Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
www.all-imm.com

SHORT COMMUNICATION OPEN ACCESS

Impact of COVID-19 in allergen immunotherapy: An Italian survey

Jaime Sánchez-López[a], Enrico Heffler[b,c], Giorgio Walter Canonica[b,c]*

[a]*Medical Department, Stallergenes Ibérica SA, Barcelona, Spain*
[b]*Department of Biomedical Sciences, Humanitas University, Milan, Italy*
[c]*IRCCS Humanitas Research Hospital, Milan, Italy*

Received 30 January 2022; Accepted 6 April 2022
Available online 1 September 2022

KEYWORDS
allergen immunotherapy;
COVID-19;
subcutaneous immunotherapy;
sublingual immunotherapy

Abstract
Allergen immunotherapy (AIT) is a common treatment for patients with allergic asthma and allergic rhinoconjunctivitis. There is evidence that the COVID-19 pandemic could have altered the administration of AIT in patients in some countries, as the pandemic caused major limitations to healthcare access and delivery. The objective of this study was to evaluate the impact of the disruption imposed by the pandemic on the perceptions and administration of AIT therapies in Italy. An online survey was carried out among Italian allergists between 22 February 2021 and 12 April 2021. The results show that Italian physicians (N=66) did not consider that the COVID-19 pandemic presented an added risk to patients with allergic asthma or rhinitis receiving AIT. Although most treatments continued, there were reduced rates of AIT therapy initiations and sublingual AIT was favored over subcutaneous AIT.

Introduction

The COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1] has had a major impact on society and created extraordinary challenges for the delivery of healthcare across the globe. The disruptive impact of COVID-19 was partly caused by the diversity and severity of its clinical manifestations, which ranged from asymptomatic to multi-organic failure and death, and by the initial lack of defined clinical protocols to combat it. Common signs of COVID-19 infection are respiratory disorders such as cough, shortness of breath, and difficulties in breathing, which could be similar to those observed in respiratory allergic disease.[2,3]

Respiratory allergies are often treated with allergen immunotherapy (AIT), the only disease-modifying treatment option available.[4] AIT actively modulates the immune system in allergy patients by reducing the production of specific IgE, regulating the Th2-polarized immune system, increasing IFN-γ production, and reducing allergic inflammation. AIT has been proven to be an effective therapy for patients with allergic asthma and allergic rhinoconjunctivitis.[5,6] Although patients with allergic asthma could have an increased risk of respiratory infections compared to those

***Corresponding author:** Giorgio Walter Canonica, MD, Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, 20090 Pieve Emanuele, Milan, Italy. *Email address:* giorgio_walter.canonica@hunimed.eu

https://doi.org/10.15586/aei.v50i5.595

with nonallergic asthma,[7] allergic asthma appears to have a protective effect against COVID-19 infection.[8] However, the possible impact of ongoing AIT in infected patients was uncertain. A joint statement by the "Allergy and Its Impact on Asthma" (ARIA) initiative and the European Academy of Allergy and Clinical Immunology (EAACI) recommended that both subcutaneous and sublingual AIT (SCIT and SLIT, respectively) could be continued in asymptomatic patients without suspicion of COVID-19 infection, but it should be discontinued in symptomatic patients, independent of disease severity, or patients with positive test results (RT-PCR).[9] This advice followed standard practice that patients experiencing an acute respiratory tract infection should temporarily discontinue AIT treatment until the infection is resolved.

Although there is evidence that the COVID-19 pandemic could have interrupted or altered the administration of AIT, there is limited data on the extent of these disruptions and their potential clinical effects.[10-12] Italy was the first European country to experience the spread of the COVID-19 virus in February 2020, which greatly impacted the healthcare system of the country,[13] and Italian physicians pioneered the organization of an allergy clinic during the breakout.[14] However, the experience of allergists with respect to ongoing or new AIT prescriptions is unknown. The objective of this survey was to evaluate changes in the perceptions, recommendations, and prescription patterns of Italian physicians as a result of the COVID-19 pandemic.

Methods

A web-based survey (SurveyMonkey®) of 18 questions was designed to evaluate, from the clinician's perspective, the impact of COVID-19 on allergic diseases and patients under AIT based on their clinical practice. The survey took place between 22 February 2021 and 12 April 2021. The responses from the physicians regarding the impact on AIT covered the period from the start of the pandemic (February 2020) to the date each physician completed the survey. Categorical variables were expressed as percentages.

