction

The term *vasomotor rhinitis* is commonly used to describe rhinitis symptoms that occur in relation to nonallergic, noninfectious triggers such as changes in barometric pressure, humidity, and temperature; strong odors; perfumes; dust; tobacco smoke; and certain foods [1•]. However, the term is misleading because the pathogenic

mechanism is not clearly established, and the symptoms are variable. Several other terms have been used to describe this condition, including *nonallergic idiopathic rhinitis*; *nonallergic, noninfectious rhinitis*; and *intrinsic rhinitis*.

Definition

Vasomotor rhinitis is best defined by the presence of chronic symptoms of rhinitis (eg, sneezing, rhinorrhea, nasal congestion, and postnasal drainage) in the absence of specific immunologic, infectious, pharmacologic, structural, hormonal, vasculitic, metabolic, or atrophic causes. It is usually not associated with nasal eosinophilia [2•]. Studies have noted that the symptoms must be present for at least 1 year for the disorder to be considered chronic [3, 4].

Classification

Vasomotor rhinitis is classified under nonallergic rhinitis, which may be subclassified on the basis of various characteristics (Table 1).

Epidemiology

Rhinitis in its allergic and nonallergic forms affects about 20% of the population in industrialized nations [5–7]. The prevalence of pure, nonallergic rhinitis underestimates the impact of this condition because it often coexists with allergic rhinitis [8]. Epidemiologic studies suggest a relative prevalence of allergic rhinitis of 76% and of nonallergic rhinitis of 23% (ratio, 3:1) [9–16, 17•]. Most studies have used skin testing to distinguish allergic from nonallergic rhinitis. These studies had several caveats (eg, skin testing

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Table 1 Differential diagnosis of nonallergic rhinitis

Syndromes of unknown etiology
Vasomotor rhinitis
Nonallergic rhinitis with eosinophils (NARES, BENARS)
Basophilic/metachromatic nasal disease
Syndromes of suggested etiology
Chronic sinusitis
Immunodeficiencies
Ostiomeatal obstruction
Metabolic conditions
Estrogen-related (oral contraceptive/hormone replacement therapy, pregnancy)
Hypothyroidism
Acromegaly
Vasculitides/autoimmune and granulomatous diseases
Sjögren's syndrome
Systemic lupus erythematosus
Relapsing polychondritis
Churg-Strauss syndrome
Sarcoidosis
Wegener's granulomatosis
Drug-induced
Topical decongestants
Systemic medications
Rhinitis with nasal polyps
Aspirin intolerance
Chronic sinusitis
Churg-Strauss syndrome
Young's syndrome (sinopulmonary disease, azoospermia, nasal polyps)
Cystic fibrosis
Kartagener's syndrome (bronchiectasis, chronic sinusitis, nasal polyps)
Structurally related rhinitis
Septal deviation
Turbinate deformation
Nasal valve dysfunction
Obstructive adenoid hyperplasia
Trauma (eg, cerebrospinal fluid rhinorrhea)
Congenital
Neoplastic
Atrophic rhinitis
Resulting from surgery
Ozena
Physical/chemical/irritant-induced
Dry air
Gustatory
Bright light
Air pollution
Occupational
Occupational rhinitis
Annoyance
Irritant
Immunologic
Corrosive

BENARS blood eosinophilia
nonallergic rhinitis syndrome,
NARES nonallergic rhinitis with
eosinophilia syndrome

results were not corroborated with the history). The prevalence of nonallergic rhinitis in children is not known [18].

The precise prevalence of different subtypes of nonallergic rhinitis is also not known. Three separate studies tried to address this issue using nasal examination, skin testing, total IgE, nasal cytology, and sinus x-rays [9, 10, 19]. These studies included 200 patients. Vasomotor rhinitis was identified as the most common subtype (71%), followed by nonallergic rhinitis with eosinophilia syndrome. Among vasomotor rhinitis patients, there was a female predominance (ratio, 2:1). The typical age at onset was late-30s to early-40s. An estimated 20 million Americans suffer from nonallergic rhinitis, with vasomotor rhinitis accounting for 14 of those 20 million [20].

Pathogenesis

No single known pathogenic mechanism underlies chronic vasomotor rhinitis. Increased sensitivity to environmental factors (eg, climate change, pollution, strong odors, perfumes) triggers symptoms in this condition. However, recent studies have suggested other potential mechanisms that could be responsible for the underlying pathologic process. These include a local IgE-mediated mechanism, nociceptive nerve dysfunction, and autonomic dysfunction [21].

