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100 Years of Immunotherapy: The Monaco Charter

Under the High Patronage of His Serene Highness Prince Albert II of Monaco

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Key Words

Allergen immunotherapy · Monaco Charter · Allergic patients · Allergy treatment · Allergic diseases

Abstract

Aims of the Monaco Charter: (1) to present the current evidence on the efficacy and safety of allergen-specific immunotherapy (SIT) and to address the reasons for its underuse in clinical practice; (2) to develop strategies to increase the awareness about the benefits and the hazards of SIT in allergic patients, lay public and healthcare professionals not trained in allergy, and (3) to make SIT accessible and affordable to eligible patients.

Facts

Allergic Diseases

General Burden and Prevalence

Allergic diseases, including respiratory allergy, skin diseases, and adverse reactions to drugs and foods, represent a major burden from both an epidemiological and an economical point of view.

Respiratory Allergies. As summarized in the World Allergy Organization (WAO) White Book [1] and according to ISAAC (International Study of Asthma and Allergies in Childhood) data [2], the worldwide prevalence of rhinoconjunctivitis ranges from 20 to 35%, and that of asthma from 10 to 20%. Respiratory allergies are of particular importance, mainly due to their high prevalence and their socioeconomic impact. In fact, those diseases are chronic in nature and therefore require long-term treatment. In addition, they induce substantial indirect costs

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due to loss of productivity (work and school absenteeism) [3, 4]. This holds true for both asthma and rhinitis. Finally, asthma and rhinitis often coexist and involve the same immunological mechanisms. Allergic rhinitis is a risk factor for the subsequent development of asthma [5].

Non-Respiratory Allergies. In addition to respiratory allergy, non-respiratory allergic diseases have a very high prevalence, e.g. atopic eczema (20%) or urticaria (15–20%). Despite their lower prevalence, food allergy (3–5%), anaphylaxis (0.1%) or insect venom hypersensitivity (1%) also pose a significant economic burden due to morbidity, hospitalization and critical care resources utilization [1].

According to an official statement of the Council of the European Union, the leading priority is to reduce health inequalities [6].

Allergen-Specific Immunotherapy

Allergen-specific immunotherapy (SIT) represents a unique modality of treatment for respiratory allergies. SIT acts not only as symptomatic treatment, but also as a biological response modifier, which changes profoundly and specifically the immunological response to allergens [7, 8].

Treatment Routes and Effects. Numerous controlled trials and meta-analyses revealed that SIT, administered either subcutaneously or sublingually, significantly reduces the symptoms of allergic rhinitis and asthma [9–11]. The reduction in symptoms consequently results in a reduced need for symptomatic medications.

Mechanisms of Action. Because of its special mechanisms of action, SIT possesses some effects not shared by pharmacological treatments, such as the persistence of the clinical benefit years after SIT discontinuation and the reduction in the risk of asthma development [12]. Those 'additional' actions of SIT have an important socioeconomic effect (i.e. reduction in disease costs in the long term), which has been formally demonstrated in specific studies [13, 14]. SIT can be considered a 'phenotype-oriented' treatment that is effective in carefully selected patients with IgE-mediated allergy in whom the causal role of the allergen(s) in eliciting symptoms is properly demonstrated.

Prerequisites. The prescription of SIT requires a detailed and accurate diagnosis to clearly identify the allergen(s) for which desensitization is instituted [15]. This is mandatory for a successful treatment.

Treating Physicians. In general, SIT is mainly prescribed and managed by allergists, but other specialists (pulmonologists, ENT specialists, pediatricians and dermatologists) are also involved in some countries [16]. Despite this, the presence of allergists seems to be largely insufficient in this specific field of immunotherapy, as shown by a recent European survey [17], and SIT is poorly known by the general population [18]. Finally, general practitioners (GPs) play a significant role, since patients often first refer to GPs: they decide the diagnostic procedures and are in charge of the follow-up of patients receiving SIT [1].

Barriers

Barriers to the Use of SIT and Unmet Needs

Several international documents, such as the WAO SLIT Position Paper [10], report the unmet needs about the scientific aspects of SIT. These include methodological shortcomings, bias in clinical trials and standardization. We herein focus on important additional issues and real barriers to the approriate dissemination of SIT, which can be summarized in the following items:

- Underappreciation of the science supporting SIT
- Complexity and time consumption in performing appropriate SIT studies compared to clinical trials with drugs
- Absence of reimbursement of SIT in most countries
- Limitation of resources available for SIT promotion due to the small size of the manufacturers' companies.

Patients. Currently, over 30% of allergic patients have never received a specific allergy diagnostic test. Knowledge about allergen SIT is low overall and varies widely by country: in Europe, 30% (country range: 10–52%) had never heard of SIT [18]. These data emphasize the surprising disparity between burden and awareness of allergic disease and its treatment.

SIT Reimbursement. As mentioned before, this is a crucial issue in most countries.

Promotion of SIT Awareness. Resources available for the promotion of SIT awareness remain scarce.

