Personalized pollen monitoring and hay fever symptom scores: a feasibility study

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Research

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Abstract

Background. Pollen is a major trigger for allergic symptoms in sensitized individuals. Airborne pollen is usually monitored by Hirst type pollen samplers located at rooftop level, providing a general overview of the pollen distribution in the larger surroundings. In this feasibility study, grass pollen-sensitized subjects monitored the pollen in their direct environment using a portable pollen sampler (Pollensniffer) and scored their symptoms, to study the relation between symptom severity and personal grass pollen exposure. For comparison the symptoms were also correlated with pollen collected by the rooftop sampler.

Methods. Nine grass pollen-sensitized individuals were enrolled in this study (May 2018) and asked to monitor personal pollen exposure using a Pollensniffer on their way to school, work or other destination, and to score their symptoms via a mobile app on a scale from 0 to 10. Daily pollen concentrations were collected by a Hirst type sampler at rooftop level. Pollen grains were analysed using a microscope.

Results. Three of the four participants with high grass pollen-specific (GPS) IgE (>9.6 kU/l) reported high symptom scores (>4) and an analysis showed a significant correlation (CC) between eye, nose and lung symptoms and the grass pollen counts collected by the Pollensniffer, as well as the daily grass pollen concentrations monitored by the rooftop sampler (CC≥0.54). In contrast, the participants with low GPS IgE levels (<9.6 kU/l) reported low symptom scores (≤4) and often other sensitizations were present. For these subjects, no significant positive correlations (CC<0.3) of symptoms with either grass pollen collected by the personal or the rooftop sampler were found.

Conclusion. Our results show that correlations between the severity of clinical symptoms of grass pollen allergic patients, and airborne grass pollen counts as determined by a personal pollen sampler (Pollensniffer) or a rooftop sampler, is restricted to patients with high GPS IgE levels, high symptom scores and no relevant other sensitizations. Based on the number of subjects included in this feasibility study, no conclusions can be drawn on the performance of the personal pollen sampler in relating symptoms and pollen exposure in comparison with the rooftop sampler.

Trial registration

The study was approved by the Committee Medical Ethics of the LUMC (approval numbers: NL63953.058.17/ P17.304).

Introduction

Late spring and summer is the period that 33 % of the European allergic population suffers from symptoms of hay fever due to grass pollen exposure (1). Grasses are present all over the world and grass pollen is one of the most important sources of allergens causing hay fever symptoms such as rhinorrhea, blocked or itchy nose, itchy or tearing eyes, and cough. Hay fever symptoms can be mild but may also have a great impact on the daily life of patients, as demonstrated e.g. by studies in adolescents
showing reduced school performance and academic achievements in symptomatic subjects (2, 3). In addition to these known effects, a new hay fever-associated phenomenon appeared in 2020, when it became apparent that some symptoms of hay fever, like rhinorrhoea, nasal obstruction and cough, were easily misjudged as symptoms of COVID-19, leading to unnecessary anxiety in hay fever patients. Informing patients when and which pollen are present in the air will help them better recognizing their symptoms as hay fever symptoms.

In Europe, a network of more than 500 stations monitor the daily airborne pollen concentrations (4). Information on how many and what type of pollen is in the air is relevant for patients, patient care and research (5). Pollen samplers used for these monitoring purposes are often located on top of buildings at a height of approximately 20-30 m. Rojo et al. (6) showed that measurements at these rooftop heights were representative for pollen concentrations at near ground. Various studies demonstrated a relationship between the overall symptom scores and pollen levels monitored by stationary samplers located at rooftop (7, 8). In a recent study, we used a mobile pollen sampler to demonstrate that pollen exposure can differ significantly from one location in a city to another (9). These findings underline the notion that allergic subjects will encounter variable pollen concentrations on their way to e.g. school or work, which may explain discrepancies between the pollen measured by the pollen monitoring station and the symptom severity experienced by patients. Therefore, especially personal sampling in the immediate environment of the patient would contribute to understanding symptom development.

Such a personal sampling approach was also found to be useful in other circumstances, as illustrated by the two cases described by Fiorina et al (9). This study showed that for two allergic patients, who could not clearly be diagnosed by skin prick tests, the responsible allergen was identified by personal sampling in the environment of these patients.

Recently, we described a portable sampler, the Pollensniffer (10), that can be conveniently used to monitor pollen at different locations including the immediate environment of a patient. This Pollensniffer was used to study the variable pollen concentrations at street level in a city (10). In the present study, we aimed to investigate whether pollen grains collected by the Pollensniffer in the immediate environment of the grass pollen allergic individuals are related to their symptoms, and to compare this relationship to that between symptoms and daily pollen concentrations monitored by conventional stationary rooftop samplers.

