Allergic Rhinitis and Bronchial Asthma

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Introduction

Inflammation – an inert response of human body – is being understood better year by year and so is complexity of diseases related to inflammation. It is accepted and well understood that both allergic rhinitis (AR) and bronchial asthma (BA) are inflammatory disease. Inflammatory mechanisms are similar; in terms of infiltration by cells - eosinophils, T cells, and mast cells, release mediators and IgE -local and systemic. Hence “One airway – One disease” is acceptable in modern treatment options while managing both.

This chapter is aiming at understanding Allergic Rhinitis with its impact over Bronchial Asthma and review evidences that direct towards better outcome in this duo that is of epidemic proportions worldwide. It is assumed that Bronchial Asthma has been well understood by the readers in terms of diagnosis and management.

Epidemiology: Allergic Rhinitis and Bronchial Asthma

The prevalence of BA and AR is increasing worldwide. Connection amongst these two has been the subject of many epidemiological investigations and shown an important overlap between both diseases. In most studies, 20–50% of AR patients had asthma, and 30% to 80% of asthmatic patients reported AR. Whether AR precedes asthma, triggers asthma or precipitates asthma are intuitive aspects that require supportive data.

The atopic status plays predominant role in this coexistence, but it is not a prerequisite. Several studies have demonstrated the strong association between rhinitis per se and asthma, both in allergic and non-allergic subjects. A large European study with sensitive interview protocols found rhinitis in 98.9% of allergic subjects with asthma and in 78.4% of non-allergic subjects with asthma.

Pathophysiology

Allergens challenging the nose will induce the influx of inflammatory cells in the lower airways and vice versa. Treating the nose will probably, in different ways, affect inflammation in lower airway. Typical early phase and late phase responses are common to both rhinitis and asthma. Studies in patients with AR exhibit bronchial hyper-responsiveness and an increase in inflammatory cells, and that nasal allergen challenge further increases this hyper-reactivity. Eosinophils have been demonstrated in the nasal mucosa of patients with asthma, even in the absence of symptoms of rhinitis. Patients with allergic rhinitis have increased numbers of inflammatory cells in their bronchial mucosa while in patients with severe asthma, sinus mucosal thickening on computed tomography correlates with the severity of lower airway disease indicated by sputum eosinophilia.

Differences and similarities between nasal and bronchial mucosa

Similarities such as a pseudo stratified epithelium and the presence of both ciliated and columnar cells resting on a basement membrane are evident. Differences are mainly at the submucosal level. The large highly developed vasculature of the nose contrasts with the smooth muscle bundles that surround the bronchial airways. Whether inflammation-induced differential symptoms represent the expression of these anatomical discrepancies needs to be established.
exhaled nitrous oxide, functional residual capacity, and diffusing capacity.

Study of outcomes of treating AR in patients with asthma has shown that not only it improves symptoms of asthma but also lowers the overall costs and reduces hospitalisations. This parallel relationship is influenced by many interactions between the nasal tract and the lower airways. The fact that the nasal passages play a major homoeostatic role by conditioning inhaled air seeds some interactions, but perhaps even more important is the bidirectional interaction that results from the systemic inflammation that is produced after local allergic reactions.

**The Link between Upper and Lower Airways**

Mechanisms have explained the link between upper and lower airways and hence the concept of “One Airway One Disease” has been accepted. Genetic factors, an anatomic link between upper and lower airways, neural interaction between the nose and the lower airway, and mediator or inflammatory-cell circulation are present as link.

Inflammatory mediators can reach the lower airway from the upper airway through the airway passages. They might also be able to reach the lower airway through the blood. A number of these mediators, such as histamine, cysteinyl leukotrienes, and some cytokines, have the ability to spill over into the systemic circulation. However, most of the cytokines have a very short half life and do not act in an endocrine fashion. Researchers suggested that inflammatory mediators such as IL-5 and GM-CSF can travel from the lung to the bone marrow, where they could stimulate the progenitors’ release to the circulation and to the target organs. It is seen that after antigen challenge, there is an increase in IL-5-producing T cells in the bone marrow and an increase in high-affinity IL-5 receptor, which is associated with an elevated number of eosinophil progenitors. This process is most likely due to retrograde migration of antigen-specific T cells from the airways to the bone marrow, where antigen-specific T cells can produce a number of cytokines and help to release and differentiate the progenitor cells. Progenitor cells can be found along the entire airway in atopic individuals and can differentiate into mature eosinophils in response to local antigen challenge.