Underappreciation. Another major barrier to the use of SIT is the underappreciation of the science supporting SIT, the efficacy of which (see above) is fully documented. This is confirmed by the fact that immunotherapy products are registered by many regulatory agencies.

Training. It is still largely insufficient in allergy (training implies the skills for a correct diagnosis and treatment) in several countries. Given the high prevalence of respiratory allergies, some forms of allergy training must be considered as an essential part of the general professional training for physicians, specialists and GPs [19, 20].

Education in Allergic Diseases. It is largely insufficient in many countries also among pharmacists [21].

Strategies

Strategies to Improve Awareness and Dissemination

Patients' Associations. They should/could play a crucial role in implementing the knowledge/awareness of an updated allergy diagnosis and they should associate with medical associations to obtain reimbursement of the treatment.

General Practitioners. The possibility to create a cohort of GPs with a special interest in allergy and with the joint task of developing and providing clinical service in primary care should be promoted wherever possible. Collaboration between primary care teams and allergists should become a social priority in this field [22, 23].

Proper Documentation. Documentation and instructions from the prescribing allergist's office as well as forms designed for complete and accurate documentation of therapy are vital components of safe administration. In addition, proper educational programs designed to raise skills in SIT within their community are required.

Patient Leaflets. A proper leaflet containing synthetic key information on allergy and SIT should be prepared in collaboration with patient organizations. This tool should be translated into different languages and promoted through media by patient organization campaigns, and distributed in doctors' offices and pharmacies.

Educational Programs. These initiatives should be finalized to GP, pharmacist and healthcare professional education. SIT guidelines (with pocket versions) for GPs and pharmacists should be prepared by their own scientific organizations in cooperation with specialists. Postgraduate schools and masters on SIT should be promoted by the allergy scientific societies.

Regulatory Authorities. Currently, allergic diseases and SIT are considered in most of the regional and national drug agencies. Allergen standardization is promoted and requested. Harmonization of regulations among countries is needed. Scientific societies should partner, at any level, to advise and promote this process.

Dissemination Strategy of the Monaco Charter and Related Documents

Target Population: Physicians and Pharmacists

Publication of the Monaco Charter

Congress Events. The aim should be to focus on the importance of curing allergies and not just to treat symptoms. The organization should be run by the GP scientific organizations (CME activities should also be part of the project).

Media Campaigns and Publications in GP/Pharmacist Journals. SIT information should be disseminated through internet websites and blogs of GPs and/or pharmacists. At present, information on SIT is missing on the vast majority of these websites worldwide. Communication in journals dedicated to GPs and pharmacists combined with media campaigns in lay press could help to achieve three goals:

(1) GPs and pharmacists will improve their skills (awareness/knowledge) in SIT.

(2) GPs and pharmacists will be less reluctant to consider SIT prescriptions to allergic patients.

(3) Allergic patients will be more aware of SIT, and demanding it to GPs and pharmacists, because of the concomitant media campaign.

Websites. Websites of GPs' (primary care practitioners and family practitioners) organizations and pharmacists should contain essential news about SIT. Links to other websites (e.g. manufacturers, allergy societies, patient organizations and educational sites) should be created.

Target Population: Allergic Patients and the General Population

Publication of the Monaco Charter

It is crucial to transmit simple and clear messages in the media (via radio, TV, newspapers and magazines, for example) to impose an effect on the public opinion. For instance, the importance of causal allergens should be stressed in order to focus on the possibility to treat the disease and not 'just' the symptoms.

SIT safety and clear messages require special emphasis:

Reassurance of the Targets about SIT Safety

General concern about SIT safety is still a barrier to its use in certain countries and/or regions; therefore, strategies to overcome this barrier should be developed.

Clear, Simple and Straight Messages about SIT

Effectiveness

Lay press is a major tool to spread messages, and, in certain countries, special focus should be placed on women's magazine, whose influence in the public arena is remarkable. The same role, possibly even more impacting, is nowadays played by blogs: the women's ones and the mothers' ones, which are formidable and successful 'by word of mouth' (network of information).

Leaflet Distribution: Leaflets created for the pharmacies and doctors' offices can be easily added as supplement to the weekly/monthly magazines dedicated to health or women, or magazines of general interest.

Patients' Association Blogs. They should contain and implement discussion and awareness on SIT. A warning on this: the control of the information to prevent misleading, incorrect or wrong news has to be considered. Thus, competent persons should take the lead and the control of these tools/initiatives.

Social Networks (e.g. Facebook or Twitter). A group called 'Allergen-Specific Immunotherapy Friends' or 'I Like Allergen-Specific Immunotherapy' can be created and led by national or international opinion leaders.

Consequently, allergic patients will be more aware of SIT, and ask their GPs and pharmacists for SIT, because of the media campaign.

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References

1 Pawankar R, Canonica GW, Holgate ST, Lockey RF (eds): The World Allergy Organization White Book on Allergy. Milwaukee, World Allergy Organization, 2011.

