Non-Allergic Rhinitis

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Grand Rounds Presentation
December 16, 2009
Define and Introduction
Etiologies
Diagnosis
Prognosis
Treatments
Define

- Rhinitis - Two or more nasal symptoms of:
  - Nasal congestion
  - Rhinorrhea
  - Sneezing/Itching
  - Impairment of Smell for more than 1 hr a day
Define

- Noninfectious rhinitis has been classified as either allergic or non-allergic.

- Allergic rhinitis is defined as immunologic nasal response, primary mediated by immunoglobulin E (IgE).

- Non-allergic rhinitis is defined as rhinitis symptoms in the absence of identifiable allergy, structure abnormality or sinus disease.
Non-allergic rhinitis has been described in many terms.

Vasomotor rhinitis, vascular rhinitis, perennial, chronic rhinitis and noninfectious perennial rhinitis.
Introduction

- Nasal function includes
  - Temperature regulation
  - Olfaction
  - Humidification
  - Filtration and Protection
Introduction

- Nasal lining contains secretion of IgA, proteins and enzymes
- Nasal Cilia propel the matter toward the natural ostia at frequency of 10-15 beats per minute
- Mucous move at a rate of 2.5-7.5 ml per minute
Introduction

- Up to 10% of the population affected by rhinitis
- 58 million American with allergic rhinitis and another 19 million with non-allergic rhinitis
- In the patient population that presents to ENT clinic, 50% diagnosed with allergic rhinitis and 50% diagnosed with non-allergic rhinitis.²
Introduction

- Problems that arise from non-allergic rhinitis (NAR) are similar to allergic rhinitis which include development of sinusitis, eustachian tube dysfunction, chronic otitis media, anosmia,
- This leads to a lack of productivity at work and frequent doctor visits
- Medical treatment side effects can cause drowsiness, epistaxis, and nasal dryness on top of the normal symptom of NAR
| Table  -- Causes of non-allergic rhinitis |

- Occupational
- Drug induced
- Rhinitis medicamentosa
- NARES
- Hormonal
- Idiopathic or vasomotor
- Atrophic and other mimickers
Arises from airborne agents at workplace.

Agents do not act through immune-mediated mechanism. They are direct irritants to the nasal mucosa and cause non-allergic hyper-responsive reactions.
Occupational Irritants

**Olfaction**
Cranial Nerve I
Sensation of odor triggered by airborne chemicals

**Common Chemical Sense**
Cranial Nerve V
Burning, irritation triggered by airborne chemicals
Occupational Irritants

- Over 205 different chemicals entities identified, including cigarette smoke and chemicals and solvents like chlorine, metal salts, latex, glues and wood dusts.
- Patients usually present with concurrent occupational asthma.
- Diagnosis is based on history or results of nasal provocation with stimulus. About 70% of patient improve in symptoms when triggers are avoided.
Drug Induced Rhinitis
Drug Induced Rhinitis

- Several common medications may induce rhinitis when administered topically or orally.
- Drugs can be divided into pharmacologic or aspiring hypersensitivity.
# Medications Contributing to Rhinitis

- Cocaine
- Topical nasal decongestants
- Phosphodiesterase type-5 inhibitors (PDE-5) -- *Sildenafil*
- Alpha-adrenoceptor antagonists
- Reserpine
- Hydralazine
- Angiotensin-converting enzyme inhibitors
- Beta-blockers
- Methyldopa
- Guanethidine
- Phentolamine
- Oral contraceptives
- Non steroidal anti-inflammatory medications
  - *Aspirin*
- Psychotropic agents
  - Thioridazine
  - Chlordiazepoxide
  - Chlorpromazine
  - Amitriptyline
  - Perphenazine
  - Alprazolam
Drug Induced Rhinitis

- Intolerance to aspirin and/or NSAIDS is unpredictable.
- It is predominately produces rhinorrhea but may be a part of a ASA triad complex involving hyperplastic rhinosinusitis, nasal polyps and asthma.
Drug Induced Rhinitis

- Pharmacologic rhinitis is infrequent and a predictable side effect.
- Usually lead to nasal congestion, but watery secretions and PND can be accompanying symptoms.
Rhinitis medicamentosa (RM) is a drug induced non-allergic rhinitis associated with prolonged use of topical nasal decongestants. Also called rebound or chemical rhinitis.

