Homeopathic Complex Remedy in the Treatment of Allergic Rhinitis: Results of a Prospective, Multicenter Observational Study

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Keywords
Homeopathic complex remedy · Seasonal allergic rhinitis · Hay fever

Summary
Background: Seasonal allergic rhinitis (SAR), also known as hay fever, is a widespread chronic respiratory disease. In treatment of SAR the use of complementary therapies is increasing, but little has been published about homeopathic complex remedies so far. Therefore, we think it is time to conduct and publish an appropriate observational study. Methods: Course of single symptoms, impairment of quality of life, general efficacy, and tolerability of a homeopathic complex remedy containing active substances on a low dilution level have been assessed and analyzed. Altogether, 123 patients with a history of allergic rhinitis of up to 45 years have been observed for about 4 weeks. Results: The majority of symptoms were shown to improve substantially and the patients’ quality of life increased clearly. The overall symptom score decreased significantly from 10.3 ± 4.7 to 3.9 ± 3.1 points (p < 0.0001), and reduction of impairment of quality of life from 5.7 ± 2.3 to 1.9 ± 1.8 score points was also significant (p < 0.0001). Rating of efficacy of study medication was markedly better than efficacy rating of previous therapies (p = 0.0193). Apart from one temporary allergic reaction, the treatment was well tolerated. Conclusion: The homeopathic complex remedy (Pascallerg®) tested in this observational study offers a useful option in treatment of SAR in children and adults.

Schlüsselwörter
Homöopathisches Komplexmittel · Saisonale allergische Rhinitis · Heuschnupfen

Zusammenfassung
Hintergrund: Saisonale allergische Rhinitis (SAR), auch bekannt als Heuschnupfen, ist eine weit verbreitete chronische Atemwegserkrankung. Die Anwendung komplementärer Therapien in der Behandlung von SAR nimmt zu, jedoch wurde bislang nur wenig zu homöopathischen Komplexmitteln publiziert. Dementsprechend ist es an der Zeit, eine entsprechende Beobachtungsstudie durchzuführen und zu veröffentlichen. Methoden: Untersucht und beurteilt wurden der Verlauf einzelner Symptome, die Beeinträchtigung der Lebensqualität, die allgemeine Wirksamkeit und die Verträglichkeit eines homöopathischen Komplexmittels, das Wirkstoffe in niedriger Potenzierung enthält. Patienten, die seit bis zu 45 Jahren an SAR litten, wurden etwa 4 Wochen lang beobachtet. Ergebnisse: Die Mehrheit der Symptome konnte wesentlich gelindert werden, und die Lebensqualität der Patienten stieg deutlich. Der Summenscore der Symptome sank signifikant von 10,3 ± 4,7 auf 3,9 ± 3,1 Punkte (p < 0,0001). Ein ebenfalls signifikanter Rückgang (p < 0,0001) zeigte sich in der Beeinträchtigung der Lebensqualität von 5,7 ± 2,3 auf 1,9 ± 1,8 Punkte. Die Wirksamkeit der Studienmedikation wurde deutlich besser bewertet (p = 0,0193) als die Wirksamkeit vorheriger Therapien. In Bezug auf die Verträglichkeit wurde die Behandlung, abgesehen von einer vorübergehenden allergischen Reaktion, gut vertragen. Schlussfolgerung: Das homöopathische Komplexmittel (Pascallerg®), das in dieser Beobachtungsstudie untersucht wurde, bietet eine nützliche Alternative in der Behandlung von Erwachsenen und Kindern mit SAR.
Background

