


Editorial

# Allergic Rhinosinusitis and Airway Diseases

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The concept of united airway disease interaction, which comprises chronic rhinosinusitis and other lower airway disorders such as asthma, has been recognized for over a decade. This concept furthers deeper comprehension on the pathophysiology and management of upper and lower airway diseases. In this Special Issue, entitled “Allergic Rhinosinusitis and Airway Diseases”, there are nine published papers which cover different interesting topics to give readers an overview of healthcare equality, advanced biomarkers, accurate diagnosis and treatment, occupational exposure-induced upper airway allergy and neoplastic disease mimicking chronic rhinosinusitis.

The equity and equality between races of patients with chronic rhinosinusitis should be considered by physicians. In fact, this issue has previously drawn the attention of the World Health Organization (WHO) [1], and was the focus of a systemic review by Weaver et al. in the Special Issue of *Sinusitis* entitled “Promoting Equity When Using the SNOT-22 Score: A Scoping Review and Literature Review” [2]. In this study, Weaver et al. [2] demonstrated the use of quality-of-life (QoL) tools to assist clinical decision-making by using SNOT-22 in patients with chronic rhinosinusitis to promote equality across diverse populations. The authors emphasized the effects of ethnicity and race on SNOT-22 scores and tried to improve equity. Based on PubMed and MEDLINE searches with appropriate keywords to find papers for a scoping review, Weaver’s study revealed, for the first time, that ethnic differences appear to exist in acute sinusitis symptomatology, and ethnic differences also exist with regard to QoL tools. Thus, the authors suggest that the evidence implies that some form of correction to QoL scores could help to promote equity for non-white patients.

Although the main theme of this Special Issue is “Allergic Rhinosinusitis and Airway Diseases”, currently, the large number of patients who have had the sequelae of COVID-19 within olfactory disorders during the post-COVID-19 phase is also a crucial healthcare problem for ENT (ear–nose–throat) physicians [3]. Therefore, in this Special Issue, Araújo et al. [4] have taken great efforts to successfully summarize the main mechanism and clinical management of anosmia in post-COVID-19 patients. This narrative review describes that olfactory disorder is one of the most common symptoms in patients with acute COVID-19 infection, and most of them recover normal neurosensory function in a short time. However, the authors emphasized that approximately 10% of patients have reported a long-term smell dysfunction which significantly impacts their quality of life. It is clear that inflammation and cellular damage can play a key role in the pathogenesis of olfactory dysfunctions. Based on this pathogenesis, the appropriate management of smell disturbances in post-COVID-19 patients should focus on the underlying mechanisms in combination with adequate smell training.

Recently, the idea of measuring the levels of fractional exhaled nitric oxide (FENO) during the COVID-19 pandemic and in patients with long-COVID has been published [5,6]. This idea might open a new field of research in the use of FENO to screen post-COVID-19



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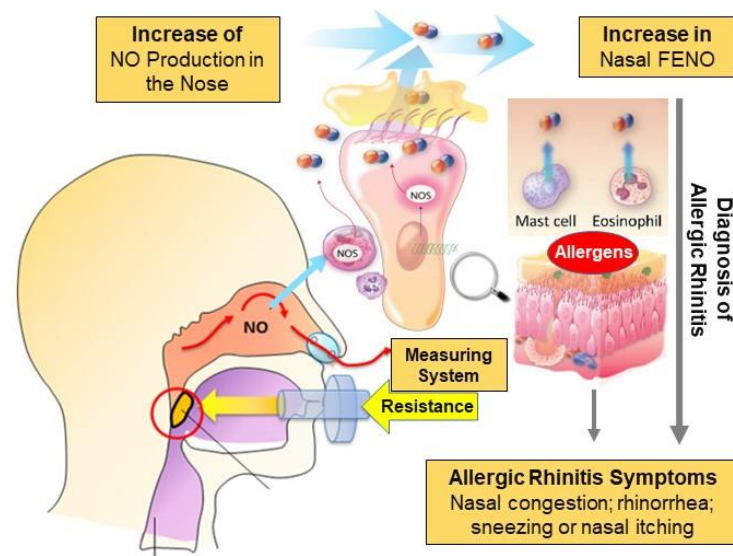
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patients with anosmia in clinical practice. Although the measurement of FENO in patients with asthma has been described in recent decades, its use in patients with allergic rhinitis (AR) remains a new area for ENT physicians [7]. In this Special Issue, Duong-Quy et al. have contributed original research on the role of nasal FENO in children with allergic rhinitis [8] to evaluate the correlations between nasal FENO and anthropometric, clinical and functional characteristics, and to determine the cut-off of nasal FENO for diagnosis of AR in the symptomatic children. This study showed that nasal FENO levels in AR patients were significantly higher than control subjects, and nasal FENO was significantly correlated with AR symptoms and nasal inspiratory/expiratory peak flows. Interestingly, the cut-off of nasal FENO for positive AR diagnosis had a very high specificity and sensitivity in AR diagnosis. These authors also concluded that the use of nasal FENO as a biomarker of AR could represent a useful tool and an additional armamentarium in the management of disease (Figure 1).



