Nasobronchial interaction

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Abstract
Upper and lower airways can be considered as a unified morphofunctional unit. In this paper, nasobronchial interactions are evaluated based on literature. To discuss nasobronchial interactions, literature review from PubMed since 1982 is evaluated. Data base was including the terms “nasobronchial interaction, nasal and bronchial”. Asthma and rhinosinusitis may be associated with environmental factors and immunological predisposition. Treatment of rhinosinusitis may decrease asthma exacerbations. It was concluded that “one airway, one disease”-concept may be accepted when considering naso-bronchial interaction. Asthma treatment should also mean treating the nose as good as treating patients with nasal symptoms. To reach the successful results it should be associated with evaluation of lung functions.

Key words: Nasal; Bronchial; Nasobronchial interaction; Reflex; Airway

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Core tip: Upper and lower airways may be accepted as unified morphofunctional unit. This concept is defined as nasobronchial interaction.

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INTRODUCTION
Upper and lower airways may be accepted as unified morphofunctional unit. Likewise rhinosinus disorders and lower airway diseases have interrelation. Inflammatory cytokines may play a role for the interaction between cells[1].

During infections of upper respiratory tract such as rhinosinusitis, asthma development may occur[2,3]. Atopic dermatitis in children, and also allergies to the
food may be the first sign for developing of allergic rhinitis (AR) and asthma[9].

In this paper, nasobronchial interactions were evaluated thoroughly by the means of literature review from PubMed since 1982. Database was depended on the terms of nasobronchial interaction, nasal and bronchial.

**NASAL FUNCTION**

Nose works as “air-conditioner”. Cold air through induces bronchospasm in asthmatic patients. Nose humidifies the air which inhaled nasally. In allergic rhinitis patients, exposure to allergens increase bronchial hyper-reactivity[10-8].

**MECHANISMS FOR NASO-BRONCHIAL INTERACTION**

Impaired nasal function, pulmonary aspiration of nasal contents, the nasal-bronchial reflex and increased absorption of inflammatory mediators in the blood stream maybe responsible for lower airway dysfunction in AR[7]. They also cause the interaction between the nose and the lung. After nasal allergen application, no allergen deposition was shown in the lungs by radiolabeled allergen[6]. Cold and dry air exposure may cause immediate bronchoconstriction[9]. Nasal provocation with methacholine also increase lower airway resistance in asthma and AR patients[9].

Mast cells and eosinophils are the major effector cells in AR and asthma[10,11]. Eosinophils migrate to the tissues from the blood and this process is depend on the expression of cytokines and adhesion molecules[12]. Vascular cell adhesion molecule-1 and E-selectin increased after nasal provocation[13]. After bronchial provocation, mast cell degranulation and increase of of basophils occur in the nasal mucosa[14].

**Impaired nasal function**

In AR, mouth breathing was observed related to the nasal obstruction. Therefore, with the lower nasal filter function, increased allergen exposure develops. This process is resulted in hyperresponsivity of the airway. If additional chronic rhino-sinusitis and/or nasal polyposis were present, surgery help to improve nasal functions. In these patients, asthma control could be done better[15]. When nose blocked with a clip, response to cat-allergen was not detected in patients with cat allergy[16].

**Aspiration of nasal contents**

Inhale particles may be removed by the help of the mucociliary clearance. With this function and beat of the cilia, particles were carried toward the pharynx. In AR patients, secretions contain inflammatory mediators and cells[7,17]. When allergens inhaled, there was swelling of the nasal mucosa[18].

**Nasobronchial reflex**

The trigeminal nerve is responsible for afferent sensory innervation of the nose. Efferent parasympathetic fibers are carried in the Vidian nerve. Vagal nerve supports afferent and efferent innervation of the lower airways[19]. Sneezing, coughing or bronchoconstriction occur with the help of reflex mechanisms. The receptors were present in the nose, trachea, larynx and respiratory tract. The are sensitive to the mechanical or chemical factors. Cold dry exposure of nasal mucosa can cause immediate bronchoconstriction in asthmatic patients[6,20,21].

Nasobronchial reflex is another mechanism for interaction between upper and lower airways. Receptors are localize in the nose, sinuses and pharynx. The signals were transferred to the medulla by trigeminal, facial and glossopharyngeal nerves[22]. In the medulla, connections with vagal nerve were performed and bronchoconstriction occur[23].

**Triggers of the reflex**

In infectious conditions of the nose and lungs, virus and bacteria may trigger the reflex system. Smoking, pollutant agents in the work places and environment may cause chronic inflammation[24]. Beta-blockers or aspirin, cold dry air exposure, and physical exercise may also trigger the AR and asthma[25].