In a press release, The European Centre for Allergy Research Foundation already warned at the beginning of January against early and stronger pollination of hazelnut and alder trees [1]. Both are wind pollinated plants and produce $2.1 \times 10^{10}$ (hazelnut) to $1.4 \times 10^{11}$ pollen grains (alder tree) per plant [2]. Just 1–10 of these huge amounts of pollen grains are enough to trigger severe symptoms of seasonal allergic rhinitis (SAR), also known as hay fever [1]. It is a symptomatic disorder of the mucous membrane of the nose induced to an IgE-mediated inflammation [3]. Unspecific stimuli which are tolerated by healthy people without symptoms cause a nasal hyperactivity. Typical symptoms of SAR are sneezing and rhinorrhea but also headache and daytime tiredness associated with ocular symptoms, such as dry, itching, and burning eyes [4, 5]. Between 10 and 28.5% of the population are affected by this chronic respiratory illness [4, 6–8]. In Germany, about 16% of the whole population and 9% of children and adolescents suffer from hay fever [9, 10], and evidence suggests that the prevalence of SAR is increasing [4]. Affected patients have to live with significant impairments in quality of life, sleep, and work performance. This also includes reduced exam performance as well as learning and attention problems in pupils and students. Additional aspects concern financial burdens of patients and society or social constraints, such as activity limitations and a higher frequency of visits to physicians [5]. Furthermore, SAR increases the risk of developing further diseases, such as upper respiratory tract infections, mainly atopic dermatitis and asthma [5, 11, 12]. It might be that the rising prevalence of asthma is not caused by pollen allergens directly but by pollen-induced rhinitis [11]. So patients need a close monitoring of their course of symptoms; reduction of symptom intensity is the most important goal of treatment [5] in combination with a high tolerability and a low risk of interactions.

Treatment possibilities of SAR include avoidance of allergens, desensitization (specific immunotherapy), and medicinal treatment. The first option is the safest, but pollen are ubiquitously present and it is impossible to avoid contact completely. Specific immunotherapies achieve good results in patients with severe courses of hay fever when drug treatment is not possible. Disadvantages may be that the specific allergens have to be found, long treatment durations with frequent visits to physicians, and risks such as anaphylaxis [4, 13, 14]. In comparison to the immune-modifying desensitization, drug therapies e.g. with antihistamines, disodium cromoglicic acid, or cortisone are symptom-releasing treatment options. Complementary treatment methods, such as classical homeopathy, often combine both treatment options: release of symptoms and support of the immune system; and they show an increasing demand [15]. The low-potency active ingredients of the homeopathic complex remedy tested in this study are used traditionally for unspecific desensitization of immune system against allergens and for treatment of characteristic SAR symptoms.

The aim of this observational study was the evaluation of safety and effectiveness of a homeopathic complex remedy in patients suffering from SAR. The study medication was a tablet containing 3 complementing and synergistic homeopathic drug substances: Alumen chromicum (Chromium(III) potassium sulfate), Acidum formicicum (Formic acid), and Gelsemium (Gelsemium sempervirens (L.) J.St.-Hil.). A higher concentration of active substances and the combination of different homeopathic preparations show that the study medication is no classical homeopathic monopreparation but similar to a phytotherapeutic drug.

Material and Methods

Study Objective

More than 50 years of experience in everyday practice documented first in a collection of experience reports in 1999 [16] lead to the hypothesis that the homeopathic complex remedy (table 1) might have a positive impact on patients suffering from typical symptoms of SAR.

Study Duration

February 2012 to July 2013.

Study Design

For the present multicenter, prospective observational study, therapists in Germany have been recruited from an internal database and via scientific field service. Concept and design of the study as well as its ethical validity and performance are based on the actual recommendations of the German Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM, German Federal Institute for Drugs and Medical Devices) and referred to the Declaration of Helsinki and Good Clinical Practice. The study was registered on ClinicalTrials.gov (trial registration number: NCT 01660737). Furthermore, this study followed the actual STROBE guidelines for items to be included in reports on observational studies [17].

Study Setting

Before the start of this study, the physicians received a briefing on the observational plan, the ethical and scientific basis of this multicenter, prospective non-interventional study (NIS) with observational character, the allocation procedure, and the therapy schedule in accordance with the study protocol. Data assessment included a physician-completed questionnaire on 3 occasions: before treatment (visit 1, baseline), after approximately 1 week of treatment (visit 2), and after approximately 4 weeks of treatment (visit 3) (table 2). The exact time points and end of documentation were set at the physicians’ own discretion. The concomitant diseases were grouped according to the ICD-10 classification. All medications apart from the study medication were classified according to the – to that time current – Rote Liste (Red List) 2012 and 2013, respectively.