- Incidence is btw 1-9%, equal sex distribution and more common in young to middle age adults and pregnant women.
Rhinitis Medicamentosa

- Nasal mucosa innervated predominately by sympathetic fibers. They release Norepinephrine, that stimulate alpha 1 and alpha 2 receptors that cause vasoconstriction.

- Sympathomimetic amines (phenylephrine) and imidazoline derivatives (oxymetazoline) both produce vasoconstriction by endogenous release of norepinephrine.
Rhinitis Medicamentosa

- Prolong use leads to reduced production of presynaptic norepinephrine and also leads to decrease sensitivity of alpha receptors causing need for larger dose for shorter acting time.

- This leads to a cycle of excessive dose which worsens their original symptoms.
Rhinitis Medicamentosa

- Risk of RM is accepted to be greatest after 10 day use of medication.
- Treatment is gradual stopping of decongestant with introduction of topical corticosteroid.
- Pt should be warned of temporary worsening symptoms. Pt should be off nasal decongestants for 3 month before any other treatment, medical or surgical, can be used for original nasal disorder.
NARES, non-allergic rhinitis with eosinophilia syndrome, is characterized on the basis of 20-25% or greater eosinophils in nasal smears of pt with rhinitis.

- There is lack of allergy by skin test, or IgE antibodies.
- Prevalence ranges from 13-33% of non-allergic rhinitis.
Numerous eosinophils on nasal mucosa
NARES

❖ Etiology is unknown, however, NARES is believed to be associated with ASA triad.

❖ This is due to the fact that NARES patients frequently develop nasal polyps and asthma later in life.

❖ Also, abnormal prostaglandin metabolism has been implicated as cause of NARES

❖ However, eosinophil counts are elevated in 20% of nasal smears of general population and not everyone with eosinophilias has symptoms of rhinitis.
Studies by Powe Et al. (2001) suggest that NARES is a local IgE mediated response that does not result in a systemic response.

Epithelium of full thickness turbinates were compared from non-allergic rhinitis, allergic rhinitis and control group, which revealed local IgE in non-allergic and allergic population, and not the controlled group. It was found that the 50% of non-allergic rhinitis pt who had negative response to skin prick tests, had a positive result to nasal allergy challenge.
Other studies (Romero et al.) have also shown positive nasal allergen challenges to skin prick test negative patients.

Therefore, skin prick test negative pt with eosinophilia may require allergen challenge before diagnosis of non-allergic rhinitis.

NARES as a subgroup responds better to nasal corticosteroids than other non-allergic rhinitis.
Hormonal Rhinitis
Hormonal Rhinitis

- Defined as rhinitis during periods of known hormonal imbalance
- Estrogens are known to affect the autonomic nervous system by increasing central parasympathetic activity, acetyl choline transferase and acetylcholine content. Also, increased inhibition of sympathetic neurons of alpha-2 receptors noted in pregnancy.
- Estrogen also believed to increase hyaluronic acid in nasal mucosa.
Hormonal Rhinitis

Therefore, the most common causes are pregnancy, menstruation, puberty and exogenous estrogen. Hormonal rhinitis in pregnancy usually manifest in the second month and continues throughout the pregnancy.

Cumulative incidence of pregnancy rhinitis was 22%, 69% in women who were smokers.
Hormonal Rhinitis

- Hypothyroidism may also be a known cause of hormonal rhinitis. In pt with hypothyroidism, edema increases in the turbinates as a result of TSH release. However, evidence is inconclusive at this time.

- Nasal congestion and rhinorrhea are the most common symptoms of hormonal rhinitis.
Idiopathic rhinitis

Also known as vasomotor rhinitis is characterized by nasal blockage and rhinorrhea, but sneezing and pruritus is lower than allergic rhinitis.

Etiology is unknown, however attempts have been made to differentiate idiopathic rhinitis on basis hyperactivity to histamine, methacholine, cold dry air or capsaicin.