Results

The survey was shared with a pool of 855 Italian physicians and a total of 66 physicians (7.7%) responded the survey. Most respondents were located in Lombardy (30.3%) and Lazio (12.2%). The majority were female (62.1%), aged 36–55 years (63.6%), and worked at public hospitals (43.9%). Of the patients treated by these physicians, 65% presented poly-sensitivities (Table 1).

Almost all respondents (92.4%) asked their patients about COVID-19 regularly during follow-up visits. Most physicians (48.5%) estimated that about 1/100 allergy patients have had COVID-19 (Table 1), in most cases "mild" (89.4%). There were no severe cases and no deaths from COVID-19 among the patients of the physicians surveyed. Asked if there had been a higher incidence of COVID-19 among patients with any specific allergic disease, 16.7% of the responders observed a higher incidence in patients with rhinitis and 9.4% with asthma, but most of them considered the disease was equal or less severe compared to other non-allergy patients. Only 7.6% and 4.6% of the physicians estimated that COVID-19 was worse for patients with asthma or rhinitis, respectively (Table 1).

Table 1 Clinical characteristics of the patients, according to the respondents.

Variable	% of respondents
Patients with allergic poly-sensitivities	65.0
Type of allergy	
Perennial	46.0
Seasonal	54.0
How many patients do you estimate had COVID-19?	
1/1000	19.7
1/100	48.5
1/10	25.8
1/5	3.0
1/3	3.0
Of your patients with COVID-19, what was its severity?	
Asymptomatic	4.6
Mild	89.4
Moderate	6.1
Severe	0
Fatal	0
Did you observe a higher incidence of COVID-19 in allergy patients?	
Food allergy patients	0
Allergic rhinitis	16.7
Allergic asthma	9.4
Of the patients with allergic asthma who had COVID-19, how severe was it compared with patients without respiratory allergy?	
More severe	7.6
Less severe	22.3
No difference	69.7
Of the patients with allergic rhinitis who had COVID-19, how severe was it compared with patients without respiratory allergy?	
More severe	4.6
Less severe	25.8
No difference	69.7

Almost all the respondents (98.5%) did not observe a higher incidence of COVID-19 among patients receiving AIT. Also, they considered that in allergy patients receiving AIT, COVID-19 was equal to or less severe than in patients without AIT (Figure 1A). However, up to 47.0% of the respondents indicated that they had reduced the prescription of new AIT during the pandemic (Figure 1B). The majority (93.0%) continued with the ongoing AIT during the pandemic, and only 5.0% recommended the interruption of AIT treatments (Figure 1C). Most of the physicians (75.8%) maintained their prescription habits, while 22.7% increased the prescription of SLIT versus SCIT (Figure 1D).

