Evidence for Self-Medication
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Allergic Rhinitis and air pollution: New clinical evidence with fexofenadine hydrochloride 180 mg

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Exposure to air pollutants and climate change are contributing factors of increasing prevalence and allergic rhinitis (AR) symptom exacerbation. Fexofenadine 180 mg has been shown effective in relieving pollen-induced air pollution-aggravated AR symptoms in a randomized, controlled clinical trial (FEXPOLSAR study) using a recognized and validated controlled allergen challenge model of AR.

Worldwide, between 10 to 30% of the population is affected by allergic rhinitis (AR) [1]. The prevalence of confirmed AR in adults in Europe range from 17% to 28.5% [2].

Allergic rhinitis is an inflammation of the nasal mucosa in response to airborne allergens such as pollen or house dust mites. Leading symptoms include sneezing, nasal itching, nasal obstruction, runny nose with clear secretion and other non-nasal symptoms such as red, itchy and watery eyes.
In recent decades, air pollution has been associated with an increased incidence of AR worldwide. Diesel Exhaust Particulate (DEP) is an essential component of air pollutants. They can interact with allergens and worsen the allergic reaction [3]. DEP particles infiltrate airway epithelial cells, inducing inflammation and cytotoxicity [4]. In addition, it has been observed that the interaction of DEP with allergens can enhance allergen induced responses, up to 50-times more than allergens alone [5].

Fexofenadine new evidence in AR symptoms aggravated by DEP

Fexofenadine HCl is a non-sedating, second-generation selective histamine H1-receptor antagonist indicated for the symptomatic treatment of seasonal AR and chronic idiopathic urticaria. Its long half-life allows a once daily intake [6]. It is marketed worldwide in about 100 countries, the approved daily dose in Europe is 120 mg or 180 mg.

Recently Ellis et al. [7] published the results of the first large study (FEXPOLSAR/NCT03664882) to demonstrate the beneficial effect of fexofenadine in reducing the symptoms of AR aggravated by air pollutant. This was a prospective, sequential, double-blind, randomized, phase 3 study, using a recognized and validated controlled allergen challenge model of AR where allergen exposure is controlled, and symptoms can be continuously monitored [7, 8].

The primary objective of the study was to demonstrate the aggravation of the AR symptoms caused by DEP.

The second primary objective was to evaluate the efficacy of fexofenadine HCl 180 mg in alleviating symptoms aggravated by DEP presence.

The study was conducted outside the pollen season in three study periods in an environmental exposure unit. A total of 257 adults were exposed to ragweed pollen in the first period of the study and, after a 2-weeks wash-out, they were re-exposed to ragweed pollen and DEP. In the treatment period of the study, 251 remaining participants were exposed again to ragweed pollen and DEP and randomized to receive fexofenadine HCl 180 mg as a single dose (n = 26), or placebo (n = 125).

Their allergic rhinitis symptoms (i.e. runny nose, sneezing, itchy nose, nasal congestion) were scored up to 12 hours. Primary endpoints were the area under the curve (AUC) of the TNSS (total nasal symptom score: sum of runny nose, sneezing, itchy nose) from basal to twelve hours (AUC_{0-12}) in periods 1 and 2, and from two to twelve hours (AUC_{2-12}) in the treatment period 3.

Looking at the first two periods of the study, a significant increase in TNSS AUC was seen in subjects exposed to

