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First comparison of symptom data with allergen content (Bet v 1 and Phl p 5 measurements) and pollen data from four European regions during 2009–2011

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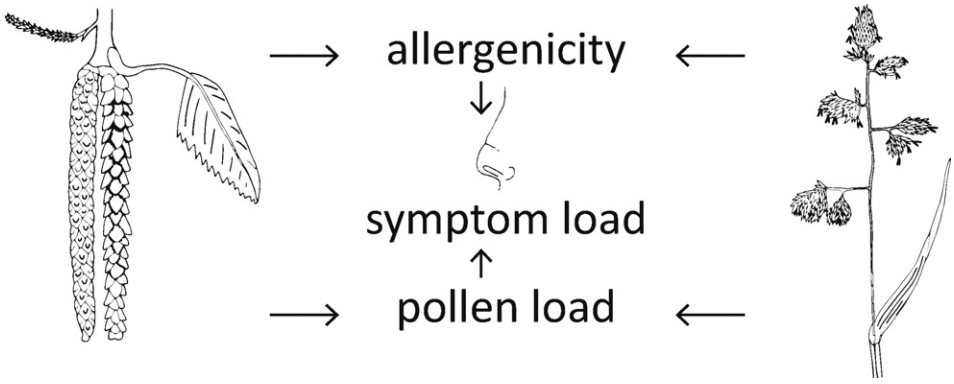
HIGHLIGHTS

- Allergen content is currently a main suspect for having a direct impact on symptoms.
- Measurements of main allergens (Bet v 1/Phl p 5) explain peaks in the symptom load.
- A direct pattern between the symptom level and the allergen content was not found.
- A focus on the development and onset of allergy symptoms is needed in monitoring.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: The level of symptoms in pollen allergy sufferers and users of the Patient's Hayfever Diary (PHD), does not directly reflect the total amount of pollen in the air. It is necessary to explain the symptom load and thus the development of allergic symptoms and to determine which environmental factors, besides the pollen load, influence variables. It seems reasonable to suspect allergen content because the amount of allergen varies throughout seasons and regions and is not always correlated with the total pollen amount.
Methods: Data on the allergen content of ambient air (Bet v 1 and Phl p 5) from 2009 until 2011 was used to compare the respective pollen and symptom loads for study regions in Austria, Germany, France and Finland.
Results: Our findings suggest that allergen amount (Bet v 1/Phl p 5) has a strong but regionally dependent impact on the symptom load of pollen allergy sufferers. Peak symptom loads can be traced with peak allergen loads. The influence of other important aeroallergens should also be assessed during the pollen season.

Abbreviations: HIALINE, EU-funded project called Health Impacts of Airborne Allergen Information Network; IgE, immunoglobulins E; PHD, Patient's Hayfever Diary; SLI, symptom load index.

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Patient's Hayfever Diary
Phl p 5
Symptom load index

Conclusion: Allergen concentrations have an impact on pollen allergy sufferers although not as clear as assumed previously. The pattern of pollen load and major allergen content distribution does not directly explain the symptom load pattern, although significant positive correlations were found. Thus, monitoring of symptoms via voluntary crowdsourcing should be considered for future pollen and symptom forecasts in order to support pollen allergy sufferers.

1. Introduction

In order to ease the burden of pollen allergy sufferers basic research is required as well as an in-depth understanding of vegetation, plant distribution, environmental pollution, aerobiology especially related to pollen information based on pollen counts. As an example, exact thresholds for a certain regional population to develop allergic symptoms (either in pollen grains per m^3 air or in allergen content in pg/m^3) were not determined (e.g. De Weger et al., 2013) and it is not known which factors are causing the diversity in the symptom levels throughout the pollen season in people affected. The history of pollen allergy has been studded with "why" questions from the very beginning. Bostock (1819) described the symptoms of pollen allergy, but was not aware of the causal agent and Blackley (1873) skin-pricked his own arm to recognize pollen as the cause of allergic symptoms. Since then innovations in various fields, including medicine, aerobiology, pollen information and molecular biology, have led to a growth of valuable knowledge for pollen allergy sufferers. Recent findings (Bastl et al., 2014; Buters et al., 2012) indicate the need for more extensive pollen information to support and optimize allergen avoidance, as it has been shown that daily pollen concentrations neither match perfectly with the symptom load of pollen allergy sufferers, nor with allergen content in the air. Up to now there is no answer to the question what the main determinant of the onset and development of allergic symptoms in pollen allergy sufferers really is. Allergen content is currently the main suspect as one of the factors causing the most impact (Brito et al., 2011). The nomenclature for allergen proteins follow the species' latin genus and species name (Phl p for *Phleum pratense*) as well as the sequence of their discover (e.g. Phl p 5 for the 5th discovered allergen of *P. pratense*). As far as we know allergen content is variable from pollen grain to pollen grain even within a taxon, e.g. birch pollen (Buters et al., 2012) and not proceeding synchronous with daily pollen concentrations (Buters et al., 2012, 2015). This is due to the fact that pollen allergens can also be present as small airborne respirable particles (Spieksma et al., 1995; Schäppi et al., 1997, 1999) and depend on pollen ripening (Buters et al., 2010). Furthermore, the pollen concentrations are not synchronous with the discomfort of pollen allergy sufferers (Bastl et al., 2014). Concluding it has to be tested whether allergen content (herein Bet v 1/Phl p 5) could be the main determinant of the symptom load. Hence, the aim of this study is to compare the measured allergen content (Bet v 1/Phl p 5) in four different regions of Europe within a retrospective study and to compare this data to the symptom load of pollen allergy sufferers during the respective pollination period in those regions to assess their relationship.