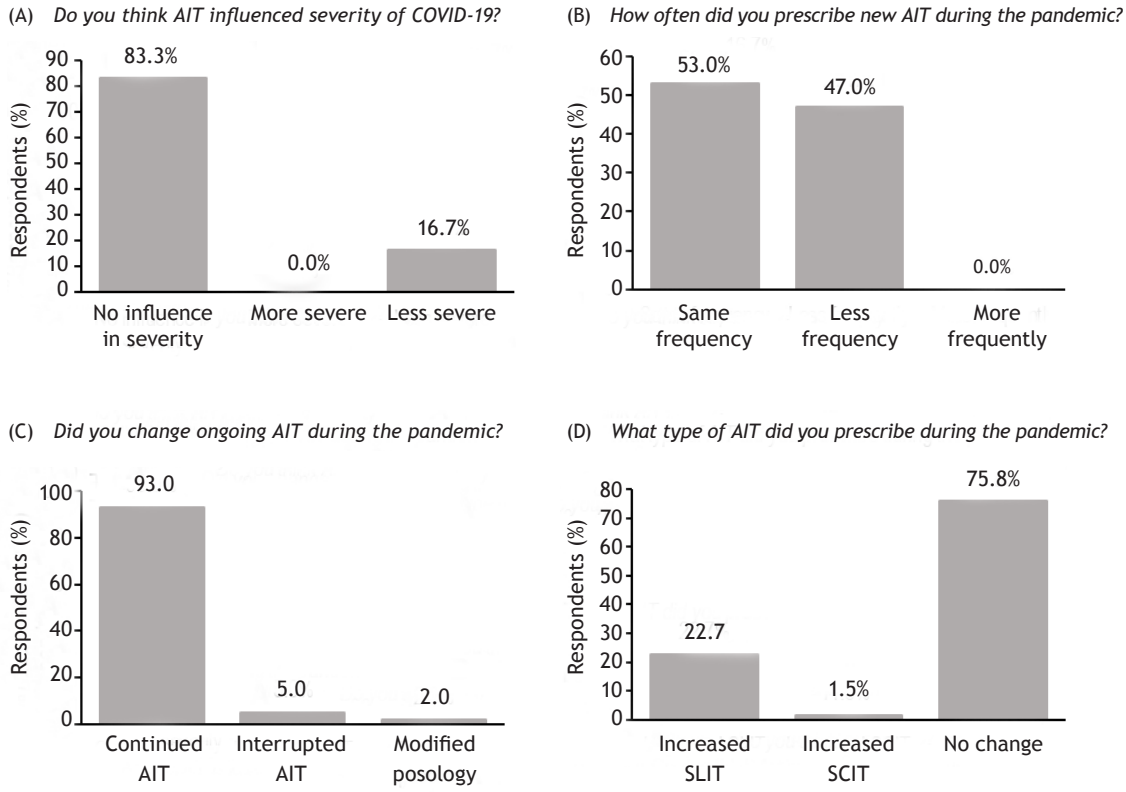

Figure 1 Influence of the COVID-19 pandemic on the perceptions and recommendations of Italian physicians regarding AIT. AIT, allergy immunotherapy; SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy.

Discussion

The survey presented here suggests that Italian physicians considered that COVID-19 did not present an added risk to patients with allergic asthma or rhinitis receiving AIT. Our data agrees with a recent international survey of allergy specialists which found that the respondents indicated that none of the allergy treatments, such as inhaled corticosteroids, AIT, or biological agents, had increased the risk of contracting COVID-19 infection.[15] The fact that almost all respondents (95.0%) recommended the continuation of AIT during the pandemic suggests good agreement with the ARIA/EAACI guidance.[9] However, our study also showed that about half of the respondents decreased the number of new AIT prescriptions during the pandemic, possibly reflecting the limitations of access to healthcare centers imposed by the pandemic, which could have restricted the initiation of new patients. This lower prescription rate agrees with the global survey, which found that 60% of physicians postponed initiation of AIT to a time point after the pandemic,[12] and with other recently published surveys,[16] but is at odds with the ARIA/EAACI guidance recommending AIT initiation as usual in patients without clinical symptoms and signs of COVID-19.[9] Although in Italy SLIT is normally the predominant AIT (87%), our finding that 22.7% of physicians increased SLIT could reflect a need to create an alternative to continuing the treatment during the pandemic lock-down. A similar trend was observed in the global survey and also in a recent survey from Spain and France.[12,16]

Although the precise reasons for reduced rates of AIT therapy initiations are unclear, our survey suggests that compliance with international clinical guidelines was high among Italian allergists. More detailed studies should be conducted to improve our understanding of how the COVID-19 pandemic affected allergy clinical practice and healthcare delivery, with the aim of improving our preparedness for potential similar disruptions in the future.

Acknowledgments

Francisco López de Saro (Trialance SCCL) provided medical writing support.

Funding

There was no funding for this study.

Conflicts of interest

JSL is an employee of Stallergenes Greer. GWC reports having received in the last 3 years research grants as well as a lecture or advisory board fees from Alk-Abelló, Allergy Therapeutics, Anallergo, Hal Allergy, and Stallergenes Greer.

Author's contributions

Study design: JSL, EH, GWC; data collection: EH, GWC; data analysis: JSL, GWC; writing of the first draft: JSL; revised and approved manuscript: JSL, EH, GWC.

