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Use of specific immunotherapy – a survey of 15,164 employed persons in Germany

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Summary

Background: The high prevalence of allergic rhinitis (AR) leads to high morbidity and costs. Specific immunotherapy (SIT) is a potentially curative therapy for AR. The decision whether or not to employ SIT is often not totally clear.

Patients and methods: In 2012/13, as part of company skin cancer screening programs, employed persons between the ages of 16–70 were asked about use of allergy-related medications and atopic conditions, as well as the use of SIT or possible reasons preventing its use.

Results: Of the 15,164 persons surveyed, 26.2% (n = 3,966) reported they had allergies that might benefit from SIT therapy. Of these, only 31.7% (n = 1,470) had undergone SIT therapy, with 63.3% (n = 931) describing the treatment as successful. The main reasons given for not undergoing SIT were relatively minor symptoms (51.2%; n = 1,278), little confidence in the success of therapy, and lack of time (12%; n = 300). Only 5.2%, n = 129) stated that avoiding allergens was sufficient or that they could not undergo SIT because of other health problems. Another 5.2% (n = 130) said they had either not heard of SIT, or had not found a place to undergo treatment.

Conclusions: Although about one-quarter of respondents reported allergies that might benefit from SIT, less than one-third had undergone treatment. The main reason was having mild symptoms; guideline or healthcare-related issues were responsible only to a limited extent.

Introduction

The prevalence of allergies is increasing in industrialized nations [1–3]. Based on current data, one-third of the German population have allergies; of these, more than half consider their allergies to be a burden [4]. Given the high prevalence of allergic rhinitis (AR) and allergic asthma, type I respiratory allergies have a significant economic impact as they lead to decreased productivity and increased absenteeism [5–7].

There are three main avenues of treatment available to the 5,000–7,500 allergy specialists in Germany:

1. Avoidance of the allergen, for instance, by reducing the house dust mite burden in one's home.
2. Symptom-oriented drug treatment, usually with non-prescription antihistamines or topical corticosteroids.
3. Specific immunotherapy (SIT).

Often also referred to as desensitization or hyposensitization, SIT is the only potentially curative treatment available

Table 1 Distribution of SIT relevant allergies.

Allergy	Frequency in percent
Grasses/grains	59.8 (CI 95% 58.2–61.3)
Early bloomers (hazelnut, alder, birch)	56.4 (CI 95% 54.8–58.0)
House dust mites	26.2 (CI 95% 24.8–27.6)
Wormwood, wall pellitory, plantain	8.5 (CI 95% 7.6–9.3)
Bee, wasp venom	2.5 (CI 95% 2.0–3.1)

for allergies. In accordance with relevant guidelines, SIT should therefore be recommended for the treatment for IgE-mediated allergies in patients for whom avoidance is impossible or inadequate, and who have no health issues preventing its use [8]. Prompt treatment is an independent factor in success and may prevent later progression of disease [9, 10]. Both sublingual and subcutaneous administration have been shown to be effective forms of treatment [11–14] and standardized preparations are now available for the most common seasonal and perennial allergens, such as early-flowering plants, grass and rye, wormwood, wall pellitory, plantain, bee and wasp venom, as well as house dust mites.

Despite the evidence of effectiveness, and the recommendation for its implementation, older data from the German National Health Interview and Examination Survey of 1998 showed that only about 11% of allergy patients had undergone SIT [15]. Patients who live in larger cities and who have a higher socio-economic status social were more likely to have undergone SIT, perhaps suggesting limited access to treatment. In addition, considering the current situation in healthcare services and the limited resources for SIT, it seems questionable whether the situation could have improved in recent years [16].

We thus conducted a survey from January 2012 to March 2013 to assess the treatment situation for allergy patients who could potentially benefit SIT, and to investigate why some patients do not use this form of treatment.

Patients and methods

During an on-site skin cancer screening program for employees at various companies, we collected information on point prevalences of self-reported allergies and their treatment [17]. In addition to the data which are routinely

Table 2 Reasons not to undergo SIT.

Reason	Frequency in percent
Low-level discomfort	51.2 (CI 95% 49.1–53.2)
No confidence in success of therapy	6.8 (CI 95% 5.8–7.8)
Lack of time	5.2 (CI 95% 4.4–6.2)
No knowledge of therapy	3.8 (CI 95% 3.0–4.5)
Avoidance is sufficient	3.6 (CI 95% 2.9–4.3)
Impossible for health reasons	1.6 (CI 95% 1.1–2.1)
No SIT therapy found	1.4 (CI 95% 1.0–1.9)
Other reasons	18.8 (CI 95% 17.3–20.3)

collected during skin cancer screening, we also focused on the use of specific immunotherapy. All employees between 16 and 70 years of age were included in the survey. The examinations were performed at the workplace by dermatologists or physician assistants who had already completed a significant portion of their dermatology training. The doctors performed the screening for the company Heigel GmbH, a private workplace screening service. Each consultation lasted about ten minutes, during which time the surveys were completed.