Participants

In accordance with recommendations of BfArM, study participants were chosen by the responsible therapist for a certain treatment and afterwards selected for participation. Then participants were enrolled after the informed written consent of the responsible therapist. Before the start of this study, the physicians received a briefing on the observational plan, the ethical and scientific basis of this multicenter, prospective non-interventional study (NIS) with observational character, the allocation procedure, and the therapy schedule in accordance with the study protocol. Data assessment included a physician-completed questionnaire on 3 occasions: before treatment (visit 1, baseline), after approximately 1 week of treatment (visit 2), and after approximately 4 weeks of treatment (visit 3) (table 2). The exact time points and end of documentation were set at the physicians’ own discretion. The concomitant diseases were grouped according to the ICD-10 classification. All medications apart from the study medication were classified according to the – to that time current – Rote Liste (Red List) 2012 and 2013, respectively.

Table 1. Composition of one tablet of study medication

| Active ingredient | Mg/tablet |
|-------------------|-----------|
| Alumen chromicum Trit. D1 (Chromium(III) potassium sulfate) | 25.0 |
| Acidum formicicum Trit. D2 (Formic acid) | 2.5 |
| Gelsemium Trit. D2 (Gelsemium sempervirens (L.) J.St.-Hil.) | 2.5 |
Table 2. Study course

| Assessment of                                      | Visit 1 | Visit 2 | Visit 3 |
|---------------------------------------------------|---------|---------|---------|
| Demographic data (sex, age, body height, body weight) | x       | –       | –       |
| Concomitant therapy due to inclusion diagnosis     | x       | –       | –       |
| Concomitant medication in general and due to inclusion diagnosis | x       | –       | –       |
| Efficacy and tolerability of previous therapy due to inclusion diagnosis | x       | –       | –       |
| Common symptoms, such as dry eyes, itchy eyes, watering eyes, bronchial complaints, sneezing, rhinitis, fatigue/tiredness, headaches (0 = not present; 3 = strong) | x       | x       | x       |
| Impact of allergy on quality of life (0 = no impact; 10 = strong impact) | x       | x       | x       |
| Efficacy of study medication in general (no efficacy (symptoms did not change or worsened); very good (symptoms completely declined)) | – (x)* | x       | –       |
| Drug changes (newly prescribed, withdrawn, dosage decreased, dosage increased) | –       | x       | x       |
| Tolerability                                         | –       | x       | x       |
| Adverse drug reactions                              | –       | x       | x       |

*If visit 2 was the last visit

consent, and a data privacy policy statement had been signed by the patient or its legal guardian. Information on possible unwanted side effects and the possibility to cancel the participation at any time without any negative impact on the treatment were given to the participant or its legal guardian. To disguise the identity of participants, a pseudonymization procedure was adopted (patient identification numbers were determined).

Concomitant criteria were defined as follows: Older than 1 year of age, history of SAR (hay fever), informed consent to participate in the study. Exclusion criteria contained children younger than 1 year of age and hypersensitivity to chrome ort/and lactose intolerance.

Doses and duration of treatment were at the respective physician’s discretion. The combination of 3 homeopathic drug substances on a low dilution level (Aluminum chromicum (Chromium(III) potassium sulfate), Acidum formicum (Aminic acid), and Gelsemium (G. sempervirens (L.) J.St.-Hil., Carolina-Jasmijn) (Pascallerg®; table 1)) has been administered as tablet via oral route. Study medication was prescribed by a therapist and bought by the patient or the patient’s legal guardian.

Variables Studied and Statistical Method

The focus laid on statistical tests for the main efficacy variables to investigate treatment effects between baseline (visit 1) and the final visit after 4 weeks (visit 3). For patients who terminated participation in this non-interventional study prior to visit 3, the last attainable value under therapy (visit 2 after 1 week) was used for analysis (if available), in accordance with the last observation carried forward (LOCF) principle. Statistical evaluations have been calculated in-house and additionally by an external statistician.