**Figure 1.** Principle of nasal FENO measurement in subjects with AR. AR: allergic rhinitis; FENO: fractional exhaled nitric oxide; NOS: nitric oxide synthase.

The use of FENO in management of asthma has been approved by many countries and international guidelines [9]; however, nasal FENO has not been approved unanimously in the management of AR. Therefore, other biomarkers used in the management of AR, such as circulating specific non-coding microRNAs (miRNAs), have been presented in another review in this Special Issue: “Allergic Rhinosinusitis and Airway Diseases”. This review, entitled “Immunological and microRNA Features of Allergic Rhinitis in the Context of United Airway Disease” and written by Naydenova et al. [10], focused on the theory involving inflammation of the upper respiratory tract in patients with AR might contribute to lower respiratory airway inflammation. These authors suggested that T-helper 17 (Th17) cells and related cytokines are also involved in the immunological mechanism of AR along with classical Th2 cells, leading to Th17-induced neutrophilic inflammation in the lungs. Definitely, the regulators of this inflammatory process could be modulated by circulating specific miRNAs, which are distinctively expressed in AR and asthmatic patients. Hence, this pathway could be considered a promising target treatment for the therapy of patients with concomitant AR and asthma.

This Special Issue has been supplemented with the study realized by Nair et al. [11] on the efficacy of saffron extract in an ovalbumin-induced airway model of allergic asthma. This study, using a very-well-known animal model to induce allergic asthma via introducing ovalbumin (OVA) into the nose, again confirmed the unification of the upper and lower airway inflammatory pathways in AR and asthma [12]. In this study, the authors used saffron (*C. sativus*) extract (CSE), a product which exerts anti-inflammatory, anti-allergic

and immunomodulatory properties, to investigate its efficacy in combination with salbutamol in the treatment of OVA-induced asthma in rats. The main results of this study demonstrated that the treatment with CSE and salbutamol significantly attenuated OVA-induced Th2 cytokine levels (TNF- $\alpha$ , IL-1 $\beta$ , IL-4, IL-13) in the bloodstream and lung tissue by ameliorating OVA-induced inflammatory influx and ultrastructural aberrations. The authors suggested that the combination of CSE and short-acting beta 2-agonist could be considered a new therapeutic strategy for the management of asthma.

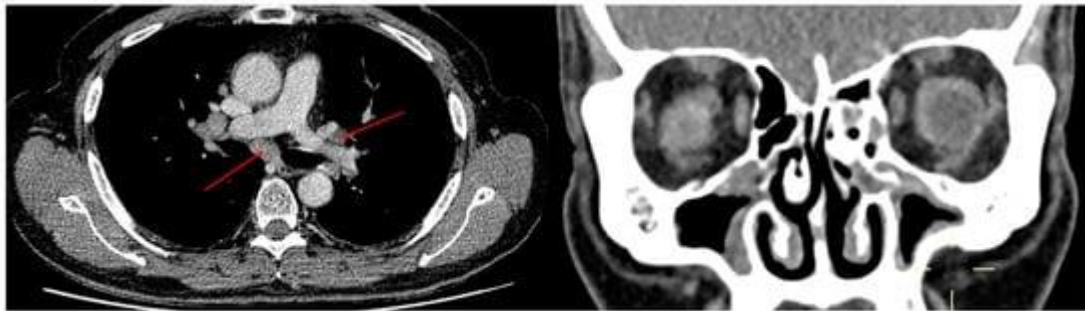
Saffron has been considered as one of the most valuable spices for centuries, and it has been used in daily foods for promoting good health and a positive mood status. Therefore, the results of Nadir's study could develop the current concept related to the use of diet in the treatment of patients with respiratory allergic diseases who did not respond to pharmacological therapy [13]. In the same scope, Calatayud-Sáez et al. [14] have published their results from the study entitled "*Effects of the Traditional Mediterranean Diet in Childhood Recurrent Acute Rhinosinusitis*" in this Special Issue. This study was conducted in a young population (1–5 years old children) who had three or more acute rhinosinusitis episodes in the period of one year from the program "*Learning to Eat from the Mediterranean*" in Spain. The main outcomes of this study showed that more than 50% of study subjects did not have any episode of acute rhinosinusitis, and KIDMED (Mediterranean Diet Quality Index) scores increased significantly. These authors stated that adoption of the traditional Mediterranean diet might have a promising effect on the prevention and treatment of recurrent acute and chronic rhinosinusitis in early ages of life.

