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Current understanding of pollen allergy: Its origin, impacting factors, treatment regime, and monitoring methods

L J Tong

Culver Academies, Culver, Indiana 46511, USA

luoshunwaijessica.tong@culver.org

Abstract. Pollen allergy is currently evolving into a major aspect regarding allergic bronchial asthma and allergic rhinitis, which are significant global health issues over the past decades. More pollen allergens are being recognized as the changing patterns of pollen exposures trigger increasing numbers of suffering patients. Impacting factors such as human-induced activities and climate change can lengthen pollen seasons as well as heighten pollen production in general. Allergen Immunotherapy (AIT) is an advancing therapeutic vaccine for pollen allergy that can modify the disease and the sensitization of allergens in patients which are less common than symptom-relieving drugs. Monitoring methods contribute greatly to the necessary observation of pollen exposure for treatment processes and the well-being of patients. Automatic monitors are being developed using technologies of different fields based on the traditional methods of pollen counting.

Keywords: Pollen allergy, Pollen allergen, Allergy monitoring, Pollen allergy treatment

1. Introduction

Pollen allergen is one of the most significant causes of type 1 allergies, which are hypersensitivity reactions triggered by immunoglobulin E (IgE) released by the immune system when encountered with the allergen, typically referring to asthma, conjunctivitis, or rhinitis [1]. Allergic reactions to pollen are also known as atopic diseases, or IgE-mediated diseases, of which allergic bronchial asthma and allergic rhinitis (AR) are the most common types, currently affecting up to 10% to 30% of the world's population in all ages, genders, and ethnic groups [2]. Allergic disorders like such have been marked with significant increases in prevalence worldwide over the past several decades. In North America, there are three major aeroallergen seasons, one of which is ragweed pollen during the summer and fall, which 10% of the US population is found sensitized to by a skin prick test survey. Results of studies over the years in North America have shown that seasonal and environmental changes may have extended the pollen seasons by 13-27 days [3]. The increasing presence of ragweed pollen by global warming is also concerned as a public health threat in Europe [4]. The intensifying of pollen exposure and the lengthening of pollen season duration caused by risk factors such as climate change greatly contributes to the increasing numbers of populations affected by allergy and asthma [5, 6].

Pollens are biological substances that are produced by the reproduction of certain plants such as trees, grasses, and weeds. All plants that produce pollen have either a considerable or slight difference in the time they bloom and release pollen. These periods of the year are also known as pollen seasons, where pollen grains are picked up by wind and distributed in the air, and when major pollen-induced allergy

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outbreaks take place. The pollen grains can be further categorized based on families and types of plants using microscopy, which use can date back to the 17th century [7]. Currently, more than 150 pollen allergens of different families of trees, grasses, and weeds are recognized by the International Union of Immunological Societies Allergen Nomenclature sub-committee. Antigens carried out by pollen grains can be recognized as threats when entering the immune system thereby provoking inflammatory responses with symptoms associated with nose, eyes, and throat [8]. Pollen allergy (pollinosis) was first explained in the 19th century as different respiratory diseases began to emerge with the study of airborne particles. The first description of pollen allergy was made by physician John Bostock at Guy's Hospital in London. The description ascribed pollen exposure to have caused a series of symptoms similar to those of hay fever (allergic rhinitis) [7]. Moreover, pollen-related food allergy has become prevalent and especially dominant in Europe, as 70% of patients diagnosed with birch pollen allergy are also allergic to certain foods. A common example refers to the 'birch-fruit-vegetable-syndrome', or the 'oral allergy syndrome', where an allergic reaction is triggered when raw fruit comes in contact with oral parts [9,10].

Sensitization to pollen is typically determined by a skin prick test or specific IgE in blood tests. Seasonal allergic symptoms of patients living in an area with defined pollen seasons or allergen exposure may also indicate a clinical diagnosis of pollen sensitization. However, a positive skin prick test alone cannot fully identify a diagnosed allergy or the severity of the allergy. The medical history of a patient needs to be consistent with the test results to further ensure the accuracy of the different test methods. Misconceptions of allergy tests can oftentimes lead to misdiagnosing or underdiagnosing of patients [11].