Target parameters were:
1. Severity of common symptoms (dry, itching, watering, and/or burning eyes; bronchial complaints; sneezing; rhinitis; fatigue/tiredness; headaches) was assessed by the therapist and evaluated by means of a 4-point scale (not present, mild, moderate, strong). A patient was defined as ‘affected’ if a symptom was at least assessed as mild at one time point of the observation. For calculation of improvements and deteriorations, a second assessment (at least ‘not present’) was necessary for the respective symptom. Based on an addition of all symptom points per visit and per patient, a sum score was calculated. Changes between 2 visits were analyzed by means of the two-sided one-sample t test.
2. The impact of patients’ allergy symptoms on quality of life was assessed at each visit via a numeric rating scale (NRS) (10-point NRS: 0 = no impact; 10 = strong impact). Changes from baseline were analyzed by means of the two-sided one-sample t test.
3. At baseline, the general efficacy of previous therapy/therapies for SAR was assessed by means of the following scale: very good (no symptoms anymore), good (symptoms clearly improved), moderate (symptoms slightly improved), no efficacy (symptoms did not change or worsened). With the same rating scale, general efficacy of the study medication was documented at the last visit. To examine the number of cases in which the previous therapy was superior, the same or worse outcome was compared by means of the (exact) Mantel-Haenszel test.
4. Furthermore the tolerability of study medication, previous therapies, and concomitant medication due to or not due to inclusion diagnosis were documented.

All data were checked for plausibility and recorded in an ACCESS database (version 2007) using double data entry. After comparison, data were exported to SPSS (version 19.0) and evaluated.

Results

Altogether, 59 therapists with a treatment focus on SAR and with at least first treatment experiences concerning the study medication were invited to collect data. Between February 2012 and July 2013, 25 physicians and alternative practitioners (10 general practitioners, 6 physicians specialized on naturopathic medicine or homeopathy, and 9 alternative practitioners) agreed to participate in the study. They returned correctly and completely filled-out case report forms of 123 patients. Therefore, the participant rate of therapists was 42.3 %. During the observational period, no patient dropped out or had to be excluded from per-protocol analysis (dropout rate = 0%) (fig. 1).

Demographic and Patient History Data

Gender distribution in the patient group with 58 men (47.2 %) and 65 women (52.8 %) was balanced. At the beginning of the therapy, the mean age of patients was 36 years, including 30 children and adolescents (6–18 years of age) and 93 adults (18–85 years of age).

The inclusion diagnosis (J30 ‘vasomotor and allergic rhinitis’) was made on average about 11 years ago with a range from 3 month to 53 years. In the majority of participants (79.7%), symptoms were present for more than 2 years. In the current season, the mean occurrence of symptoms began 2.4 weeks before the beginning of this study.

About 43.1 % of patients showed an allergic reaction to just one kind of plants (trees, grasses, herbs or others), while about 56.9%
reacted allergic to a combination of different kind of plants or to a combination of plants with other allergens. The most frequent examples for ‘other types of allergy’ were animal hair (31.3%) and house dust (12.5%).

Period of observation enfolded an average duration of 1.4 ± 0.4 weeks (n = 9) including visit 1 and visit 2, or a mean duration of 4.5 ± 1.3 weeks (n = 114) including all 3 visits (table 2). After the last visit, more than 70% of participants continued treatment with study medication. The average daily dose was 5 tablets (with a range of 1–10 tablets) which is in accordance with the recommended dose for one day. In the course of treatment, frequency of intake and amount of study medication could be reduced.

During the observation period, 54 patients (43.9 %) received previous drug therapy due to inclusion diagnosis (mostly antiallergics); only 15 of these patients continued their medication during the study. A subgroup analysis showed that duration of symptoms was more than 2 years in all of these 15 patients. In the course of the study, changes in dosage of concomitant antiallergics showed an addition in 2 cases, a reduction in 2 cases, and a stop in 5 cases. In patients without concomitant medication due to inclusion diagnosis during observation, 76.9 % suffered from these symptoms for more than 2 years, and for 23.2% a duration of complaints of less than 2 years were documented. The overall symptom score was slightly lower in the group with additional medication (8.5 ± 5.0 in comparison to 10.6 ± 4.7).

Side effects of previous medication occurred in 19 patients (35.2%). At the beginning of the observational study, 32 patients (26.0%) suffered from concomitant diseases and took at least one concomitant drug. These included antihypertensives, psychopharmaceuticals, thyroid gland therapeutic agents, and gastrointestinal drugs.