**Increased absorption of inflammatory mediators in the blood stream**

Increase in the eosinophil count is detected in AR and asthma patients in the blood[26]. Nasal provocation, performed with methacholine, also increases the lower airway resistance. It may be said that systemic mediators may induce lower airway resistance[9]. In AR and asthma, inflammatory cells and progenitors may play a role[27-29].

**RHINOSINUSITIS AND ASTHMA**

**Symptoms of rhinosinusitis**

Syptoms of rhinosinusitis are known as nasal congestion, discharge, purulence and postnasal drip; hypoxia, facial pressure, fever, halitosis, dental pain and headache. Chronic rhinosinusitis (CRS) may damage to the mucociliary clearance. CRS is an independent risk factor for asthma[2,3,30,31].

**Epidemiology**

Rhinosinusitis and asthma were coexistently detected in 34%-50% of patients. In asthmatic patients, concomitant rhinosinusitis were present up to 84%[24].

**Clinical appearance**

In rhinosinusitis patients, there is the possibility of having asthma. When nasal disease was treated, asthma control maybe easier due to the reducing of...
branched hyperresponsiveness. Therefore, therapeutic approach to asthma and rhinosinusitis should be planned together\cite{32}.

Treatment
Medical treatments or surgery for rhinosinusitis help the reduce of respiratory symptoms and improve the asthma. Cold air inhalation causes the decrease FEV1 in asthmatic patients\cite{45}.

AR AND ASTHMA

AR is a risk factor for asthma development\cite{33}. Whereas, in same cases, asthma starts first. Exercise induces bronchoconstriction in most asthmatic patients. It may be related to to alterations in the osmolarity of the liquid covering the epithelial layer. This process may be resulted release of chemical mediators originating in mast cells\cite{34}.

Epidemiology
In 19%-38% of AR patients, there are concomitant asthma. Moreover, 30%-80% of asthmatic patients also have AR. Rhinitis symptoms were reported in 98.9% of allergic asthmatics and in 78.4% of non-allergic asthmatics\cite{35}. Bronchial hyperreactivity was observed in most of the AR patients\cite{36}. In AR patients, 40% have involvement of the lower airways. Additionally, allergic asthma patients have concomitant rhinitis symptoms as a 80%\cite{37,38}.

Potential mechanisms
The allergic response starts with the uptake of the antigen by antigen presenting cells, in particular dendritic cells\cite{39,40}. Dendritic cells present the antigen to T lymphocytes in the regional lymph nodes\cite{41,42}. B cells recognize antigen with surface immunoglobin (sIg) receptors. The T cell receptor recognizes antigens and activation of the it stimulates the naive T helper cell, a Th0 cell. It differentiates to either a Th1 or a Th2 subset\cite{43,44}.

Activation of Th1 cell causes the release of IL-2 and INF-y. Additionally IL-4, IL-5, IL-10 and IL-13 are also produced by Th2 cells. Th2 cytokines are also involved in IgE synthesis (IL-4, IL-10)\cite{45,46}.

Nerve growth factor (NGF) and NGF receptors are expressed in the nasal mucosa\cite{47}. In patients with AR and allergic asthma, serum levels\cite{48,49}; and nasal and bronchial fluid levels of NGF increase\cite{50,51}.

Microbial stimuli
Exposure to endotoxins reduces the risk of developing allergic rhinitis and asthma during the first years of life. Chlamydia pneumoniae infection has been suggested as a possible causative factor for asthma\cite{52}. It was also reported as protective against the development of asthma in children\cite{53}. In infancy, bacterial infection is associated with a reduced prevalence of atopic eczema, allergic rhinitis and asthma\cite{54}. Viral respiratory infections stimulate nasal allergic inflammation in atopic patients; and virus-induced airway hyperresponsiveness develops\cite{55}.

Treatment
The medical treatment of AR reduces the risk of asthma-related events in asthmatic patients\cite{56}. Nasal corticosteroids stabilize bronchial hyperreactivity in allergic rhinitis patients with seasonal asthma\cite{37,59}. The leukotriene receptor antagonists are less effective than antihistamines and nasal steroids in upper airway disease\cite{60,61}.

Allergen immunotherapy reduces asthma symptoms. This therapy also improves nasal disease\cite{62,63}. By immunotherapy, progression of allergic rhinitis to bronchial asthma may be prevented. Specific immunotherapy with seasonal allergic rhinitis significantly reduced the asthma development risk\cite{59,65}.

UPPER AIRWAYS AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

The correlation between chronic obstructive pulmonary disease and upper airway inflammation are reported. The relation between nasal and bronchial inflammation by estimating the IL-8 concentration were reported\cite{66}.

CONCLUSION

Upper and lower airways are thought as one functional entity. Local allergen exposure of the respiratory system induces mucosal inflammation. A “unified airway” concept suggests that the upper and lower airways function as a single unit\cite{67}. The nasobronchial interaction may be suggested as present in airway. Trigger agents for naso-bronchial reflex are important to initiate the symptoms.

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