Entropy: Local IgE Synthesis

Entropy refers to localized allergy in the nasal cavity without positive skin prick tests, elevated serum IgE, or serum allergen-specific IgE [22]. The presence of allergic inflammatory cells in the nasal mucosa supports such localized IgE production. Earlier nasal biopsy studies did not show a difference in lymphocytes, antigen-presenting cells, eosinophils, or other IgE-positive cells between idiopathic, nonallergic rhinitis patients and control participants [3, 23]. Previous use of nasal corticosteroids may have confounded the results in these studies. However, a more recent study of perennial, nonallergic rhinitis patients revealed a higher density of total (CD3+), activated (CD25+), and allergen-naïve (CD45RA+) T lymphocytes in the nasal mucosa than that seen in healthy control participants [22]. CD4+ and other lymphocytes were found to be the same in number in idiopathic rhinitis and allergic rhinitis patients but higher compared with control participants. Nasal lavage fluids contained low levels of IgE to dust mite in 22% of 50 nonallergic rhinitis patients [24]. Acoustic rhinometry was positive in 50% of these patients after nasal challenge with Der p 1. The nasal lavage fluid of the idiopathic rhinitis patients had significantly higher

levels of eosinophil cationic protein compared with that of control participants. Local IgE production may occur in patients with nonallergic rhinitis, and increased numbers of high-affinity IgE receptors have been found in some patients with chronic nonallergic rhinitis [25]. This phenomenon of local IgE production was demonstrated in two ex vivo studies in which there was production of allergen-specific IgE in nasal explants of patients with nonallergic rhinitis [26, 27]. In contrast, not all studies have found evidence supporting the existence of entropy [28]. Initial and subsequent allergen challenges with multiple glycerinated extracts were negative in most patients. Additionally, Khan [29•] recently challenged the concept of entropy. None of the patients who had an initial positive challenge (5 of 20 perennial nonallergic rhinitis patients) had a positive reaction on subsequent challenge [29•]. Future studies using nasal allergen challenge in patients with allergen-specific IgE in nasal fluid may be helpful in resolving the issue of entropy.

Nociceptive Dysfunction

Various chemical and mechanical sensations from the nasal mucosa are carried by sensory- afferent nerve endings and perceived at the cortical level. Sensations (eg, heat, cold, and burning) are transmitted through fast conducting Aδ fibers, and discomfort, paresthesia, and gentle touch are transmitted through C fibers [30]. They may also convey sensations of mechanical stretch when there is swelling of the epithelial cells and the blood vessels that supply the nasal mucosa [31]. Distinct chemicals interact with distinct sensory proteins on epithelial cells and the nerve endings to induce neural depolarization. Mediators such as bradykinin, histamine, and amines act on stimulatory receptors. One such example is the capsaicin receptor TRPV1 (TRP vanilloid-1). TRPV1 is activated by capsaicin, ethanol, local anesthetics, and temperature greater than 42°C. Topical capsaicin has been shown to reduce congestion in vasomotor rhinitis compared with allergic rhinitis [32], which suggests nociceptive nerve dysfunction in individuals with nonallergic rhinitis. Chronic fatigue syndrome patients with nonallergic rhinitis have altered response to hypertonic saline nasal administration that causes more pain and no glandular secretory response [33]. These patients also have increased sinus tenderness compared with healthy controls and those with allergic rhinitis [34]. All these findings indicate the possibility that trigeminal hyperresponsiveness, hyperalgesia, and allodynia may be present in this group of patients.

The effect of cold, dry air on airway functions is significant in idiopathic, nonallergic rhinitis. Nonallergic rhinitis patients demonstrate a dose-dependent airflow

obstruction following cold air inhalation. Such a dose-dependent response is absent in allergic rhinitis patients and individuals without rhinitis [35]. Hyperresponsiveness of the cold-sensing neural afferents present in the nasal mucosa of idiopathic rhinitis patients mediates such a response. Measurement of nasal airflow resistance by acoustic rhinometry after inhalation of cold, dry air is currently the standard for objective identification of idiopathic, nonallergic rhinitis patients [36]. In “skier’s rhinitis,” exposure to cold air leads to excessive nasal blockage with copious discharge. This results from a hyperactive, afferent, cholinergic, parasympathetic reflex arc and can be blocked by topical anticholinergic medications [37]. In gustatory rhinitis, eating activates oral trigeminal receptors that recruit parasympathetic cholinergic reflexes and produce glandular secretion. This suggests an increased sensitivity of sensory receptors to irritant stimuli with increased parasympathetic reflex arc activity and resultant increased glandular secretion [38].