2 Asher MI, Montefort S, Björksten B, Lai CK, Strachan DP, Weiland SK, Williams H, ISAAC Phase Three Study Group: 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;368:733–743.

3 Lamb CE, Ratner PH, Johnson CE, Ambegaonkar AJ, Joshi AV, Day D, Sampson N, Eng B: Economic impact of workplace productivity losses due to allergic rhinitis compared with select medical conditions in the United States from an employer's perspective. Curr Med Res Opin 2006;22:1203–1210.

4 Nathan RA: The burden of allergic rhinitis. Allergy Asthma Proc 2007;28:3–9.

5 Shaaban R, Zureik M, Soussan D, Neukirch C, Heinrich J, Sunyer J, Wjst M, Cerveri I, Pin I, Bousquet J, Jarvis D, Burney PG, Neukirch F, Leynaert B: Rhinitis and onset of asthma: a longitudinal population-based study. Lancet 2008;372:1049–1057.

6 Samoliński B, Fronczak A, Kuna P, et al: Prevention and control of childhood asthma and allergy in the EU from the public health point of view: Polish Presidency of the European Union. Allergy 2012;1398–1404.

7 James LK, Durham SR: Update on mechanisms of allergen injection immunotherapy. Clin Exp Allergy 2008;38:1074–1088.

8 Akdis CA: Therapies for allergic inflammation: refining strategies to induce tolerance. Nat Med 2012;18:736–749.

9 Bousquet J, Lockey R, Malling HJ: WHO Position Paper. Allergen immunotherapy: therapeutic vaccines for allergic diseases. Allergy 1998;53(suppl 44):1-42.

10 Bousquet J, Van Cauwenberge P: Allergic rhinitis and its impact on asthma (ARIA) WHO Position Paper. J Allergy Clin Immunol 2001;108:S147–S334.

11 Canonica GW, Bousquet J, Casale T, Lockey RF, et al: Sublingual immunotherapy: World Allergy Organization Position Paper 2009. WAO J 2009;2:223–281.

12 Passalacqua G, Canonica GW: Specific immunotherapy: beyond the clinical scores. Ann Allergy Asthma Immunol 2011;107:401–406.

13 Canonica GW, Passalacqua G: Disease modifying effect and economic implications of sublingual immunotherapy. J Allergy Clin Immunol 2011;127:44–45.

14 Berto P, Frati F, Incorvaia C: Economic studies of immunotherapy: a review. Curr Opin Allergy Clin Immunol 2008;8:585–589.

15 Valenta R, Ferreira F, Focke-Tejkl M, Linhart B, Niederberger V, Swoboda I, Vrtala S: From allergen genes to allergy vaccines. Annu Rev Immunol 2010;28:211–241.

16 Potter PC, Warner JO, Pawankar RS, Kaliner MA, Del Giacco S, Rosenwasser LJ, et al: Recommendations for competency in allergy training for undergraduates qualifying as medical practitioners: a position paper of the World Allergy Organization. WAO J 2009;2:150–154.

17 Warner JO, Kaliner MA, Crisci CD, Del Giacco S, Frew AJ, Liu GH, Maspero J, Moon HB, Nakagawa T, Potter PC, Rosenwasser LJ, Singh AB, Valovirta E, Van Cauwenberge P, World Allergy Organization Specialty and Training Council: Allergy practice worldwide: a report by the World Allergy Organization Specialty and Training Council. Int Arch Allergy Immunol 2006;139:166–174.

18 Chivato T, Valovirta E, Dahl R, de Monchy J, Bloch Thomsen A, Palkonen S, Jacobsen L: Allergy living and learning: diagnosis and treatment of allergic respiratory disease in Europe. J Investig Allergol Clin Immunol 2012;22:168–179.

19 Ryan D, Levy M, Morris A, Sheikh A, Walker S: Management of allergic problems in primary care: time for a rethink? Prim Care Respir J 2005;14:195–203.

20 Levy ML, Walker S, Woods A, Sheikh A: Service evaluation of a UK primary care-based allergy clinic: quality improvement report. Prim Care Resp J 2009;18:313–319.

21 EFA Book on Respiratory Allergies. Bruxelles, EFA, 2011 (http://www.efanet.org/documents/EFABookonRespiratoryAllergies-FINAL.pdf).

22 Charron M, Kramer J, Crocetti S: Allergy immunotherapy in the primary care setting: integrating national practice standards to promote safe delivery. J Nurs Care Qual 2006;21:187–193.

23 Pinnock H, Thomas M, Tsiligianni I, Lisspers K, Ostrem A, Stallberg B, Yusuf O, Ryan D, Buffels J, Cals JWL, Chavannes NH, Henrichsen SH, Langhammer A, Latysheva E, Lionis C, Litt J, van der Molen T, Zwar N, Williams S: The International Primary Care Respiratory Group (IPCRG) Research Needs Statement 2010. Prim Care Respir J 2010;19(suppl 1):S1–S20