An appropriate diet, such as the traditional Mediterranean diet, may be useful for subjects who are allergic with airborne and/or food allergens. For these subjects, skin prick tests (SPT) have been considered as a relevant examination technique to detect respiratory or food allergens, although the level of specificity remains a challenge for the treatment with specific desensibilization [15]. Therefore, the atopic status assessment with SPT or specific immunoglobulin (sIgE) in subjects with asthma or AR is always a milestone in identifying potential risk factors and triggers provoking loss of disease control. A recent study in asthmatic children published by Lazova et al. [16] demonstrated that there was a moderate to strong correlation between multiscreen ImmunoCAP Phadiatop/fx5 and Euroimmun sIgE titers against aero-allergens—cats, mites, tree mix and food allergens—soy, wheat, rice, apple and peanut. This study also showed that good sensitivity and specificity were observed for EUROIMMUN Pediatric (food allergens) compared with the gold standard ImmunoCap/fx5. The authors of this study suggested that the immunoblotting technique is an easily applicable, cost-effective and reliable alternative to ImmunoCAP Phadiatop/fx5 in diagnosing atopic children.

In addition to airborne and food allergens, some evaporated chemical products used in industry could be the cause of airway allergies in workers [17]. This crucial problem has been clarified by the study realized by Kashyap et al., published in this Special Issue of *Sinusitis* [18]. This study included tannery workers of Kanpur city in India who were frequently exposed to chromium during the leather tanning process. The authors found that the severity of nasal and sinus allergies increased with age and work duration in the tannery, and workers with occupational exposure were more likely to develop sinus problems than those without exposure. The authors suggest that this high risk of occupational factors could be eliminated by improving the overall working conditions and ensuring necessary protective regulations for the tannery workers to reduce upper airway allergies and other carcinogenic factors.

This Special Issue, "*Allergic Rhinosinusitis and Airway Diseases*", concludes with the ninth paper presenting an interesting clinical case, entitled "*Low-Grade B Cell Lymphoproliferative Disorder Masquerading as Chronic Rhinosinusitis*", reported by Chen et al. [19]. In this case report, a 72-year-old man was referred by his general practitioner for symptoms mimicking chronic rhinosinusitis unresponsive to local corticosteroid treatment and antibiotics. Although the histopathology result taken from the middle turbinate biopsy revealed chronic non-specific inflammatory changes with mixed microbial flora, the patient

was consequently referred to hematology specialists, as recommended previously [20]. Then, a combination of serum and radiological findings (chest CT scan: mediastinal and hilar lymphadenopathy; Figure 2) was used to perform the clinical diagnosis of B-cell lymphoproliferative disorder. The authors of this case report recommend that patients with chronic rhinosinusitis who present with atypical clinical features such as nasal crusting and treatment resistant organisms may have underlying immunosuppression.



**Figure 2.** Transverse CT chest image with arrows indicating mediastinal and hilar lymphadenopathy. Coronal CT sinus image depicting disease affecting the ethmoid bullae and ostio-meatal complex [19].

In conclusion, this Special Issue, entitled “Allergic Rhinosinusitis and Airway Diseases”, successfully raises more awareness of rhinosinusitis and its comorbidity with other airway diseases. Hence, the concept of united airway disease interaction comprising upper and lower airway diseases should be recognized in patient management programs. Progress in diagnosis, with the use of the advanced biomarkers and relevant imagery techniques associated with accurate treatment of chronic rhinosinusitis and lower airway diseases, should continue to be developed in the future.

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