Participants were asked whether they had any allergies or prior atopic diseases (neurodermatitis, asthma, hay fever). Patients who reported having allergies, for which specific immunotherapy is available [18], were further asked whether they had undergone SIT (“Have you ever undergone desensitization?” yes-currently; yes-previously; no.) Table 1 lists the allergies for which preparations have been approved in Germany and are available. Patients were then asked about treatment success or reasons for declining treatment: “Was desensitization successful?” (yes/no). “Why have you not yet undergone SIT (Why has no desensitization been performed)?” Table 2 lists the possible answers. We also asked how often patients used allergy medications: “In the past 12 months, did you take any other medications to treat your allergy or allergies?” (yes-consistently, yes-sometimes, no). For data collection, we developed and used a specific data mask for entering characteristic values. Four data sets were removed due to missing age. All data were anonymous.

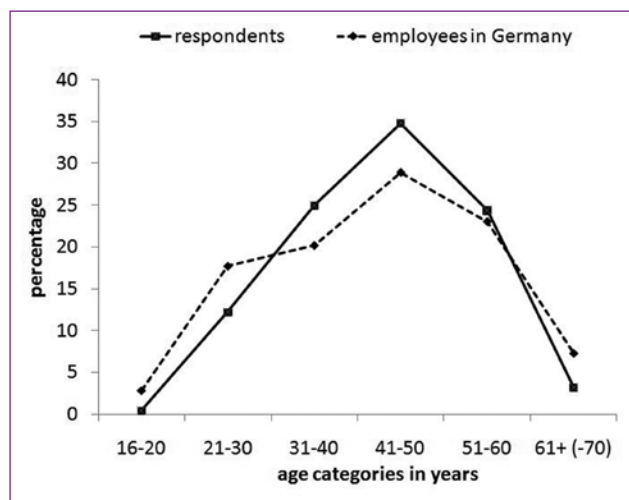


Figure 1 Ages of the respondents and the employed population in Germany.

The age structure for all employees in German was compared with the random sample to determine generalizability. All analyses were performed using SPSS 19. To simplify clinical interpretation, measures of central tendency were calculated as a binomial percentage, as well as mean and dispersion with 95% confidence intervals (95% CI).

Results

Study population

Between 1 January 2012 and 26 March 2013, a total of 15,164 employed persons aged 16 to 70 years were surveyed and examined. 32.0% (95% CI, 31.2% – 32.8%) of participants were women; the average age was 43.5 years (95% CI, 43.4% – 43.7%). The age distribution roughly corresponded to the age distribution of all employed persons in Germany (Figure 1). 38.2% of survey participants (95% CI, 37.4% – 38.9%) reported having allergies. 25.4% of participants with allergies had undergone SIT. Table 3 shows the frequency of neurodermatitis/flexural eczema, bronchial asthma, or rhinitis/allergic rhinoconjunctivitis as an underlying atopic disease.

Table 3 Frequency of underlying atopic conditions in percent.

	All respondents	Respondents with allergies that might benefit from SIT	Respondents who had undergone SIT
Atopic dermatitis, flexural, eczema	4.9% (CI95% 4.6–5.2)	9.2% (CI95% 8.3–10.0)	10.2% (CI95% 8.6–11.6)
Bronchial asthma	5.4% (CI95% 4.6–5.2)	15.8% (CI95% 14.7–16.9)	21.9% (CI95% 19.7–24.0)
Allergic rhinitis, rhinoconjunctivitis	20.3% (CI95% 19.6–20.9)	72.5% (CI95% 71.2–73.9)	81.4% (CI95% 79.3–83.4)

Employees with allergies which could be treated by SIT

26.2% (95% CI, 25.4% – 26.9%) of participants reported having allergies which could be treated by SIT. With an average age of 42.5 years (95% CI, 42.2% – 42.8%) they were somewhat younger, although the percentage of women – 30.1% (95% CI, 28.6% – 31.5%) – was comparable. The most common allergens were grass and grain allergies, along with allergies to early-flowering plants and house dust mites (Table 1). Employees with allergies which could be treated by SIT often reported having more than one allergy; participants reported an average of 1.53 (95% CI, 1.51% – 1.56%) allergies which could be treated by SIT. Consistent use of allergy medication was reported by only 2.1% (95% CI, 1.7% – 2.6%), and occasional medication use by 34.8% (95% CI, 33.3% – 36.3%). 31.7% (95% CI, 35.5% – 38.6%) of employees with allergies which could be treated by SIT had undergone desensitization.