None of the test have been able to differentiate it from other forms of rhinitis.
Idiopathic rhinitis (IR) is usually diagnosis of exclusion.

Therefore, it is solely diagnosed on patient complaints.
Idiopathic Rhinitis

- Exclusion criteria for IR
  - Positive allergy test
  - Smoking
  - Nasal polyps
  - Pregnancy
  - Medications affecting nasal function
  - Beneficial effects of nasal corticosteroid spray (NARES)
Idiopathic Rhinitis

- IR have no significant difference in nasal mucosal lymphocytes, antigen-presenting cells, eosinophils, macrophages, mast cells or IgE positive cells compared to controls.

- A significant reduction of immunocompetent cells in nasal mucosa of IR pt treated with nasal steroids did not reduce nasal complaints.

- Therefore IR is believed not be causes by inflammation.
Idiopathic Rhinitis

- Studies have suggested autonomic dysregulation, neuropeptide or nitric oxide hyperactivity.
- However, none of these studies have been conclusive.
Atrophic rhinitis et al

- A number of conditions can produce the same signs and symptoms of rhinitis.
- Structural conditions mimic rhinitis include deviated septum, nasal tumors, enlarged adenoids, hypertrophic turbinates, and atrophic rhinitis.
- Immunologic conditions include Wegener’s granulomatosis, sarcoidosis, and polychondritis.
Diagnosis
PATIENT HISTORY QUESTION

What are your nasal and sinus symptoms? Do they include:

- Nasal discharge
- Congestion/blockage
- Postnasal drainage
- Episodes of sneezing
- Nasal itching
- Itchy eyes
- Epiphora

Do you have environmental allergies (e.g., hayfever)?

- Have you undergone allergy testing?
- Have you been treated for allergies?
- Are there certain situations or environments in which your symptoms are worse or in which they are better? For example, home, work, indoors, or outdoors?
- Are there certain times of the day or year during which your symptoms are worse or better?
- Did your environment change before the onset of your symptoms?
PATIENT HISTORY QUESTION

- What type of work do you do?
- Are you exposed to chemicals in your occupation?
- Have you noticed an increase in nasal or sinus symptoms around certain chemicals/aromas?
- Did your symptoms begin when you started taking certain medications?
- What medications have you tried for your symptoms?
- Of the medications you have tried, have any resulted in the improvement of your symptoms?
- Do you have a history of chronic sinusitis?
- Do you have a history of nasal and/or sinus polyps?
- Are you sensitive or allergic to aspirin?
- Have you undergone sinus surgery?
- Do you have asthma?
A comprehensive head and neck examination includes nasal endoscopy.

- Boggy and edematous mucosa with clear mucoid secretions suggest noninfectious rhinitis.
- Inflammation and purulent discharge from middle meatus suggest active infection.
- Areas of blanched mucosa with prominent vessels suggest chemical exposure.
- Atrophy of mucosa is seen in aging, prior surgery or drug abuse.
- Look for septal deviations, choanal stenosis, polyps.
Treatment
Patient education is key for initial treatment.

Pt are frequently not aware of triggers that incites their congestion

Avoidance of inciting factors, change in environment, using mask and protective equipment

Associated medications can be discontinued or changed

If exposure and medications cannot be changed, then medical therapy is next line of treatment.
Treatment

- Immunologic therapy has no benefit to non-allergic rhinitis and therefore it is important to distinguish the disease before considering starting immunotherapy.

- Nasal saline lavage has minor decongestant benefits and improves mucociliary function in both allergic and non-allergic rhinitis.
Topical nasal steroids are widely used for treatment of NAR.