2. Association Between Pollen Allergy and Environmental Factors

Climate change and anthropogenic environmental factors significantly alter and prolong pollen emission seasons and production rates. Due to global warming, warmer temperature has been constantly observed over the past decades. The increase in temperature has shifted the start of pollen seasons by 3-22 days in advance for spring-flowering taxa and delayed by 27 days for late-flowering taxa, therefore extending the duration of pollen seasons [12]. In the datasets of temperature and the monitoring of pollen count and pollen season duration over the world recorded over the span of approximately 26 years, 76% of the monitoring locations observed an increase in pollen load, and 65% observed an extension in the duration of the season due to the increase of temperature [13]. *Ambrosia artemisiifolia* (ragweed) pollen, one of the most common and widespread pollen allergens, were planted in the urban areas in Baltimore and were found to flower earlier and produce higher concentrations of pollen than in rural areas where carbon dioxide (CO_2) levels and temperature were lower by 30% and 0.2 degrees Celsius, respectively [14]. The increases in production of ragweed pollen were up to 55-90% as a result of increasing CO_2 levels. Moreover, C3 and C4 grasses, both warm and cool season grasses, also displayed increased growth rates of 44% and 33%, stimulated by elevated CO_2 levels. Studies that have been conducted to observe allergens and pollen emission of ragweed pollen showed that allergens of ragweed may remain active even after traveling long distances under different weather conditions and indicated that human-induced CO_2 emissions enhance its allergenicity [15].

Aside from climate change and environmental factors, human-induced activities such as diesel exhaust and secondary pollutants are also associated with the change in pollen emissions. The World Health Organization (WHO) states that traffic-caused air pollution may increase the population affected by allergies as a positive correlation was presented between living along busy streets with traffic and allergic sensitization [16-18]. The air pollutants not only affect humans, but also allergens. Pollen allergens are found to be impacted by long-term air pollution and ozone levels in a study using birch pollen samples. Skin prick tests of aqueous pollen extracts (10 mg/mL) of pollen samples exposed to different levels of ozone were implemented on patients and results show that the allergenicity of the samples with higher ozone exposure indicates a higher allergic potential of birch pollen [18]. By 2100, CO_2 levels are expected to reach 730-1020 ppm from 400 ppm currently and Ozone (O_3) levels from 30-40 ppb to 42-80 ppb. Based on the expected levels of both greenhouse gases in 2100, overall pollen production is expected to increase by around 200% at the increased CO_2 level and 165% at the increased O_3 level [19].

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3. Treatment

When addressing pollen-induced allergies or IgE-mediated allergies in general, there is a plentiful variety of medications available to temporarily relieve or prevent allergic symptoms. For instance, decongestants and antihistamines, some of the most common prescriptions given to alleviate allergy inflammation, are able to block symptom-causing chemicals secreted as a result of the immune response. However, while medications are safely and effectively used by many patients, a significant number of patients encounter side effects such as nausea, insomnia, drowsiness, elevated blood pressure, and more serious side effects such as stroke and intracranial bleeding due to varying types of body constitution and backgrounds of existing diseases [20].

On the other hand, Allergen Immunotherapy (AIT), an advancing therapy used for over 100 years, is another widely suggested approach for treatment, as it is proven to be successful in potentially modifying the disease in the long term. AIT is identified as a therapeutic vaccine, which relies on repeated exposure to specific pollen allergens to treat allergic inflammation of seasonal allergic asthma patients caused by the same pollen allergen. This method was first recorded in 1911 by Leonard Loon, in an attempt to inject grass pollen extract into a patient who was found allergic to grass [21]. Recent research demonstrates that a reduction in Th2 and Th17-producing cytokines, such as IL-4, IL-5, and IL13 contributes to the relief of allergy symptoms. AIT enhances the production of antibodies that compete and suppress the reactive activities of the allergy-triggering cells. Thereby, more of the suppressor cells are able to reduce the levels of symptom-triggering cytokines [8].