**Methods**

**Participants**

Participants were recruited in March and April 2018 using social media and posters in the region of Leiden. Fifty-five individuals responded and 18 individuals living in the region of Leiden were invited for a 1st visit (Figure 1). Living within 30 km of the Leiden University Medical Center (LUMC) was relevant to compare the symptom scores with the daily pollen concentrations assessed using a rooftop sampler at
the LUMC. Three individuals were excluded due to one or more of the following exclusion criteria: 1) a clinically relevant pet allergy and the very pet at home; (2) immunotherapy, currently or within the last five years; (3) daily use of inhaled corticosteroids for asthma; (4) daily use of oral corticosteroids; (5) pregnant or breast feeding; (6) chronically blocked nose; (7) other significant disease (e.g. severe cardiovascular or pulmonary disease, malignancy or autoimmune diseases), where significant is defined as any disease that in the opinion of the investigator would put the safety of the subject at risk by participation. After signing an informed consent, fifteen individuals provided venous blood samples and the serum levels of allergen-specific immunoglobulin E (IgE) were determined by ImmunoCAP (Thermo Scientific, the Netherlands) using a panel of allergens: grass (gX1); birch (t3); mugwort (w6) house dust mite (d1); fungi (mx1); dog (e5); cat (e1). Three individuals appeared to be negative for grass pollen (<0.34 kU/L) and were excluded; the remaining twelve grass pollen IgE positive individuals were included in the study.

The study was approved by the Medical Ethics Committee of the LUMC (approval numbers: NL63953.058.17/ P17.304). All participants provided written consent after receiving a verbal and written explanation of the study.

Study design

Following inclusion, participants were provided with a subject number (S01-S18) and they received instructions on how to use the mobile application (see later) and the Pollensniffer, either by holding the device in their hand when going on foot, or by mounting the device on their bicycle. The participants were asked to perform the measurements on their first walk or bicycle tour of the day, for instance on their way to work or school during the total time they were outside (exposure time) and to score their symptoms with the mobile application within the next 3 hours after collecting pollen. Since the route to school or work varied for each participant, the monitoring time was also different. The sample slides containing the pollen were stored. The participants were asked to collect pollen and score symptoms during 14 days within the next month starting on May 26. The daily pollen concentrations collected at rooftop level in that period are shown in Figure 2. Participants were asked not to use any medication for their allergic symptoms, starting three days before the first measurement. During the study period the participants could contact the clinical research unit for questions or problems. In two cases, the Pollensniffers required small adjustments during use and three participants had issues with the sample slides. After the study period, the participants returned the Pollensniffers and their sample slides.

Mobile phone application. An application for mobile phones was developed on which users could log in via a personal password, which was linked to their subject number. Users could score their symptoms of eyes, nose and lungs on a scale of 0-10. Upon entering the scores, both location and time were recorded. The data were anonymously stored on a local server.

Collection of symptoms- and pollen data
Symptom scores were extracted from the server when all symptom scores were submitted (June 20th, 2018). In the Pollensniffer, pollen grains were collected on a Melinex strip covered with Vaseline. The strip was stained with a safranin solution (0.002 % w/v) and mounted on a microscopic slide and differential pollen counts were obtained using microscopy (10).

For the daily pollen concentrations, the microscopic slides from the Hirst type sampler (rooftop level counts) were scanned using the microscope in three longitudinal bands corresponding to 1 m\(^3\) collected air in 24 h, to obtain daily concentrations (11).

Data analysis

A Shapiro-Wilk test showed that the pollen data from the Pollensniffer or from the Hirst type sampler on the roof were not normally distributed. After log-transformation, the pollen data were normally distributed. Pearson correlations coefficients were calculated between the log-transformed pollen data and the individual eye, nose and lung symptom scores of the participants. The grass pollen-specific (GPS) IgE levels of the participants were not normally distributed and thus the geometric mean of the IgE levels was determined instead of the arrhythmic mean.

All statistical analyses were performed using the statistical software package STATA 14.2 (StataCorp, TX, USA).

Results

Participant description

The age of the participants varied between 19 to 56 yr. The group consisted of 3 males and 9 females. The first day of the study period appeared to be a day with very high grass pollen counts (Figure 2) and three participants decided to leave the study since they could not meet the criterium not to use medication; 2 males and 7 females completed the study. The GPS IgE levels in the serum of these patients varied between 1.4 to 93 kU/L with a geometric mean of 9.6 (Table 1).

Collection of pollen

Since the participants were asked to collect the pollen on their way to school or work during the time they were outside, the collection time varied for the different samples in a range from 15-40 minutes. The participants were asked to collect pollen on 14 different days spread over the 4 weeks (May 28\(^{th}\) and June 20\(^{th}\), 2018). Most participants (6) collected pollen for 14 days or more, while some (3) participants could only collect pollen during 9, 11 or 13 days. Most samples were collected on a bicycle (Table2). The range of pollen collected by the participants varied hugely; the lowest number of pollen grains was 2 and the highest number 4017 pollen grains (Table 2).