Course of Symptoms

The following frequencies of symptoms have been documented (N = 123 patients = 100%, multiple answers were possible): sneezing (87.0%), rhinitis (82.9%), itching eyes (82.1%), fatigue/tiredness (75.6%), watering eyes (66.7%), burning eyes (61.8%), bronchial complaints (43.9%), headaches (43.1%), and dry eyes (37.4%). Concerning 5 symptoms (itching eyes, burning eyes, sneezing, rhinitis, fatigue/tiredness), 51.3–67.4% of affected patients suffered from a moderate or strong intensity before treatment. At the end of observation, in most of these patients at least 82.8% (concerning symptom fatigue/tiredness) and up to 89.1% (concerning symptom dry eyes) of severity was reduced from moderate/strong to mild/not present. In general and independent from the baseline intensity, at least 82.1% (concerning symptom fatigue/tiredness) and up to 95.6% (concerning symptom dry eyes) of all those patients affected were symptom-free or had only mild symptoms. In the majority of participants, a clear improvement of symptomatology has been documented (71.7–89.4%) (fig. 2), in some patients symptoms did not change (7.9–28.3%) or deteriorate (0–6.5%). Concerning all symptoms, a good reduction was detectable after one visit, but there was also a tendency to a substantially reduction after a longer observational period and a second visit. Even in cases where allergy symptoms had existed for over 45 years, efficacy was good to very good in 3 out of 4 patients.
Comparison of the mean overall score of symptoms between start and end of the observational period showed a significant reduction of 7.1 points from 10.3 ± 4.7 to 3.2 ± 3.1 points (p < 0.0001, one-sample t test, two-sided).

Subgroup analysis showed no difference in efficacy for different age groups or for the time that had passed since first occurrence of allergy. Although the overall score at baseline visit was higher in the patient group without concomitant medication due to inclusion diagnosis, the value at the end of observation was comparable (3.1 ± 3.1 in comparison to 3.7 ± 3.0).

Impairment of Quality of Life

The impact of the allergy on the general well-being was assessed at each visit by means of a numerical rating scale. All in all, 115 patients reported a negative impact at visit 1. In more than 97% of these participants the quality of life improved during treatment (fig. 2). The corresponding score decreased significantly by 66.7% from 5.7 ± 2.3 to 1.9 ± 1.8 points (p < 0.0001, one-sample t test, two-sided). A subgroup analysis showed no relevant difference in patients with or without concomitant medication due to inclusion diagnosis.

Efficacy in Comparison to Previous Medication

In accordance to the above-mentioned results, the general efficacy of study medication assessed by patients via NRS was stated as very good (symptoms completely declined) by 48.8%, as good (symptoms clearly improved) by 35.3%, or as moderate (symptoms slightly improved) by 12.2% of patients. Only 2 patients (2.4%) reported that their symptoms did not change or worsen.

Most patients who received previous drug therapy due to inclusion diagnosis (54 patients) before the beginning of the study assessed the efficacy of their previous medication as moderate (48.1%) or good (37.0%). Only these 54 patients (with an available assessment of the previous medication) were included in a comparison of mean efficacy assessments. The comparison showed that the efficacy of study medication was rated significantly better than the efficacy of previous therapy (p = 0.0193 at the 5% level, calculated via (exact) Mantel-Haenszel test).

Tolerability and Safety

A good tolerability without side effects was reported for 122 (99.2 %) of the participants. In one case (0.8%) the tolerability was described as bad because of a temporary allergic reaction (rash around mouth and pustules on the décolleté) that occurred 11 days after beginning of treatment. The patient recovered completely without further treatment, the causal relationship to study medication was assessed as possible.

Discussion

Clinical data on treatment of SAR patients with homeopathic complex remedies is rare (one exception is [18]). With the present prospective, multicenter observational study we intended to close this gap to some extent. We have decades of experiences with the study medication in everyday practice and conducted a first documentation with the character of an observational study in 1999 including 365 patients with SAR [16]. In this documentation, 61.4% of patients became symptom-free or felt a clear improvement following the administration of study medication. In the current study, this amount of patients is more than 20% higher. This difference might be the result of different study populations, regional differences, changed weather conditions, etc. A smaller number of patients with a higher sensitivity towards outliers might also be a factor. The very low proportion of patients with unchanged symptoms as well as the good tolerability could be confirmed.