However, numerous features of AIT concerning its reliability and safety of resources remain questionable, causing its use to be relatively less prevalent [22]. Targeted studies have shown that the discontinuation of immunotherapy had no significant change in the immediate sensitivity of an allergen throughout a three-year period. However, the proclivity of immediate sensitivity to the same allergen became increasingly noticeable after a three-year period, indicating that AIT remains debatable for its long-term effects on patients [23].

Regardless of the developed mechanisms of AIT, efforts are being made to better address issues of standardization and potential side effects or harms in the long run. As the understanding of the mechanics of allergic reactions increases worldwide along with the accessibility of research and lab proficiency, numerous advancements regarding vaccination techniques and the incorporation of biotechnological products in therapy mark the improvements in the progressing clinical trials [24].

4. Monitoring

Monitoring of pollen counts provides crucial information for increased numbers of pollen allergy patients worldwide, affecting up to 10-30% of adults and 40% of children in 2021. Currently, pollinosis are more prevalent than ever as an outcome of climate change and human-induced pollution. Moreover, altering environmental and anthropogenic factors affect the durations of pollen seasons, typically causing an increased exposure to pollen and triggering of allergic reactions [25]. Therefore, the demand for real-time monitoring has shown significance through treatment methods for pollinosis and other respiratory diseases appearing to be associated with pollen concentrations [26]. In North America and Europe, the medical score reflecting the treatment effect of 2363 patients receiving allergy immunotherapy is shown to be dependent on daily pollen counts [27].

Historically, pollen monitoring referred to counting under a microscope using Hirst pollen traps, one of the first and most traditional methods. The first Hirst pollen traps were made to estimate the exposure of pollen in the air for the development of treatment. The first station that holds a continuous pollen record, from Cardiff in the UK, utilized a Hirst pollen trap since 1954. Hirst pollen traps samples from airborne pollen particles that are fixed to a slide and require human operators to manually count the number of pollen under the microscope. [28] This method is time-consuming and labor-intensive which fails to provide up-to-date information with a reasonable margin of error. However, Hirst traps serve as the foundation for advancing monitors that better assure consistency and regularity [29].

In the past decade, automatic pollen monitors were proposed and developed using different technologies. In 2018, an inventory presented a total of 879 running pollen traps around the world,

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majorly Hirst method-based, with more than half accounted for in Europe, coupled with automatic monitors mostly found in Japan [28]. Pollen metabarcoding is one of the automatic monitoring approaches by which qualitative (pollen types) and quantitative (pollen counts) analysis can be achieved at the same time by identifying DNA sequences in a large-scale sample of different pollen types. However, test trials still indicate the presence of negative and false results as the barcode may generate gaps depending on the sample size [30]. The BAA500 developed in Munich, Germany, is an automatic monitor system based on image recognition and analysis. Using a sample of more than 480, 000 particles, the performance of the BAA500 automatic system was assessed, which accurately identified 93.3% of the pollen in the sample, but 27.8% of the pollen in the test sample was only identified manually. The image-analysis monitors are also largely based on adhesive surfaces like the Hirst pollen traps, indicating that real-time information could not be provided easily [31]. Aiming to achieve real-time monitoring, the successful uses of laser optics technology in other fields were brought to attention in Japan. Monitors utilizing laser optics were developed to provide automatic and simultaneous information by an algorithm that created the ideal region of each pollen type using scatter plots and scattering of laser lights. Yet, this method fails to identify pollen counts when more than one pollen taxa is present [32]. Overall, although there may be uncertainties, automated pollen counting has great potential for more accessible online reporting and enhancing monitors.

5. Conclusion

Allergic disorders triggered by pollen present a significant health issue worldwide as it affects millions of people worldwide. However, as pollen allergy continues to be potentially more impactful through changing environmental conditions, treatment and monitoring approaches should be further improved to benefit patients experiencing pollen allergy.

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