Participants S03 and S16 had some minor incidents handling 2 and 3 slides, respectively, and participants S04 had an incident with the sampling box which may have affected the integrity of the
sample slides. All these slides were microscopically analysed, and although no discrepancies with the other slides was observed, there may be a chance that the number of pollen grains on the slides was affected by the incidents (see also later).

In all Pollensniffer samples, grass pollen was by far the most numerous pollen type. Other allergenic pollen types, like tree pollen, birch, alder, ash or oak, never exceeded 1% of the number of grass pollen. Weed pollen, such as sorrel, plantain or mugwort, never exceeded 5% of the number of grass pollen in the samples.

**Correlation between symptoms and pollen collected by Pollensniffer**

In a first analysis, we found significant correlation between either one of the clinical symptom scores and the pollen count in the Pollensniffer samples for only three participants. We noticed that these 3 participants were the ones with the higher GPS IgE levels and the higher symptom scores. Based on this observation, the participants were split into 2 groups, according to their GPS IgE levels. Since the IgE levels were not normally distributed we took the geometric mean of the GPS IgE levels to divide the participants into group 1 (GPS IgE levels > 9.6 kU/L) and group 2 (£ 9.6 kU/L) (Table 1). The different symptoms were correlated with the pollen collected by the participants. Three of the four participants (S01, S06 and S15) from group 1 (high GPS IgE levels) showed a significant correlation (Figure 3 and Table 3) for one (S01 and S15) or two (S06) types of symptoms. These participants had no other sensitizations or other sensitizations with low specific IgE levels (Table 1), and their range of symptom scores was large (from 0 to > 5). The scatter plot of results from participant S07 (Figure 3, Table 3) showed a non-significant moderate correlation for lung symptoms; some data points correlated by increasing symptoms with increasing number of pollen collected, but other data points show a 0-score for the symptoms when relative high numbers of pollen were collected (Figure 3).

The five participants in group 2 (low GPS IgE levels) showed moderate, none or even negative correlation and between the symptoms and the pollen collected (Figure 3 and Table 3). Participant S04 showed a moderate positive correlation. Participants S16 and S03 both had incidents with 2 or 3 slides but leaving out the data points belonging to those slides did not significantly alter the outcome of the analysis. These participants had very low IgE levels to grass pollen and their symptom scores were low (< 2). Participant S14 submitted the symptom scores during the evening and may have scored the symptoms over the whole day and not directly after exposure during the sampling. Participant S18 showed no or negative correlations with all types of symptoms. This participant had relatively high IgE level towards house dust mite and trees. Furthermore, this participant had received grass pollen immunotherapy more than 10 years ago. These conditions might have affected the relation between grass pollen and symptoms.

These results show correlations between the severity of symptoms and the personal grass pollen exposure especially in patients with high GPS IgE levels, high symptom scores and no other relevant sensitisations.

**Correlation between clinical symptoms and daily pollen concentrations at rooftop level**
We next investigated the relationship between these symptom scores and the pollen counts derived from the nearby local pollen monitoring station collected at rooftop level at the LUMC. Significant positive correlations between symptom scores and daily pollen counts were found in the group with the high GPS IgE levels (group 1, Table 4). For participants S01 and S15 the same type of symptoms, that correlated significantly with the Pollensniffer pollen counts, showed a significant correlation with the daily rooftop pollen concentrations. Participant S06, that showed significant correlations for lung and nose symptoms with the pollen collected by the Pollensniffer, did not show a significant correlation for any type of symptoms with the daily pollen counts at rooftop level. In contrast, symptoms of participant S07, which showed only non-significant moderate correlation with the Pollensniffer pollen counts, correlated for lung symptoms significantly with the daily rooftop pollen concentrations (Table 4). Two of the participants (S14 and S18) with low IgE levels even showed a significantly negative correlation with the daily pollen concentrations at rooftop level. These findings illustrate that also when using pollen counts from the rooftop sampler, correlation with symptom scores were especially found in those patients with high symptom scores, high GPS IgE levels and no other relevant sensitizations.

**Discussion**

To our knowledge, this is the first study to correlate personal exposure to outdoor pollen and the severity of allergic rhinitis symptoms in grass pollen allergic participants. In this feasibility study, nine grass pollen allergic participants were enrolled. The participants collected pollen on their first walk or bike tour during the day and the number of collected pollen was related to the symptoms developed after this activity. The time span a participant collected the pollen in the Pollensniffer varied between 15–40 min, depending on the way of transport (walking or biking) and the distance to the destination. All pollen collected during this exposure time were analysed. This set up enabled us to directly correlate the symptoms of the participants to the number of pollen grains, to which they had been exposed.