**Approach to AR and BA**

With both being very simple to pick up on history and good clinical examination, complacency is common for clinicians and that leads to poor outcome or persistence of symptoms or failure to control. Following are a few methodical steps for **Confirmation of Co-existence of AR with BA**

1. **When to suspect AR coexisting with BA?**
   - Symptoms and signs of AR can be very mild as local or severe as systemic. Most of those with AR experience nasal congestion or obstruction as the predominant symptom, while some experience mainly ocular symptoms like watering - lacrimation and itching.
   - Many times patients are unaware of typical symptoms, presence of following leads to suspicion especially symptoms that suggest continuous or recurrent upper respiratory tract infections.
     - Frequent sore throats
     - Hoarse voice
     - Persistent mouth breathing, especially in children
     - Snoring
     - Feeling of pressure over sinuses
     - Recurrent headaches
     - Recurrent serous otitis media, especially in children
     - Coughing, especially in children
     - Halitosis
     - Poor sleep and daytime fatigue or poor concentration
     - Persistent respiratory symptoms despite stable, well controlled asthma, appropriate treatment and good lung function on spirometry.

2. **When and how to investigate for AR with BA?**
   - Consider further investigations in patients having any of the findings listed here.
     - Poorly controlled asthma despite appropriate treatment and good adherence
     - Difficult-to-treat eczema or skin allergies
• Food allergies
• Persistent rhinitis (including nasal obstruction) that have not responded to a trial of intranasal corticosteroid treatment
• Persistent nasal obstruction, congestion, post-nasal drip and a reduced sense of smell for ≥ 12 weeks (suggests chronic sinusitis)
• Persistent unilateral nasal obstruction (suggests foreign body or tumour)
• Persistent unilateral bleeding (suggesting tumour, a granulomatous condition or vasculitis)
• Suspected diffuse nasal polyps (with or without history of asthma)

If any of above is present, following are the steps to be carried out.
A. Review asthma control, including spirometry before and after bronchodilator.
B. Consider routine haematological and radiology investigations
C. Consider arranging allergy tests (skin prick test or allergen-specific IgE/RAST blood test)
D. Consider CT Scan for intranasal pathology.

Treatment of AR and BA

Better understanding of the mechanisms of asthma and allergic rhinitis in recent years. Few have led to the development of new therapeutic agents while others may be the basis for further new drug entities.

The currently available therapies for AR and BA mainly include anti-inflammatory compounds and bronchodilators. Anti-histamines and Des-sensitisation has some role to play though.

**Group A - Anti Inflammatory Agents**

**Steroids:** Till date, Inhaled or instilled Corticosteroids (IC) therapy is the most effective anti-inflammatory treatment for AR and BA. However, the effects of the long-term use of ICs on bone metabolism and the associated risk of osteoporosis remains controversial. Some studies have shown a reduction in bone mineral density and results of such studies suggest a risk of osteoporosis with higher doses of ICs. Corticosteroids, however, do not fully suppress the production or release of eicosanoid mediators, thromboxane and leukotriene B4. Probably this is a sub group of steroid resistant patients, who are taking larger than usual daily oral corticosteroid dose and showing inadequate symptom control.

**Leukotriene Receptor Antagonists:** Role of cysteinyl leukotrienes is known to play a pivotal role in asthma and allergic rhinitis. At present, the scientific evidence does not support the substitution of leukotriene receptor antagonists for inhaled glucocorticoids, which remain first line therapy for asthma but it has certainly gained edge in management of AR.

**Group B - Bronchodilators**

Short-acting β2 agonists (SABA) are used as rescue therapy for relief and prevention of acute symptoms. Long-acting bronchodilators are also combined with anti-inflammatory medications for long-term control and nocturnal asthma. Sustained release theophylline, is a mild bronchodilator, used principally with inhaled corticosteroids for nocturnal asthma.