All symptoms chosen for evaluation are widespread among people suffering from SAR [4, 15]. Out of these, the most frequent were sneezing, rhinitis, itching eyes, and tiredness/fatigue. Independent from severity, and kind of symptom alleviation was achieved in the majority of patients. Patients with short histories of SAR as well as participants with existing symptoms for more than 45 years responded very well to the complex homeopathic treatment. A small group of 15 patients (21.2%) received an additional medication due to inclusion diagnosis. At baseline visit, these patients showed a tendency to lower symptom intensity, but the difference in overall sum score is still small if a full efficacy of additional medication is expected. However, for general statements concerning this topic the group size is not large enough. Although patients without concomitant medication started with slightly higher symptom intensity, the overall score of symptoms at the end of observation was the same in both groups. A comparison also showed that participants from the small subgroup tended to have a longer duration of complaints, but a general influence of the duration of symptoms on the efficacy or tolerability was not detectable.

Considering all patients, a positive development is reflected in the 62.1% reduction in the overall score of symptoms and in the high increase in quality of life.

Concerning the average of quality of life, different questionnaires (from VAS to Rhinoconjunctivitis Quality of Life Questionnaire) and several treatment opportunities (from antihistamines to homeopathics, from immunotherapy to acupuncture) have been used in past studies [19–24]. Therefore, a comparison to already existing data is not possible in detail. In general, an average improvement of a general quality of life score ranges from 24.0% to 66.7%, so the result achieved with the homeopathic complex remedy in the presented study (66.7%) might be at the upper end of range. Of course, a direct comparison between different treatment opportunities is necessary to confirm these results.

No side effects have been reported for nearly all participants. No sedative effects – typical adverse reactions associated with antihistamines – occurred. The opposite turned out to be the case: At baseline, in most patients tiredness/fatigue was one of the most frequent and most severe symptoms. After treatment with the homeopathic complex remedy for 1–4 weeks, in 83.9% of affected patients’ tiredness/fatigue declined or at least clearly improved.

The results show that it is possible to adjust the treatment individually. Possible factors, such as age of the patient, the period...
since diagnosis, or concomitant medication due to inclusion diagnosis had no impact on the good treatment results. In case of positive development of disease, a reduction of study medication has been proven effective. A further advantage concerning the compliance in children and adults is the small tablet which can be swallowed or melt under the tongue easily.

In further examinations, these results should be confirmed and directly compared in a randomized comparative effectiveness trial vis-à-vis standard therapy, classical homeopathy or placebo.

Limitations
The limitations are characteristic for an officially required design of a multicenter, prospective observational study, e.g., lack of a placebo group and randomization. No difference between patients suffering from intermittent or persistent forms of disease was made. The open character and the sensitivity of safety and effectiveness may also be limitations. On the other hand, this type of study offered the possibility to prove the medication’s tolerability and effectiveness until 5 weeks of follow-up in everyday life beyond a strictly controlled environment of a clinical study.

Conclusion
We suggest that the homeopathic complex remedy tested in this observational study leads to a relief of symptoms typical for SAR and improves the quality of life. It offers a useful option in treatment of children and adults.