In this study, the pollen grains were collected by two types of pollen sampler. The small, portable Pollensniffer which collects pollen in the environment of the patient, and the Hirst type stationary pollen sampler on the roof of the LUMC, collecting the pollen produced in the region. In a previous study using the portable Pollensniffer for street level measurements, we showed that pollen counts at a certain time point can significantly differ at various locations in a city (10). This may be one of the reasons why the symptoms of allergic patients living in the same region differ (8). We had expected to find a better correlation between symptoms and the pollen collected with the Pollensniffer in the direct environment of the participant, than between symptoms and the pollen concentrations monitored at rooftop level. However, pollen sampled by either method showed for three out of nine participants a significant relation with the symptoms. These participants had high GPS IgE levels and often high symptom scores. The relation between high specific IgE levels and symptom severity has also been found in other studies (12, 13). A larger range in symptom scores will result in better correlation with increasing grass pollen concentrations compared to symptom scores that vary only 1 or 2 scales. Furthermore, participants in this high-level GPS IgE group did not have significant other sensitizations that might have interfered with the symptom development caused by grass pollen.
The five participants with low GPS IgE often also had sensitizations to other allergens and they showed no or even negative correlations with the Pollensniffer-derived pollen counts or daily pollen concentrations determined at rooftop level. The mild symptoms (S03) or the multiple sensitizations for e.g. house dust mite, tree pollen or cat (S04, S14 S16, and S18) may help to explain the absence of a significant relation with the grass pollen. Also, the grass pollen immunotherapy of patient S18, given more than 10 years ago, most likely still protected this participant from symptom development upon exposure to grass pollen.

The main outcome of this feasibility study is that focussing on relevant traits of patients is important when studying the relationship between symptom scores and pollen sampled in the patient’s environment. To establish such relations, it appeared to be relevant to enrol participants with high levels of GPS IgE, and thus most likely severe symptoms, and preferentially low levels of sensitizations to other allergens since these may contribute to symptom development independent of grass pollen exposure. In our participants group the number of participants with a high GPS IgE level was rather low. This was also caused by the fact that three participants with high levels of GPS IgE levels dropped out of the study, since withdrawing their medication was not possible due to the severity of their symptoms. Since it was an inclusion criterium of the study not to use medication, these participants had to leave the study. Although we aimed to study symptom development without interference of medication, we realize that this prerequisite might have hampered the inclusion of best suitable candidates. For future studies, it is recommended to reconsider this requirement and consider allowing the use of specific medication during the study period; this medication use could be added into the symptom score resulting in a combined symptom-medication score (14, 15), or used as a confounder in the analysis.

During the analysis of the pollen slides, we noticed a clear difference in size among the grass pollen grains in both the samples of the Pollensniffer as well as in the samples of the rooftop sampler (data not shown). Most likely this reflects the presence of pollen from various grass species in the samples, which may differ in allergenicity and in potential to induce symptoms. Since the routes to work or school are different for each participant, they may collect, not only different amounts of grass pollen, but also different grass pollen species with varying allergenic potential. This could influence the correlation with between the symptoms and the number of grass pollen. However, currently we cannot study this further in detail, since we cannot distinguish the different species in our microscopic analysis. Analysis by Next Generation Sequencing of the different grass species (16, 17) could be used in future studies to relate the symptoms to the number of the different grass pollen species.

In this feasibly study, the number of participants with severe symptoms was too low to draw conclusions regarding the performance of the Pollensniffer in relating symptoms to the personal pollen exposure compared to pollen monitored at roof top level. Our results indicate that it is relevant to select participants with high IgE levels, severe symptoms and no other relevant sensitizations to reveal correlations between personal pollen exposure and symptom development.

**Abbreviations**
Declarations

Ethics approval and consent to participate

The study was approved by the Medical Ethical Committee of the Leiden University Medical Center (CME # NL63953.058.17). All clinical investigations were conducted according to the principles expressed in the 1964 Helsinki declaration and its recent amendments. Written informed consent was obtained from all the participants in the study.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and analysed during the current study are not publicly available since individual privacy of the participants could be compromised, but anonymized data sets are available from the corresponding author on reasonable request.

Competing interests

All authors declare that they have no competing interests.

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Authors contributions

LdW: conceptualization, recruitment of patients, methodology, data management, analysis of data, writing original draft; PvH: patient screening, review & editing of the manuscript; MM: project management, review & editing of the manuscript, BB: patient recruitment and screening, data management, review & editing of the manuscript; FM: methodology, review & editing of the manuscript; PSH: conceptualization, supervision, review & editing of the manuscript

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