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382(8):727-33. https://doi.org/10.1056/NEJMoa2001017
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506. https://doi.org/10.1016/S0140-6736(20)30183-5
3. Hagemann J, Onorato GL, Jutel M, Akdis CA, Agache I, Zuberbier T, et al. Differentiation of COVID-19 signs and symptoms from allergic rhinitis and common cold: An ARIA-EAACI-GA2 LEN consensus. Allergy. 2021;76(8):2354-66. https://doi.org/10.1111/all.14815
4. Bousquet J, Lockey R, Malling HJ. Allergen immunotherapy: Therapeutic vaccines for allergic diseases. A WHO position paper. J Allergy Clin Immunol. 1998;102(4 Pt 1):558-62. https://doi.org/10.1016/s0091-6749(98)70271-4
5. Dhami S, Nurmatov U, Arasi S, Khan T, Asaria M, Zaman H, et al. Allergen immunotherapy for allergic rhinoconjunctivitis: A systematic review and meta-analysis. Allergy. 2017;72(11):1597-631. https://doi.org/10.1111/all.13201
6. Dhami S, Kakourou A, Asamoah F, Agache I, Lau S, Jutel M, et al. Allergen immunotherapy for allergic asthma: A systematic review and meta-analysis. Allergy. 2017;72(12):1825-48. https://doi.org/10.1111/all.13208
7. Woehlk C, von Bülow A, Kriegbaum M, Backer V, Porsbjerg C. Allergic asthma is associated with increased risk of infections requiring antibiotics. Ann Allergy Asthma Immunol. 2018;120(2):169-176.e1. https://doi.org/10.1016/j.anai.2017.11.015
8. Yang JM, Koh HY, Moon SY, Yoo IK, Ha EK, You S, et al. Allergic disorders and susceptibility to and severity of COVID-19: A nationwide cohort study. J Allergy Clin Immunol. 2020;146(4):790-8. https://doi.org/10.1016/j.jaci.2020.08.008
9. Klimek L, Jutel M, Akdis C, Bousquet J, Akdis M, Bachert C, et al. Handling of allergen immunotherapy in the COVID-19 pandemic: An ARIA-EAACI statement. Allergy. 2020;75(7):1546-54. https://doi.org/10.1111/all.14336
10. Larenas-Linnemann DE, Epstein T, Ponda P, Bernstein D, Williams P, Creticos P. Gaps in allergen immunotherapy administration and subcutaneous allergen immunotherapy dose adjustment schedules: Need for prospective data. Ann Allergy Asthma Immunol. 2020;125(5):505-506.e2. https://doi.org/10.1016/j.anai.2020.07.015
11. Aytekin ES, Soyer Ö, Şekerel BE, Şahiner ÜM. Subcutaneous Allergen immunotherapy in children: Real life compliance and effect of COVID-19 pandemic on compliance. Int Arch Allergy Immunol. 2021;182(7):631-6. https://doi.org/10.1159/000514587
12. Pfaar O, Agache I, Bonini M, Brough HA, Chivato T, Del Giacco SR, et al. COVID-19 pandemic and allergen immunotherapy-an EAACI survey. Allergy. 2021;76(11):3504-16. https://doi.org/10.1111/all.14793
13. Ricci G, Pallotta G, Sirignano A, Amenta F, Nittari G. Consequences of COVID-19 outbreak in Italy: Medical responsibilities and governmental measures. Front Public Health. 2020;8:588852. https://doi.org/10.3389/fpubh.2020.588852
14. Malipiero G, Paoletti G, Puggioni F, Racca F, Ferri S, Marsala A, et al. An academic allergy unit during COVID-19 pandemic in Italy. J Allergy Clin Immunol. 2020;146(1):227. https://doi.org/10.1016/j.jaci.2020.04.003
15. Tanno LK, Demoly P, Martin B, Berstein J, Morais-Almeida M, Levin M, et al. Allergy and coronavirus disease (COVID-19) international survey: Real-life data from the allergy community during the pandemic. World Allergy Organ J. 2021;14(2):100515. https://doi.org/10.1016/j.waojou.2021.100515
16. Rodriguez del Rio P, Caimmi D, Rico P, Vidal C, Carmen M, Pintoiu IM, et al. Real-life report of allergen immunotherapy management during the COVID-19 outbreak in France and Spain. Clin Exp Allergy. 2021:cea.14043. https://doi.org/10.1111/cea.14043