More than half of patients said that the main reason they had not undergone SIT was that their symptoms were too mild (Table 2). Health-related limitations, or lacking access or knowledge of treatment options, were reported by fewer than 5% of patients. A significant number of respondents (18.8%) stated “other” reasons for not using SIT.

SIT participants

The average age of employees who had undergone SIT was 43.7 years (95% CI, 43.2% – 44.1%); the percentage of women was somewhat lower (25.6%; 95% CI, 23.4% – 28.0%). Consistent medication use was reported by 2.9% (95% CI, 2.1% – 3.8%), and occasional use was reported by 37.8% (95% CI, 35.1% – 40.1%). SIT was considered successful by 63.3% (95% CI, 60.8% – 66.0%) of employees. Among those who reported successful SIT, 2.3% (95% CI, 1.4% – 3.3%) reported consistent use and 33.4% (95% CI, 30.4% – 36.3%) occasional use of medication; among those reporting unsuccessful SIT, consistent medication use was reported 4.1% (95% CI, 2.4% – 5.8%) and occasional use by 45.3% (95% CI, 41.0% – 49.7%).

Discussion

The present study collected data from 15,164 employees on the prevalence of allergies, focusing on the use of SIT. The main determinant of SIT use appeared to be symptom severity. Inadequate health care structures, or lacking knowledge of SIT as a treatment option, played only a smaller role. Most patients felt that their treatment was successful; therapy was also related to decreased use of allergy medications. Only 3.6% of respondents with allergies that could be treated by SIT said that allergen avoidance alone was sufficient. This in turn means that, once an allergy has been confirmed by a physician, in accordance with German guidelines, there would be an indication for initiating SIT with an approved preparation, as long as there are no health-related reasons preventing treatment (which was reported by only a few participants) [8]. This is all the more important when one considers that prompt treatment with SIT, along with younger age, are predictors of successful treatment [8, 19]. Yet, international recommendations on SIT advise therapy only if medication alone is inadequate, so perhaps this overestimates the number of patients who could benefit from treatment [20, 21]. On the other hand, the more restrictive recommendations may be due less to the suitability of SIT and more to its high direct and indirect costs [22].

The high percentage of respondents (18.8%) who reported “other” reasons for not using SIT could indicate relevant reasons which were not asked by our standardized survey. Given that the survey is based on self-reports, other relevant reasons for not using SIT could be lack of confirmation of diagnosis by a physician (e.g., through prick testing) or fear of injection. This would be in line with the large number of respondents who said they refused to undergo SIT because their symptoms were too mild, although it is ultimately unclear. Typical methodological limitations should also be taken into consideration. Misclassification is conceivable, especially considering that the survey was based on self-reported data; in the framework of our study, it was impossible to compare patient self-reports with existing medical findings or diagnoses. In addition, due to its voluntary nature, as part of a company health intervention, there is a potential selection bias. Yet, given that the survey was announced as a skin screening, there was presumably no specific selection in terms of allergic diseases or SIT.

Taking this factor into account, if one compares the present data with the results from the 1998 German National Health Interview and Examination Survey, the overall rate of allergies is largely comparable to the present results [15]. Yet, the reported rate of using SIT was about 14% lower (absolute percentage) than in current studies. This may be due to greater acceptance or selection as a result of comparing different populations. The differences in the reported success rates of

SIT are even greater: respondents in the current study were 20% more likely (absolute figure) to say that SIT was successful or had led to an improvement of their symptoms. This result could be because the present study focused on allergies for which standardized and approved preparations are available. Yet, if one compares the data in terms of success rates of SIT with a smaller, partial analysis of recently published data from a representative sample in Germany, the results are similar for those with pollen allergies [4].

Summary

About one-quarter of employees surveyed reported having allergies which could be treated with SIT. Yet, fewer than half of them had undergone SIT, although they were generally aware of it and it was available. Most patients said that their symptoms were too mild to warrant its use; taken together, health-related issues and adequate avoidance of the trigger were named by only about 5% of respondents. Considering the high level of awareness of patients and the availability of treatment, further discussion is needed about the indication for using SIT as a treatment option in accordance with relevant guidelines.