Autonomic Dysfunction

Vasomotor rhinitis has also been linked to autonomic dysfunction. Autonomic nervous system testing was performed in 19 patients with vasomotor rhinitis compared with 75 matched control participants in one study [39]. These rhinitis patients had significant abnormalities in their pseudomotor, cardiovagal, and adrenergic subscores. The authors concluded that the sympathetic nervous system is hypoactive or that there is an imbalance between the parasympathetic and sympathetic system rather than a hyperactive parasympathetic system. Nasal trauma has been mentioned as a possible triggering factor for this autonomic dysfunction [40]. Midfacial pain syndrome has many features resembling tension-type headaches. The pain is symmetric and may involve the root of the nose, the bridge of the nose, the peri- or retro-orbital regions, or the cheeks. Patients describe nasal pressure, heaviness, or tightness and feel that their nostrils are blocked even when there is no obstruction to nasal flow. CT scans and nasal endoscopy are typically normal [41].

Clinical Presentation

Symptoms of vasomotor rhinitis range from obstructive/congestive to secretory/rhinorrhea. Concomitant ocular symptoms tend to be minimal, and symptoms of nasal and palatal itch, as well as sneezing spells are uncommon [12]. Headache, postnasal drip, facial pressure, throat clearing, and coughing are common. Vasomotor rhinitis patients fall into two categories: “runners,” who have wet rhinorrhea,

and “blockers” with nasal blockage [8]. Patients with rhinorrhea tend to have an enhanced cholinergic response, whereas blockers have nociceptive neurons with heightened sensitivity to innocuous stimuli [8]. In a survey of 678 rhinitis patients, nasal blockage was the predominant symptom in those with vasomotor rhinitis, whereas allergic rhinitis patients experienced more rhinorrhea, sneezing, and eye irritation [42]. Asthma was more common in the allergic group. Togias [11] reported that nonallergic patients had fewer sneezes and conjunctival symptoms, but rhinorrhea and congestion did not distinguish between the allergic and nonallergic groups. Vasomotor rhinitis is generally perennial and not worsened by allergen exposure [6]. However, seasonal exacerbation of vasomotor rhinitis during shifts in temperature, humidity, or barometric pressure during the spring and fall may be confused with seasonal allergic rhinitis [43]. The environmental triggers that do not affect healthy people but affect vasomotor rhinitis patients include strong odors; exposure to cold air; changes in temperature, humidity, and/or barometric pressure; and ingestion of alcoholic beverages.

Diagnosis

The diagnosis is based on the clinical history and exclusion of other known causes of rhinitis (eg, allergic, noninfectious, inflammatory, or immunologic). Patients with appropriate nasal symptoms (as described previously) triggered by one or more of the aforementioned environmental triggers are likely to have vasomotor rhinitis [6]. The absence of other atopic diseases in the patient or in the family supports the diagnosis as well. The onset of nasal symptoms in older patients (> 35 years of age) without history of atopy, seasonal variation, or specific allergen exposure–related symptoms but induced by nonspecific triggers (eg, perfume) suggests a greater than 99% likelihood of a vasomotor rhinitis diagnosis [44]. The nasal mucosa usually appears normal but may appear red and beefy [45]. Nasal and peripheral eosinophilia are absent, as are positive skin tests or allergen-specific serum IgE assays. Serum IgE is usually normal as well.

Treatment

Once a diagnosis of vasomotor rhinitis has been made, every measure should be undertaken to avoid environmental triggers as much as possible. These may include odors (eg, cigarette smoke, perfumes, bleach, and formaldehyde), automobile emission fumes, light stimuli, temperature changes, and hot and spicy foods.

Patients with chronic vasomotor rhinitis generally are less responsive to pharmacologic therapy than those with allergic rhinitis [46–48]. Two medications (eg, intranasal steroids and the topical antihistamine azelastine) have been useful in treating the total symptom complex of chronic nonallergic rhinitis. In addition to this, ipratropium bromide has been approved to treat rhinorrhea.

A stepwise pharmacologic approach may be used in which the initial intervention is chosen based on the patient's predominant symptoms. A topical anticholinergic would be the first choice if the only symptom was rhinorrhea. However, a topical nasal corticosteroid would be the first choice if the symptoms were congestion and obstruction. In patients with rhinorrhea and nasal congestion, a topical antihistamine (eg, azelastine) would be very helpful. Again, topical azelastine and a topical nasal steroid can be combined if neither alone is effective.

