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Research Article

Allergen-Specific Immunotherapy: A Possible Role in the Incidence and Course of SARS-Cov-2 Infection in Allergic Patients

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Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has a high impact on patients with chronic diseases. The vast majority of studies indicate that allergic diseases do not represent a risk factor for COVID-19 susceptibility nor cause a more severe course of disease and allergic patients were recommended to continue allergen-specific immunotherapy (AIT) throughout the Covid-19 pandemic. Studies to evaluate the role of allergen-specific immunotherapy in SARS-CoV-2 infection have not yet been performed.

The aim of our study has been to evaluate, through specific questionnaires, the incidence and the disease severity in allergic patients receiving AIT compared to non-treated allergic patients. We also evaluated the quality of life and the psychological impact of the SARS-CoV-2 pandemic in these patients.

The data collected confirmed that allergic diseases are not a risk factor to SARS-CoV-2 infections and showed, for the first time, that patients receiving AIT have a lower incidence and a milder course of SARS-CoV-2 infection compared to non-treated allergic patients. Furthermore, patients receiving AIT have a better quality of life and a lower psychological impact of the SARS-CoV-2 pandemic.

However, further studies are needed to confirm the protective role of AIT against SARS-CoV-2 infections and to elucidate the underlying immunological mechanisms.

Keywords: Allergen-specific Immunotherapy; allergy; quality of life; compliance; Covid-19; SARS-CoV-2

Introduction

Coronavirus disease 2019 (COVID-19) is a highly contagious and infectious disease caused by the novel coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [1].SARS-CoV-2 has multiple clinical presentations from asymptomatic to severe lung injury and multiorgan disease, especially in older individuals and those with chronic comorbidities [2].

Regarding the relationship between SARS-CoV-2 infection and allergies, several studies highlighted that atopic patients are protected against severe course of SARS-CoV-2 infection and the genetic predisposition to any allergic disease is associated with reduced susceptibility to COVID-19 [3,4,5]. The possible mechanisms that could be associated with reduced susceptibility to the virus are: the over-expression of Th2 response that could limit tissue damage induced by inflammatory cytokine storm associated with Th1 responses in COVID-19 and the reduced expression of ACE2, the SARS-CoV-2 receptor.

Allergen immunotherapy (AIT) is the only curative approach for specific type I allergy [6].

AIT involves the gradual administration of increasing amounts of allergen that selectively modulate the allergen-specific Th2 immune response, through the induction of allergen-specific regulatory T (Treg) and B cells (Breg) and the increase in production of anti- inflammatory cytokine, such as IL-10 and TGF-β [7,8,9].

Because there is a potential protective effect driven by a Th2 response and an inflammatory cytokine storm associated with Th1 responses in COVID-19, allergic patients have been recommended to stop AIT in case of SARS-CoV-2 infection and continue it in the absence of infection or after healing [10,11,12,13].

There are no reports on whether a history of AIT will reduce the risk of infection and severe outcome in COVID-19 patients.

The aim of our study is to evaluate the incidence of SARS-CoV-2 infection in allergic patients receiving AIT versus non-treated allergic patients to find a possible protective role of AIT against SARS-CoV-2 infection. We also evaluated compliance to AIT and the psychological impact of the SARS-CoV-2 pandemic in allergic patients.

Material and Methods

Study Population

A total of 431 patients (209 males and 222 females) aged 18-70 with allergic rhinitis, food allergy and venom allergy were enrolled in this study. 257 patients received AIT with aeroallergens and bee or vespid venom, 174 were not treated. Data were collected from June 2020 to November 2021 at Fondazione Universitaria Policlinico A. Gemelli IRCCS.

Diagnosis and treatment of hymenoptera venom allergy was determined according to the EAACI guidelines [14]. Diagnosis and treatment of allergic rhinitis (AR) and asthma were in accordance with ARIA and The Global Initiative for Asthma (GINA) guidelines [15,16].

Questionnaires

Patients were assessed using anamnestic questionnaire (administered online, over the phone or in person during clinical follow-up), regarding personal information and questions about the allergic disease diagnosed, ongoing therapy (AIT or drug therapy), compliance to AIT, possible SARS-CoV-2 infection and its course.

Quality of life was assessed using the Short-Form 36-Item Health Survey (SF-36) and Health- Related Quality of Life-4 (HRQOL-4) questionnaires [17,18].

Statistical Analysis

The population has been described in its demographic and clinical characteristics applying descriptive statistics techniques. Qualitative variables have been presented as absolute frequencies and percentages. Quantitative variables have been summarized with mean and standard deviations. The normality of data has been verified with the Kolmogorov–Smirnov test. Proportions were compared applying the Chi-square test. A p-value < 0.05 was considered statistically significant. All the statistical analyses have been performed with SPSS 25.

Results

431 patients (209 males and 222 females) were included in the present study.

257 (59,6%) were undergoing allergen-specific immunotherapy, while the remain 174 (40,4%) allergic patients were not treated and represented the control population (Figure 1). During the COVID-19 pandemic, 85 patients (19,7%) suffered from SARS-CoV-2 infection: 21 were undergoing AIT and 64 were not treated (Table 1; Figure 2; Figure 3). Most of the patients evaluated had had a mild form of SARS-CoV-2 infection; only 4 patients referred a more severe infection and of these 1 was receiving AIT and 2 were untreated. None of the patients who had contracted SARS-CoV-2 infection has been hospitalized confirming the protective role of allergic diseases.