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References

- 1 Asher MI, Montefort S, Björkstén B et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006; 368: 733–43.
- 2 Asher MI, Stewart AW, Mallol J et al. Which population level environmental factors are associated with asthma, rhinoconjunctivitis and eczema? Review of the ecological analyses of ISAAC Phase One. *Respir Res* 2010; 11: 8.
- 3 Sly RM. Changing prevalence of allergic rhinitis and asthma. *Ann Allergy Asthma Immunol* 1999; 82: 233–48; quiz 48–52.
- 4 Augustin M, Franzke N, Beikert FC et al. Allergien in Deutschland – Häufigkeit und Wahrnehmung in der Bevölkerung. *J Dtsch Dermatol Ges* 2013; 11: 514–21.
- 5 de laHoz Caballer B, Rodríguez M, Fraj J et al. Allergic rhinitis and its impact on work productivity in primary care practice and a comparison with other common diseases: the Cross-sectional study to evaluate work Productivity

- in allergic Rhinitis compared with other common diseases (CAPRI) study. *Am J Rhinol Allergy* 2012; 26: 390–4.
- 6 Kauppi P, Salo P, Hakola R et al. Allergic rhinitis alone or with asthma is associated with an increased risk of sickness absences. *Respir Med* 2010; 104: 1654–8.
- 7 Lamb CE, Ratner PH, Johnson CE et al. Economic impact of workplace productivity losses due to allergic rhinitis compared with select medical conditions in the United States from an employer perspective. *Curr Med Res Opin* 2006; 22: 1203–10.
- 8 Kleine-Tebbe J, Bufer A, Ebner C et al. Die spezifische Immuntherapie (Hyposensibilisierung) bei IgE-vermittelten allergischen Erkrankungen. *Allergo Journal* 2009; 18: 508–37.
- 9 Burgess JA, Matheson MC, Gurrin LC et al. Factors influencing asthma remission: a longitudinal study from childhood to middle age. *Thorax* 2011; 66: 508–13.
- 10 Shaaban R, Zureik M, Soussan D et al. Rhinitis and onset of asthma: a longitudinal population-based study. *Lancet* 2008; 372: 1049–57.
- 11 Boyle RJ, Elremeli M, Hockenhull J et al. Venom immunotherapy for preventing allergic reactions to insect stings. *Cochrane Database Syst Rev* 2012; 10: CD008838.
- 12 Abramson MJ, Puy RM, Weiner JM. Injection allergen immunotherapy for asthma. *Cochrane Database Syst Rev* 2010: CD001186.
- 13 Calderon MA, Alves B, Jacobson M et al. Allergen injection immunotherapy for seasonal allergic rhinitis. *Cochrane Database Syst Rev* 2007: CD001936.
- 14 Radulovic S, Wilson D, Calderon M, Durham S. Systematic reviews of sublingual immunotherapy (SLIT). *Allergy* 2011; 66: 740–52.
- 15 Hommers L, Ellert U, Scheidt-Nave C, Langen U. Factors contributing to conductance and outcome of specific immunotherapy: data from the German National Health Interview and Examination Survey 1998. *Eur J Public Health* 2007; 17: 278–84.
- 16 Kleine-Tebbe J, Ackermann-Simon J, Hanf G. Role of allergen-specific immunotherapy (desensitization) for the treatment of allergies in Germany. Current situation. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2012; 55: 343–50.
- 17 Augustin M, Herberger K, Hintzen S et al. Prevalence of skin lesions and need for treatment in a cohort of 90 880 workers. *Br J Dermatol* 2011; 165: 865–73.
- 18 Paul-Ehrlich-Institut. Therapie-Allergene (Stand Bundesanzeiger Nr. 112, vom 28.07.2011, Seite 2707). 2011.
- 19 Brehler R, Klimek L, Kopp MV, Virchow JC. Specific immunotherapy-indications and mode of action. *Dtsch Arztebl Int* 2013; 110: 148–58.
- 20 Bousquet J, Schunemann HJ, Samolinski B et al. Allergic Rhinitis and its Impact on Asthma (ARIA): achievements in 10 years and future needs. *J Allergy Clin Immunol* 2012; 130: 1049–62.
- 21 vanCauwenberge P, Bachert C, Passalacqua G et al. Consensus statement on the treatment of allergic rhinitis. *European Academy of Allergology and Clinical Immunology. Allergy* 2000; 55: 116–34.
- 22 Zuberbier T, Bachert C, Bousquet PJ et al. GA(2) LEN/EAACI pocket guide for allergen-specific immunotherapy for allergic rhinitis and asthma. *Allergy* 2010; 65: 1525–30.