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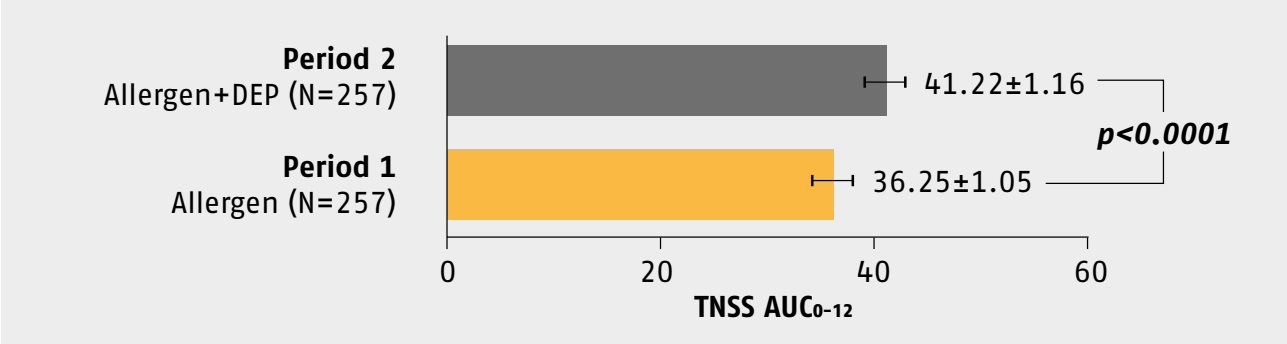

Fig. 1. Symptoms of allergic rhinitis due to ragweed pollen were significantly stronger with the simultaneous presence of DEP. Adapted from Ellis et al., 2021 [7].

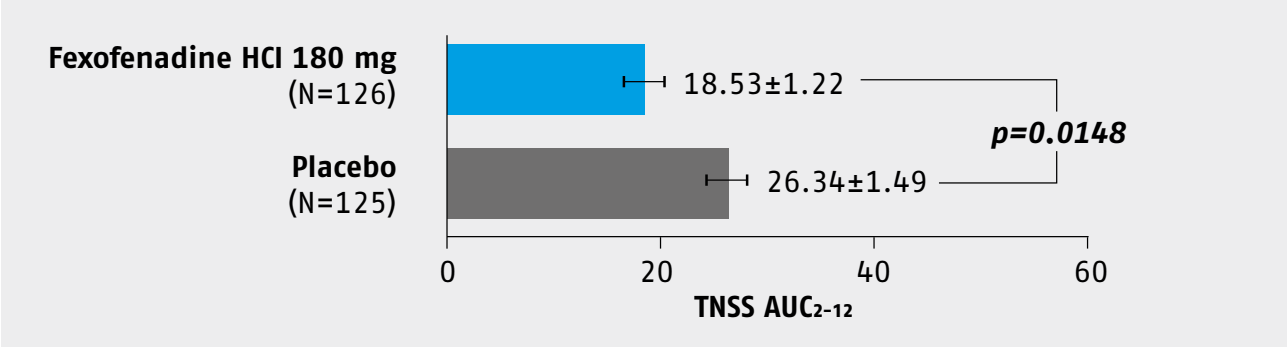

Fig. 2. The fexofenadine group showed significantly fewer symptoms of allergic rhinitis than the placebo group after allergen exposure with the simultaneous presence of DEP. Adapted from Ellis et al., 2021 [7].

both ragweed pollen (allergen) and DEP compared to those exposed to ragweed pollen alone (**Fig. 1**, $p < 0.0001$). In the third period of the study, fexofenadine HCl 180 mg significantly reduced the air pollutant-aggravated AR symptoms compared to patients receiving placebo ($p = 0.0148$) (**Fig. 2**). The mean percent symptoms reduction compared to placebo related to the individual symptoms was as follows: sneezing (39.2%), rhinorrhoea (28.8%), watery eyes (27.5%), blocked nose and red or burning eyes (24.8%), nasal itching and itchy eyes (23.0%), ear, palate or throat itching (18.6%).

Summary

Allergic Rhinitis sufferers want a quick relief of their symptoms with restoration of their usual daily life and work productivity. Second-generation non-sedating oral antihistamines are recommended in the treatment of AR [9]. Rapid onset of action in improving SAR symptoms has been observed with once daily administration of fexofenadine-HCl [10].

Air pollutants such as DEP can aggravate AR symptoms [5]. Fexofenadine-HCl 180 mg showed an improvement of SAR symptoms aggravated by DEP. Sneezing is particularly reduced, important for AR sufferers during the COVID-19 pandemic for when early mild COVID-19 symptoms may be confused with or co-occurrent with AR and, as uncontrolled hay fever may increase the risk of viral dissemination[11].

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