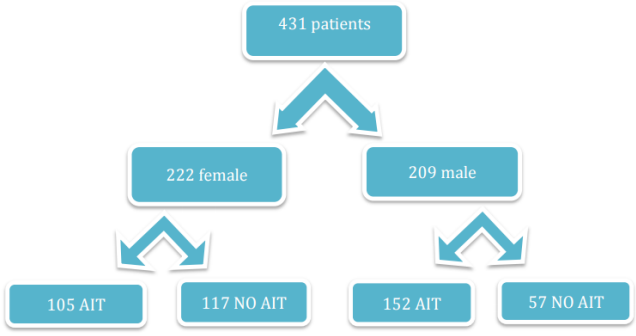

Figure 1: Characteristics of the Population Examined

Features	n, (%)
Female	222 (51.5%)
Male	209 (48.5%)
Allergen-specific Immunotherapy (AIT)	257 (59.6%)
SARS-CoV-2 infection	85 (19.7%)

Table 1: Cases of SARS-CoV-2 infection referred.

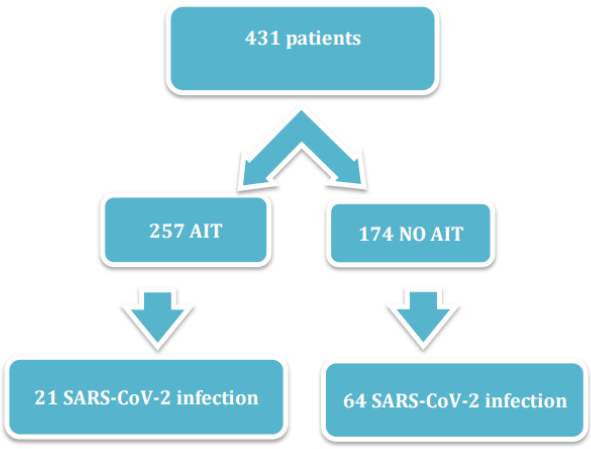

Figure 2: Cases of SARS-CoV-2 Infection Reported in Allergic Patients Treated and Untreated

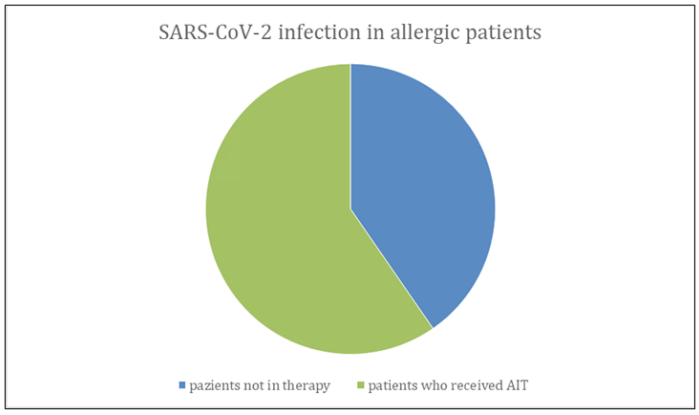

Figure 3: SARS-CoV-2 Infection Reported in Allergic Patients Treated and Untreated

These data evidence a possible protective role of AIT in patients infected with SARS-CoV-2 (p< 0,005).

Several studies have shown that COVID-19 pandemic has reduced compliance to AIT [19-23].

The data collected confirmed a reduced compliance to AIT which was higher in female patients than in male patients (47.3% vs 72.7%, p< 0,005). (Table 2)

	AIT	NO AIT	p-value
SEX			P<0.005
Female	105 (47.3%)	117 (52.7%)	
Male	152 (72.7%)	57 (27.3%)	
SARS-CoV-2 infection	21 (8.2%)	64 (36.8%)	P<0.005

Table 2: Compliance to Allergen-Specific Immunotherapy

Furthermore, the questionnaires aimed at assessing the quality of life of patients (SF-36 and HRQOL-4), highlighted a better quality of life and a lower psychological impact of the SARS- CoV -2 pandemic in patients undergoing treatment with AIT (Tables 3 and 4).

	p-value (AIT vs NO AIT)
General health	0.053
Health change	0.554
Physical functioning	0.693
Role limitations (physical)	0.007
Role limitations (emotional)	0.089
Social functioning	0.052
Pain	0.017
Energy/fatigue	0.247
Emotional-well being	0.01

Table 3: Short-Form 36-Item Health Survey (SF-36) In Allergic Patients

	AIT	NO AIT	p-value
a) General health (%)			0.079
Excellent	78 (30.4%)	43 (24.7%)	
Very good	114 (44.4%)	69 (39.7%)	
Good	60 (23.3%)	55 (31.6%)	
Fair	5 (1.9%)	5 (2.9%)	
Poor	0 (0%)	2 (1.1%)	
b) Days of not good physical health (mean, SD)	1.72 (4.62)	4.21 (7.97)	0.048
c) Days of not good mental health (mean, SD)	2.77 (6.16)	4.89 (8.68)	0.016
d) Days of normal activities influenced by health (mean, SD)	0.67 (2.84)	4.60 (9.13)	<0.005

Table 4: Health-Related Quality of Life-4 (HRQOL-4) in Allergic Patients.

Conclusions

In conclusion, the data collected showed that the protective role of allergic diseases versus SARS-CoV-2 infections and the reduced compliance to AIT during Covid 19 pandemic described in the literature were confirmed in patients enrolled in this study.

For the first time, the possible protective role of AIT in preventing SARS-CoV-2 infection and in determining a mild clinical course of Covid-19 was highlighted.

Furthermore, our study showed a reduced quality of life especially in allergic patients not subjected to AIT, probably due to less control of allergic symptoms and the risk of worsening during SARS-CoV-2 infection.

The study had some limitations: data collected were self-reported by the patients and the sample examined is too small to define the real impact of immunotherapy in the prevention or during the COVID19 disease. Further studies are required to confirm this data and to elucidate the underlying immunological mechanisms.

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