They work on the nasal mucosa by decreasing neutrophils and eosinophil chemotaxis, reduced mast cell release and thus decrease edema and inflammation.
## Topical Nasal Steroids

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Dosage</th>
<th>Multiple that Suppresses HPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone</td>
<td>Dexacort</td>
<td>TID</td>
<td>Any dose greater than TID</td>
</tr>
<tr>
<td>Beclomethasone</td>
<td>Vancenase</td>
<td>BID-QID</td>
<td>5 times the QID dosing</td>
</tr>
<tr>
<td></td>
<td>Beconase</td>
<td>BID-QID</td>
<td>5 times the QID dosing</td>
</tr>
<tr>
<td></td>
<td>Vancenase AQ DS</td>
<td>QD</td>
<td>5 times the QD dosing</td>
</tr>
<tr>
<td></td>
<td>Beconase AQ</td>
<td>BID</td>
<td>5 times the BID dosing</td>
</tr>
<tr>
<td>Flunisolide</td>
<td>Nasalide</td>
<td>BID</td>
<td>3.5 times the BID dosing</td>
</tr>
<tr>
<td></td>
<td>Nasarel</td>
<td>BID</td>
<td>3.5 times the BID dosing</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>Nasacort</td>
<td>QD</td>
<td>16 times the QD dosing</td>
</tr>
<tr>
<td></td>
<td>Nasacort QD</td>
<td>QD</td>
<td>16 times the QD dosing</td>
</tr>
<tr>
<td>Budesonide</td>
<td>Rhinocort</td>
<td>QD</td>
<td>4 times the QD dosing</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>Flonase</td>
<td>QD</td>
<td>8 times the QD dosing</td>
</tr>
<tr>
<td>Mometasone</td>
<td>Nasonex</td>
<td>QD</td>
<td>20 times the QD dosing</td>
</tr>
</tbody>
</table>
Fluticasone propionate, budesonide and beclomethasone are the only topical steroids approved for NAR.

Efficacy is inconsistent. They must be tried for a minimum of 6 wks.

With the exception of NARES, topical steroids sprays do not provide the same reliefs as they do to allergic rhinitis.
Treatment

- Antihistamines have been shown to have inconsistent results.
- Histamine release is the pathophysiology indicated for AR.
- For this reason, they are considered a poor choice for NAR.
# Commonly Prescribed Antihistamines

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First generation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>Benadryl</td>
<td>25–50 mg Q 4–6 hours PRN</td>
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<tr>
<td></td>
<td></td>
<td>6.25 mg Q 4–6 hours (pediatric)</td>
</tr>
<tr>
<td>Clemastine</td>
<td>Tavist</td>
<td>1–2 mg BID-TID PRN</td>
</tr>
<tr>
<td></td>
<td></td>
<td>.5 mg BID (pediatric)</td>
</tr>
<tr>
<td>Chlorpheniramine</td>
<td>Chlor-Trimeton</td>
<td>4 mg Q 4–6 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 mg Q 4–6 hours (2–6 year olds)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 mg Q 4–6 hours (6–12 year olds)</td>
</tr>
<tr>
<td><strong>Second generation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acrivastine</td>
<td>Semprex D</td>
<td>8 mg TID</td>
</tr>
<tr>
<td>Loratadine</td>
<td>Claritin</td>
<td>10 mg QD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 mg QD (2–12 year olds)</td>
</tr>
<tr>
<td><strong>Third generation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fexofenadine</td>
<td>Allegra</td>
<td>60 mg BID</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30 mg (6–11 year olds)</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>Zyrtec</td>
<td>10 mg QD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5–10 mg QD (6–11 year olds)</td>
</tr>
<tr>
<td><strong>Topical</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azelastine</td>
<td>Astelin</td>
<td>2 sprays per nostril BID</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 spray per nostril BID (5–12 year olds)</td>
</tr>
</tbody>
</table>
Of the antihistamines, Azelastine intra-nasally has been efficacious for all forms of NAR, including Idiopathic Rhinitis.

It is an H1 receptor antagonist, that also inhibits synthesis of leukotrienes, kinins, cytokines and free radicals.

However, the exact mechanism of action for relief of symptoms is unknown.
Treatment

- The anticholinergic drug Ipratropium bromide, which is mainly used for treatment of asthma, has been shown to be effective in reducing the severity and duration of rhinorrhea in NAR.

- The strength of 0.03% is the dose for NAR, initially two sprays TID. Once symptoms abate, the dose should be lowered slowly until one spray BID.
Mast cell stabilizers such as cromolyn, are effective only for allergic rhinitis and have no benefit with non-allergic disease.