Intranasal Glucocorticoids

Multiple studies have shown the effectiveness of topical nasal steroids in the treatment of nonallergic rhinitis [49–52]. Integrated analysis of three double-blind, randomized, prospective, placebo-controlled studies involving 983 patients with nonallergic rhinitis with and without nasal eosinophilia (674 were classified as not having nasal eosinophilia) found that intranasal fluticasone propionate at a dose of 200 or 400 µg was significantly more effective than placebo in both groups [52].

Topical Azelastine

Topical azelastine has been found effective in randomized controlled studies [53, 54]. Two multicenter, randomized, placebo-controlled trials showed significant improvement in all symptoms within the first week of treatment [54]. Azelastine may mediate its anti-inflammatory actions through its ability to diminish eosinophil activation, adhesion molecule expression, and cytokine generation [55, 56]. The starting dose is typically two sprays per nostril twice daily.

Ipratropium Bromide

Ipratropium bromide (0.03%) nasal spray is recommended for treating patients with vasomotor rhinitis who have prominent rhinorrhea. The recommended dose typically is two sprays per nostril three times daily. It can also be used as needed or prior to exposures that cause rhinorrhea (eg, cold air) or before eating. Ipratropium bromide (0.06%) is available and intended for short-term use only (eg, rhinorrhea associated with a common cold). Two separate multicenter, placebo-controlled trials have demonstrated

the effectiveness of ipratropium bromide in controlling rhinorrhea [57, 58].

Adjunctive Therapies

Decongestants

No study has evaluated the efficacy of decongestants in chronic vasomotor rhinitis patients. These agents can be added if the previously described therapies are not effective. A short course of pseudoephedrine can be used if patients do not have coexisting hypertension. The usual dosing of pseudoephedrine is 30 to 60 mg orally up to three times daily.

Phenylephrine hydrochloride is also widely available but may be less effective than pseudoephedrine in the treatment of rhinitis symptoms [59•].

Nasal Saline

Daily nasal lavage or saline sprays can also be useful and should be used immediately prior to intranasal glucocorticoids or azelastine. This intervention may be helpful for postnasal drainage. It is effective in nonallergic rhinitis and chronic rhinosinusitis [59•, 60, 61].

Over-the-counter bulb syringes and bottle sprayers also may be helpful. The system should deliver an adequate volume of solution (> 200 mL/side) into the nose to be effective. Homemade or commercially prepared solutions can be used. Nasal lavage can be performed once or twice daily depending on the severity of symptoms. Intranasal saline sprays are useful for relieving postnasal drip, sneezing, and congestion associated with nonallergic rhinitis. Saline sprays are less effective than larger-volume nasal lavage, but they are more convenient for some patients [62].

Miscellaneous Therapies

Topical nasal capsaicin is an effective therapy in idiopathic nonallergic rhinitis [32]. This treatment can reduce nasal congestion for up to 6 months. Low daily dose amitriptyline (20 mg/d) for 6 months has been shown to be beneficial in treating midfacial syndrome [41].

Surgical Approach

Various surgical procedures have been used in cases in which medical management has failed. At least 6 to 12 months of medical therapy should be used before

considering surgical therapy. Turbinectomy can be performed to improve congestion. Long-term dryness and crusting may occur following a turbinectomy. This may be the result of an increase in nasal airflow or diminished secretions. The extreme or end stage of this process is atrophic rhinitis. Patients may also experience a sense of nasal congestion in the absence of a reduction in airway patency. This is believed to be caused by the alteration of the passage of air (perhaps diminished turbulence) through the nasal passages, which produces the perception of nasal obstruction. Laser turbinectomy has been reported to preserve nasal cytology and ciliary motility compared with the conventional approach [63]. Other surgical methods (eg, vidian nerve resection, electrocoagulation of the anterior ethmoidal nerve, and sphenopalatine ganglion block) have been used with varying success rates. Both procedures carry potential risks [64–66].

Conclusions

Vasomotor rhinitis, or nonallergic idiopathic rhinitis, is a heterogeneous group of disorders characterized by chronic nasal congestion, rhinorrhea, or combination of the two. The exact pathogenesis of this disorder remains unknown, although nociceptive and autonomic nerve dysfunction have been identified in many patients. The diagnosis is made by excluding other causes of chronic rhinitis. Combination therapy with topical nasal steroids and topical antihistamine can be useful in most patients. Selected patients can benefit from topical anticholinergic agents as well as other adjunctive therapies.

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- Of major importance

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