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References
1 Colli M, ECARF (European Centre for Allergy Research Foundation): Die ersten Pollen fliegen schon. Press release, 09.01.2013, Berlin. www.ecarf.org/aktuelles/presse-und-information/news/details.html?tx_ttnews[tt_news]=16266&cHash=c840b73c0f686a8f343807b32b9ef08 (access 15.01.2015).
2 Piotrowska K: Ecological features of flowers and the amount of pollen released in Corylus avellana (L.) and Alnus glutinosa (L.) Gaertn. Acta Agrobotanica 2008, 61:33–39.
3 Hansel F: Clinical and histopathologic studies of the nose and sinuses in allergy. J Allergy 1929;1:43–70.
4 Small P, Kim H: Allergic rhinitis. Allergy, Asthma & Immunology 2011;7(suppl 1):53.
5 Pawankar R, Canonica GW, Holgate ST, Lockey RF, Bauchau V, Durham SR: Prevalence and rate of diagnosis of allergic rhinitis in Europe. Eur Respir J 2004, 24:758–764.
6 Bousquet J, Khalturin N, Cruz AA, et al.: Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2) LEN and AllerGen). Allergy 2008;63(suppl 86):8–160.
7 Mullol J, Valero A, Alobid I, et al.: Allergic Rhinitis and its Impact on Asthma update (ARIA 2008). The perspective from Spain. J Invest Allergol Clin Immunol 2008;18:327–334.
8 Robert Koch Institut, Bundeszentrale für gesundheitliche Aufklärung [eds]: Erkenntnis – Bewerten – Handeln: Zur Gesundheit von Kindern und Jugendlichen in Deutschland. Berlin, RKI, 2008.
9 Deutscher Allergie- und Asthmahandbuch: Pollenallergie: Heuchernapfen. www.daah.de/allergien/pollenallergie/beuchernapfen/ (access 15.01.2015).
10 Leynaert B, Neukirch C, Kony S, et al.: Association between asthma and rhinitis according to atopic sensitization in a population based study. J Allergy Clin Immunol 2004;113:86–93.
11 Bacher C, Borchard U, Wedi B, et al.: Leitlinie der DGAi – Allergische Rhinosinusitis. Allergo J 2003, 12:182–94.
12 Armentia A, Carballada F, Carretero P, et al.: Postmarketing study for assessment of tolerability of a grass allergen immunotherapy tablet (GRAZAX) in patients with rhinitis or rhinoconjunctivitis. J Investig Allergol Clin Immunol 2012;22:485–490.
13 Pastorello EA, Losappio L, Milani S, et al.: 5-grass pollen tablets achieve disease control in patients with seasonal allergic rhinitis unresponsive to drugs: a real-life study. J Asthma Allergol 2013;4:127–133.
14 Gruendingl C, Schimetta W, Frass M: Real-life effect of classical homeopathy in the treatment of allergies: a multicenter prospective observational study. Wien Klin Wochenschr 2012;124:11–17.
15 Schmitz-Bohm C, Leitzmann F, Koch H, et al.: Qualität von Medikamenten: Faustregel für ausgewählte Arzneimittel. Berlin, Deutscher Arzneimittel-Verlag, 2007.
16 Krück B, Werner B: PASCALLERG®. Sammlung von Erfahrungsbereichen 1999. Acta Biologica 2000;1:43–50.
17 Von Ems L, Altmann DG, Egger M, et al.: The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. PLoS Med 2007;4:e296.
18 Weiser M, Gegenheimer LH, Klein P: A randomized equivalence trial comparing the efficacy and safety of Lufia comp.-Heel nasal spray with cromolyn sodium spray in the treatment of seasonal allergic rhinitis. Forsch Komplementarmed 1999;6:142–148.
19 Ciebiada M, Ciebiada MG, Knicieck T, Dubuske LM, Gorski P: Quality of life in patients with persistent allergic rhinitis treated with Montelukast alone or in combination with Levocetirizine or Desloratadine. J Investig Allergol Clin Immunol 2008;18:343–349.
20 Goossens S, Leceman G, Aertgeerts B, et al.: Evaluation of the quality of life after individualized homeopathic treatment for seasonal allergic rhinitis. A prospective, open, non-comparative study. Homeopathy 2009;98:11–16.
21 Hashemi SM, Oskhovat A, Amini S, Pourghasemian M: Comparing the effects of Botulinum toxii A and Cetirizine on the treatment of allergic rhinitis. Allergol Immunol 2013;62:245–249.
22 Li XM: Complementary and alternative medicine in pediatric allergic disorders. Curr Opin Allergy Clin Immunol 2009;9:161–167.
23 Moreno-Accilò A, Moreno C, Ojeda P, et al.: Efficacy and quality of life with once-daily sublingual immunotherapy with grasses plus olive pollen extract without updosing. J Invest Allergol Clin Immunol 2007;17:399–405.
24 Valero A, Iquiez I, Giralt J, Bartra J, del Cuvillo A, Molló J: Rupatadina improves nasal symptoms, quality of life (EPSPRINT-15) and severity in a subanalysis of a cohort of Spanish allergic rhinitis patients. J Invest Allergol Clin Immunol 2011;21:229–235.