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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Untreated allergic rhinitis is a major risk factor contributing to motorcar accidents

To the Editor,

Allergic rhinitis is a common allergic disease with increasing prevalence, recent estimates suggesting an incidence in excess of 30% of individuals in the European Union.^{1,2} While often trivialized, allergic rhinitis is crucially linked to impairments in information processing and changes in attention-related cognitive processes.³ This has a measurable impact on performance at work or school but an under-investigated implication is the effect of untreated allergic rhinitis on driving motor vehicles.

A recent study has assessed the effect of nasal provocation of seasonal allergic patients on driving performance.⁴ The results showed that when individuals were symptomatic and untreated, their driving ability was significantly impaired. When engaging in a secondary memory task during driving, their performance deteriorated further. The magnitude of impairment was relevant and comparable to that seen with a blood alcohol level of 0.5%, the legal limit in many countries.⁴

While this is an excellent clinical study, it does not necessarily represent the real-life situation in chronic disease where sleep disturbances may exacerbate impairment of psychomotor performance, including driving.⁵⁻⁷ We now present the results of a real-life survey of 513 regular car drivers with seasonal allergic rhinitis on the effect of their disease on their ability to drive and the measurements they took to reduce the possibility of accidents.

Initiated and funded by the company autoscout24, Berlin, Germany, a nationwide survey was performed in Germany involving a representative sample of 513 regular car drivers who suffered from seasonal allergic rhinitis. The group comprised 262 males and 251 females between the ages of 18 and 65. The drivers were asked three questions by trained interviewers by telephone. In the questions, rather than using the term seasonal allergic rhinitis, the German term "hay fever" was used, which is the commonly known term in that country. In addition to counting the number of respondents for each answer, the replies were divided into sex and into age groups 18-29, 30-39, 40-49 and 50-65 years.

The first question asked was "Do you think that hay fever impairs your ability to drive?" More than three quarters of the respondents said that it did with 13% saying that it is sometimes so

bad that they have to refrain from driving (Figure 1). There was no significant sex or age difference between the answers.

The second question asked was "Have you ever had an accident attributed to your hay fever or have you ever experienced a near-accident situation which can be attributed to this?" To this question, 36 respondents (7%) replied yes, they had. Interestingly, approximately twice as many men than women and twice as many respondents under rather than over 40 years old responded yes to this question.

The third question asked was "What measures do you take to relieve your hay fever symptoms while driving?" Multiple answers were allowed here. The results (Figure 2) showed that while the majority (57%) of respondents kept the windows and roof closed while driving, it is surprising that less than half took anti-allergic drugs, such as H₁-antihistamines, or turned the air conditioning to recirculating before driving. Furthermore, 46 respondents (9%) did nothing to relieve their hay fever symptoms before driving. The only sex difference in these answers was that more men than women equipped their car with a pollen filter. With regard to age, fewer of the younger age group kept their windows and roof closed or equipped their car with a pollen filter than the other age groups. However, this younger age group were more likely to take anti-allergic drugs than their older counterparts.

The primary findings of this survey are that more than three quarters of the individuals with seasonal allergic rhinitis interviewed replied that their disease bothered them when driving and 7% stated their disease had contributed to an accident or near-accident situation. However, less than half took drug therapy to relieve their symptoms before driving.

The figure of 7% of the respondents reporting an accident or near-accident situation may seem small, but is it? Approximately 60% of the 500 million people living in the European Union hold a valid driving licence.⁸ If it is assumed that around one-third of these 300 million citizens has seasonal allergic rhinitis then that gives a figure approximately 7 000 000 accidents or near accidents. All of these could have been prevented by appropriate treatment as detailed in the ARIA guidelines.⁹

Almost as disturbing is that 60% of respondents failed to take pharmacotherapy to relieve their symptoms before driving. This is