**Group C – Antihistamines**

**Oral antihistamines:** Second-generation, less sedating oral H1-antihistamines are effective in managing AR symptoms of rhinorrhoea, sneezing, nasal itching and ocular symptoms, but are less effective for congestion. Cetirizine, Levocetirizine, Loratadine, Desloratadine or Fexofenadine are used in preference to older, more sedating antihistamines. All appear to be equally effective overall.

**Intranasal antihistamines:** Reduce all symptoms of AR. Some have a more rapid onset of action than intranasal corticosteroids. These are as effective as newer, less sedating oral H1-antihistamines, but are generally less effective than intranasal corticosteroids for the treatment of AR.

**Group D – Specific Allergen Immune Therapy - (Desensitisation)**

**Sublingual immunotherapy** is effective for the treatment of allergic asthma in adults and for allergic rhinitis in adults and children aged 5 years and over. However, it is unclear which patients will benefit most. Sublingual immunotherapy is better tolerated than subcutaneous immune therapy.

**Subcutaneous immunotherapy** is effective for the treatment of BA and AR, especially in adults with allergies to pollens. It may also be effective in adults with allergies to animal dander, house dust mite and some fungi. Subcutaneous immunotherapy is associated with local adverse effects (e.g. injection-site swelling) and, less frequently, serious systemic adverse effects and anaphylaxis is very rare (estimated as 1.4 serious adverse events per 100,000 doses). The majority of adverse events occur soon after beginning treatment.

Consider specific allergen immunotherapy (sublingual immunotherapy and subcutaneous immunotherapy) only for patients with a clinical history of allergy and documented positive allergen-specific IgE test. Both forms of specific allergen immunotherapy require 3–5 years of treatment.
Group E - Not Recommended In AR

**Intranasal decongestants:** A limited role in the management of AR - they should only be used for very short courses (up to 5 days maximum). Repeated or long-term use can cause rebound swelling of nasal mucosa necessitating dose escalation (Rhinitis Medicamentosa), with a risk of atrophic rhinitis. Intranasal decongestants might be considered for a patient with severe nasal congestion to gain rapid relief of symptoms until the full effect of intranasal corticosteroids is achieved.

**Oral decongestants:** Pseudoephedrine or phenylephrine should not generally be used in the management of AR. They are indicated for short-term use only e.g. acute infectious rhinitis. They are associated with adverse effects including palpitations, tachycardia and insomnia.

**Oral corticosteroids:** should be avoided as a treatment for AR. In exceptional circumstances, their use might be considered in consultation with an allergy specialist.

**Guidelines for treatment of AR and BA**

Various guidelines from various agencies are available for the management of AR and BA. ARIA (Allergic Rhinitis and its Impact on Asthma) World Health Organisation (WHO) evidence-based document addresses AR and BA together. The National Asthma Education and Prevention Programme (NAEPP) in US addresses questions about the asthma management by using a systematic review of the clinical studies, while Global Initiative for Asthma (GINA) discusses about management of asthma by patient education, monitoring severity of disease, avoiding exposure to risk factors, establishing individual medical plans for long term management of asthma and regular follow up.

**Key Points**

- Allergic rhinitis and Bronchial asthma are both chronic heterogeneous disorders, with an overlapping epidemiology of prevalence, health care costs and social costs in quality of life.
- Both are inflammatory disorders with similar pathophysiology and both share treatment approaches.
- Each disorder has an array of treatments used separately in controlling these atopic disorders, from inhaled corticosteroids, beta₂-agonists and antihistamines to anti-leukotrienes and newer monoclonal antibody-based treatments.
- All available drug therapies are generally successful at controlling symptoms of AR or BA or Both. However, there is a group of patients with persistent symptoms, frequent exacerbations and pulmonary abnormalities despite maximum standard therapy.
- Cure of rhinitis would prevent only some cases of new-onset asthma. Potential risk of BA and its management options should be discussed cautiously with patients of AR.

**References**

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