2. Material and methods

2.1. Allergen content

This retrospective study uses Bet v 1 and Phl p 5 measurements of four countries (Austria, Germany, France and Finland), which took part in the HIALINE study during the period of 2009 to 2011 (Buters et al., 2015, 2012). The values obtained were used for comparison with symptom data in the study presented here. The procedure of allergen measurement of Bet v 1 and Phl p 5 is described in detail in Buters et al. (2010, 2012, 2015). The Bet v 1 and Phl p 5 air content values derive from the pollen grains trapped in the Chemvol® sampler and were measured as pg/m^3 (Buters et al., 2012). The HIALINE study (Buters et al., 2012, 2015) only indirectly tested whether free allergen (D'Amato et al., 2008), apart from that encapsulated in the pollen grains, was present in the air and only focused on one major allergen protein per pollen type. The term "allergen content" is thus used in this work as in former works (Buters et al., 2010, 2012, 2015) and refers to Bet v 1 and Phl p 5. Hence, it does not mean the whole content of possible allergens (major and minor allergens, free and encapsulated) in the air.

2.2. Symptom data

The Patient's Hayfever Diary (PHD) provided symptom data for this study. This free online web-based tool has also been available as the "pollen app" since 2013 in some countries (Austria, Germany; Kmenta et al., 2014) and is a highly practicable tool for both scientists and pollen allergy sufferers (e.g. Bastl et al., 2014; Karatzas et al., 2013; Kmenta et al., 2014; Voukantsis et al., 2013). Its wide distribution in several European countries, as well as the growing number of users every year, provide a large and valuable dataset concerning pollen allergy symptoms (e.g. Bastl et al., 2014). We used the methodology described in Bastl et al. (2014) to calculate the symptom load index (SLI) based on the PHD symptom data for each study region during 2009–2011. This includes normalizing the data to come to an alternated symptom score ranging from a minimum of 0 to a maximum of 10. In the following, the average symptom score is calculated for the respective season in the respective region. The whole PHD data for each country was not used, only the data from the region where the allergen measurements were performed following the regional definitions in EAN and the PHD (Austria: Pannonian lowlands; Germany: Allgäu, Oberbayern, Bayrischer Wald; France: Rhône-Alpes; Finland: southern Finland). This procedure avoids a levelling of the results. The birch or grass pollen season was also calculated based on local pollen data, namely the centre of allergen measurement (Vienna, Lyon, Turku, Munich). We assume that the allergen content is representative for the region, as the pollen concentrations are, and we thus confirm that the period of the respective pollen seasons is used as the basic reference due to their pre- and post-season availability to summarize the allergen measurement values during the season and the SLI calculation during the very same defined pollen season within the region. Datasets (daily symptom reports) and PHD user numbers vary per year and are still on the rise (Table 1). Over all regions, seasons and years, we used the data from 4115 users and their 65,250 datasets for analysis. The detailed breakdown per pollen season and year is listed respective of the region, together with the time period chosen in Table 1. Results are listed in Table 2 together with the sum of allergen content during the pollen seasons 2009–2011. PHD symptom datasets have already proven to give relevant and stable insight into the allergenic burden of a population on a national, regional and local level (Bastl et al., 2015b). This is also true when applied during a short pollen season with only a minor fraction of the population affected (Bastl et al., 2015a).

2.3. Data presentation

Note that allergen measurements were not performed in Austria in 2009, and therefore no symptom and pollen data was retrieved for this year. The sample size of the symptom data was too small in 2009 for some regions, since the PHD was introduced in that year and was