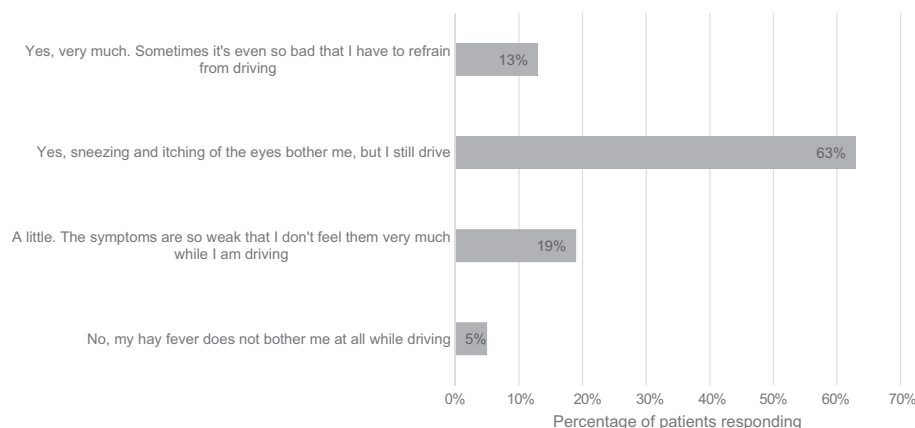


FIGURE 1 Do you think that hay fever impairs your ability to drive?

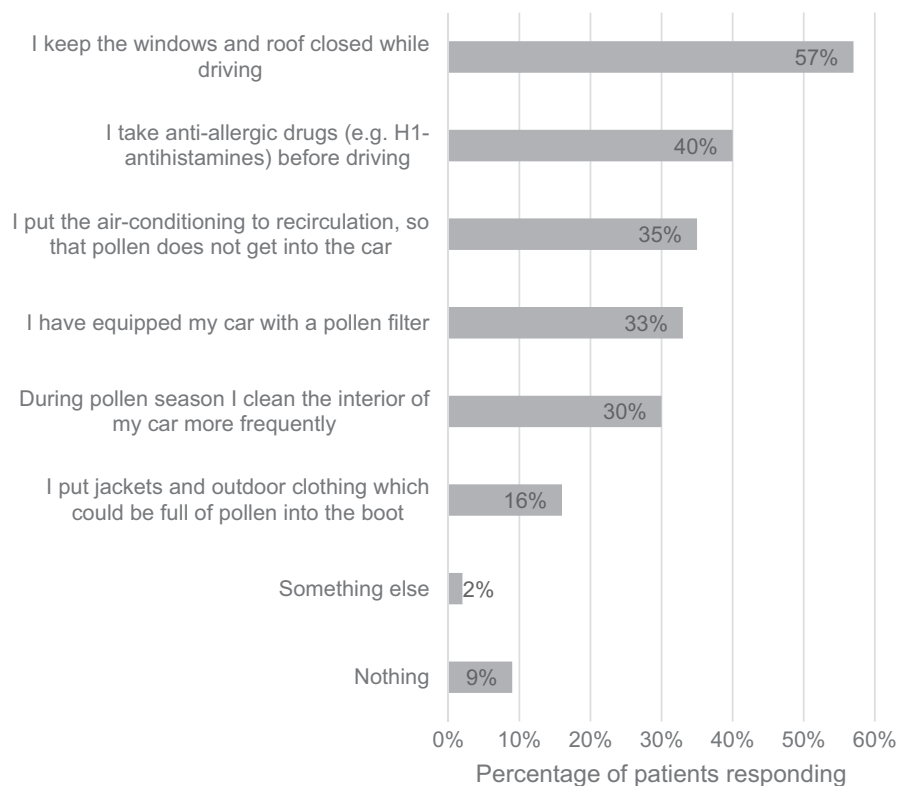


FIGURE 2 What measures do you take to relieve your hay fever symptoms before or while driving?

consistent with the report of Zuberbier et al¹ that up to 90% of allergic persons are untreated or insufficiently treated. Even in the absence of regular therapy, a single dose of a second generation H₁-antihistamine (cetirizine) 45 minutes before allergen provocation and 2 hours before a simulated driving test was sufficient has been shown to be sufficient to restore driving ability.⁴

In conclusion, more than three quarters of the individuals with seasonal allergic rhinitis are bothered by their symptoms when driving and 7% stated their disease had contributed to an accident or near-accident situation. However, less than half took drug therapy to relieve their symptoms before driving.