No studies to date have been identified looking at the efficacy of leukotriene modifiers in treatment of non-allergic rhinitis.
Capsaicin has been shown to be of benefit to Idiopathic Rhinitis.

Nasal Capsaicin, the pungent agent of hot red peppers, results in rhinorrhea, nasal blockage and sneezing through c-fibers (pain receptors).

Repeated application of capsaicin, however, lead to desensitization and degeneration of C-fibers.
Treatment

- Dosage is five high dose treatments of intranasal capsaisin over 1 day at 1 hr intervals after local anesthesia or five treatments spread out over 2 wks.
- Up to 75% of patients will show long lasting (from 4 month to over 1 yr.) relief of symptoms.
- Even after symptom free period is over, a repeat dose of capsaisin will most likely repeat itself.
- A lower dose capsaicin formulations nasal sprays can be found OTC at pharmacies and used in higher frequencies.
Surgery is reserved for failed medical therapy only.

Nasal polyps, inferior turbinate hypertrophy and septal spurs may obstruct nasal cavity and block the action of topical medications.
Silver nitrate has been studied as therapy. Topically it has been shown to down-regulate nasal mucous membranes stimuli. Clinical trials show improvement over placebo at 6 month interval for most patients. Local irritation and anosmia was rare side effect. A 20% solution was most effective dose that did not cause harmful irritation. Applied by cotton tip applicator for 1 minute once a wk for 5 wks.
Submucosal resection, vidian neurectomy or the combination of the two have been shown to be efficacious in treatment of symptoms.
Since 1961, vidian neurectomy has demonstrated as treatment for persistent rhinorrhea.

Initially done as transantral, recently endoscopic transnasal approaches are used, which have less morbidity (decreased lacrimation and dysesthesia)

Efficacy has been documented up to 88% with symptoms ceasing.
Many surgical techniques are available to treat inferior turbinate hypertrophy.

A randomized control trial of 382 pt with 6 yr. follow up found sub-mucous resection with lateral displacement to be statistically better in terms of efficacy to turbinectomy, laser or cryotherapy or electrocautery
Treatment

- Recently Ikeda et al (2006) showed benefit to combined vidian neurectomy and inferior turbinate resection for intractable chronic rhinitis.

- Fifty-six pt enrolled showed improvement of >80% in symptomatic nasal obstruction, discharge, sneezing, and quality of life. Four pt had complication of anosmia, one showed hyperesthesia.
Follow up


- A sample of 180 pt diagnosed with NAR during 2000-2004 was reevaluated in 2007 by questionnaires, spirometry, skin prick testing and IgE testing.

- Pt with NAR experienced worsening disease (52%), increased persistence and severity (9-12%), and new comorbidities (24%) of asthmas and conjunctivitis.
Follow up

- Sensitization to allergens not present at initial evaluation was detected by skin prick or IgE measurement in 24% of the patients initially diagnosed with NAR.
- This suggested that sensitization of allergens is likely to appear at a later date in adults.
Follow up

- Sanders et al (2009) also noticed variability in allergen content in 5 different skin prick test (up to 10 fold difference in concentration).

- Therefore it is possible that many apparent cases of non-allergic rhinitis may be misdiagnosed allergic rhinitis.
Conclusion

- Non-allergic Rhinitis is diagnosis of exclusion of allergic IgE mediated causes.
- NAR is typically given diagnoses when no identifiable cause is given, which is up to 50% of cases seen in ENT practices
- History and physical exam findings are as important an allergy testing in diagnoses
Conclusion

- Avoidance of irritative substance, medication changes and monitor of hormonal balance are important initial steps to treatment.

- Topical nasal steroids and topical H-1 receptor antagonist Azelastine are FDA approved medications for use of non-allergic rhinitis.

- Anticholinergic medications and capsaisin treatment have been proven beneficial, whereas mast cell stabilizers and leukotriene modifiers have not.
References


4. Bachert C. Persistent rhinitis—allergic or non-allergic? *Allergy* 2004; 59[Suppl 76]:11-15


References