The data presented here show an association between allergic rhinitis symptoms and the ability to drive in a real-life study. This study design allows to represent the real-life situation of patients but since it has its weaknesses, prospective controlled studies

regarding this association are desirable and should also be considered in areas of governmental funding as accidents have a high relevance in society.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

Keywords

allergy treatment, epidemiology, prevention, quality-of-life, rhinitis

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Effect of sex on group 2 innate lymphoid cells in the airways of mild and severe asthmatics

To the Editor,

Asthma is predominately observed in males in childhood but during and after puberty there is a shift favoring females.¹ Consequently, sex hormones have been implicated in the pathogenesis of asthma. Group 2 innate lymphoid cells (ILC2s) are critical modulators of allergic asthma, secreting large quantities of type 2 cytokines, interleukin 5 (IL-5), and interleukin 13 (IL-13).² Greater numbers of lung-extracted ILC2s are found in female compared to male allergen-sensitized mice.³ Testosterone upregulates ILC2 expression of killer cell lectin-like receptor G1 (KLRG1) that binds to E-cadherin inhibiting cell proliferation and activation.^{3,4} Additionally, androgen signaling downregulates CD25, an important ILC2 proliferation signal.⁵ Androgen-dependent regulation of ILC2s may mediate differences in asthma prevalence and severity between the sexes.

In a retrospective study of consenting adult mild atopic asthmatics (MA) and severe eosinophilic asthmatics (SA), we assessed the effect of sex on sputum and blood levels of canonical type-2 cells, ILC2s, and CD4+ T lymphocytes. We included nonsmoking MA (n = 38 [15 male, 23 female], FEV₁ ≥ 80% predicted, methacholine

PC₂₀ ≤ 16 mg/mL, dual-phase response to whole lung allergen challenge, intermittent β₂ agonist use) and SA (n = 30 [13 male, 17 female], FEV₁ < 80% predicted, methacholine PC₂₀ ≤ 8 mg/mL, sputum eosinophilia > 3%, mean ICS/LABA > 880 µg/day; mean prednisone > 7.5 mg/day). Blood and sputum were collected at baseline for all asthmatics and sputum at 24 hours postallergen, for a subgroup of MA (n = 19) (Table S1). By flow cytometry, we gated on ILC2 and CD4+ T cells phenotypes that are upregulated in eosinophilic asthmatic responses within the airways (Figure S1).⁶ Procedures were reviewed and approved by the institutional ethics board. See Data S1 for methodological details.

For MA, all demographic characteristics were comparable between the sexes except for BMI, which was higher in males. Both sexes demonstrated similar allergen-induced changes in FEV₁, methacholine airway hyperresponsiveness, total leukocyte counts, and sputum eosinophilia (Table S2). At baseline, we found significantly higher absolute ILC2 numbers in sputum from females compared to male with MA (Figure 1A). When expressed as a percentage of CD45+ cells, the between-sex difference in total ILC2s was lost (Figure S2A). No significant sex differences in type 2 cytokine-positive sputum ILC2s (Figure 1B-D) or blood ILC2s (Figure 1E-H) were found at baseline. Total sputum ILC2 numbers in all MA increased significantly 24 postallergen (Figure 1I) but no significant sex

Abbreviations: BMI, body mass index; EAR, early asthmatic response; FEV₁, forced expiratory volume in one-second; ICS, inhaled corticosteroid; ILC2, type 2 innate lymphoid cell; IL, interleukin; LABA, long-acting beta agonist; LAR, late asthmatic response; MA, mild asthmatic; Methacholine PC₂₀, provocative concentration of methacholine inducing a 20% fall in FEV₁; SA, severe asthmatic; TCC, total cell count.