

Summary

At the beginning of SARS-CoV-2 pandemic, in the absence of "targeted" therapies, the national health authorities have introduced some measures aimed at reducing the spread of infection in the community [lockdown, social distancing, personal protective equipment (PPE), personal hygiene and disinfection of living environments]. All the containment measures have led to both positive and negative effects in patients with allergic diseases. We believe that further studies should be undertaken to investigate the possible correlations between SARS-CoV-2 infection and allergy, from a broader perspective. In particular, the risk factors for the development of undesirable effects should be investigated, especially in healthcare professionals forced to use PPE and sanitizing agents for a long time. However, since the COVID-19 pandemic probably will not be short-lived, the use of such protective aids will necessarily be widespread even in the general population. Therefore, further studies on the materials used for the production of PPE and sanitizing agents would be necessary to reduce their sanitizing and, in some cases, toxic potential.

1 - Introduction

The role of allergic diseases and related treatments as a possible risk factor for severe SARS-CoV-2 infection has started to be investigated since the beginning of the COVID-19 pandemic, on 11th March 2020. In patients with asthma, it has been postulated that high doses of inhaled corticosteroids might facilitate the replication of the virus in the airways, with detrimental effects especially in case of poorly controlled asthma.

The lack of specific therapies against SARS-CoV-2 pushed the Authorities to strict measures aimed at spread control: lockdown, social distancing, personal protective equipment (PPE), personal hygiene and disinfection of living environments. As a consequence, the effect of SARS-CoV-2 and of the above-mentioned measures on allergic diseases has become a matter of interest too, in the allergy field.

The purpose of this contribution is to provide an update on this topic and elucidate pros and cons for allergic patients.

2 - Effects of SARS-CoV-2 and lockdown on allergic diseases

Particular attention has been paid to the overall effect of lockdown in patients with allergic respiratory diseases (1). It is likely that the reduction of respiratory infections due to lockdown, social distancing, face masks, and hand washing had a role in the improvement of some clinical outcomes such as reduction of asthma hospitalizations (2,3), both in adults and children (4). It has been suggested that the lockdown and the consequent changes in exposure to different kinds of pollution may have different -and sometimes opposite- effects in patients, depending on the type of sensitization, namely worsening of clinical symptoms in patients sensitized to "indoor" allergens, and improvement in those sensitized to "outdoor" allergens (5). In addition, pandemic and lockdown had an impact not only on respiratory allergies, but also on food allergy.

2.1 - Respiratory allergy: effects in indoor environments

It has been hypothesized that lockdown might be a risk factor for development of allergic diseases due to the more prolonged exposure to sensitizing proteins and chemical agents present in indoor environments (6). During the lockdown, higher levels of pollutants and in particular polycyclic aromatic hydrocarbons (PAHs) were found, compared to the pre-COVID-19 period, due to the increase of domestic activities (e.g. cooking, cleaning, heating) (7), and despite the decreased production of outdoor pollution and consequently of its level in indoor environments (8).

As expected, the “home confinement” due to pandemic has had negative clinical effects on patients with allergic rhinitis to dust mites. In fact, a worsening of upper airway symptoms, as well as an increase in the use of specific drugs (anti-H1 agents, nasal steroids, decongestants, etc.), has been documented in spring 2020, compared to spring 2019 (9). Similar results have been demonstrated by Yucel et al. (10) in a group of children with rhinitis and / or bronchial asthma with or without sensitization to dust mites.

In the other hand, a substantial improvement in asthma symptoms (assessed by Asthma Control Test, drug use, frequency of exacerbations, etc.) has been observed during the 2020 lockdown compared to the same period of the previous year. The lower frequency of any viral infections due to school closures was considered the main cause of the favourable course of asthma in children (10). However, in children with associated mite allergic rhinitis it has been showed a significant increase in the severity of nasal and conjunctival symptoms in the period March-May 2020, compared to the same months of 2019. No significant increase in the same nasal/ocular symptoms was reported in subjects with asthma and non-allergic rhinitis (10).

2.2 - Respiratory allergy: effects in outdoor environments

During the pandemic period, an improvement of allergic rhinitis has been demonstrated in patients sensitized to "outdoor" allergens, especially to pollens (5), but also regardless of the type of allergen (11). Damialis et al. (12) demonstrated, in 31 countries, that high atmospheric levels of allergenic pollens were associated with high rates of SARS-CoV-2 infections regardless of the subjects' atopic status. Just before the start of the SARS-CoV-2 pandemic, the same authors had highlighted that high allergenic pollen counts had an effect facilitating the spread of respiratory viruses as pollens were able to reduce the innate immune defenses against viruses (13).

Recently, Gelardi et al. (14) have demonstrated a significant improvement in sino-nasal clinical outcomes (e.g. nasal obstruction, postnasal discharge, thick nasal discharge etc.) and a decrease of drug use in patients with seasonal allergic rhino-conjunctivitis from pollen in Italy during the lockdown, compared to the same period in 2019.

2.3 - Effects on food allergy

Musallam et al.(15) have shown that food allergic reactions (FARs) occurred with a significant lower incidence during the lockdown period (April-May 2020) compared to the previous 3 months. There are several possible explanations for this finding. For example, primary caregivers may have been more careful in feeding their allergic children, to minimise the need of medical aid and access to the emergency room during the pandemic, or they had to eat home-made food instead of meals from restaurants due to the restrictions which is likely to decrease the frequency of unintentional FARs (13). Moreover, Nachshon et al (16) have observed, in Israel, a significant reduction in the rate of home epinephrine-treated reactions during the COVID-19 lockdown (March 15-April 30, 2020), in patients undergoing oral immunotherapy (OIT) for food allergy, compared with the events occurred over the same time frame from 2015 to 2019. These results suggest that potentially avoidable triggers (e.g. exercise, fatigue, infections) may contribute significantly to the rate of adverse reactions during OIT (16).

3- The role of filtering masks in allergy

The use of face masks is particularly widespread to prevent inhalation of chemical agents in areas with high levels of pollution or in professional environments (e.g paint workers) (17,18). Especially in Asian countries, surgical masks are used to prevent the spread of seasonal viruses such as influenza (19). In allergy practice, PPE together with nasal filters and "barrier" materials are the most common devices to avoid contact with allergens (20). PPE (associated with the use of gowns, shoe covers and protective goggles) are essential tools in the prevention of both occupational allergy in individuals who work with animals (e.g. in animal housing), and passive transfer of animal allergens from work environments to private houses (21,22).

Unsurprisingly, the massive use of PPE has led to significant inconveniences in the millions of people who have been forced to wear PPE for many hours a day (23). Difficulties in breathing, communicating and recognizing faces, dermatological issues, sweating etc. represent the most common discomforts reported by patients (23).

3.1 - Possible role of filtering masks in pollen allergy

Very few studies have shown the effectiveness of PPE in people with allergic rhinitis. Dror et al. (24) have documented that the use of professional PPE (surgical or N95) reduced the severity of symptoms of chronic allergic rhinitis (regardless of the type of allergen) in healthcare professionals. The nurses scored their allergic rhinitis symptom severity before and after wearing face masks for 1 week at work. Godoh et al. (25) documented a reduced penetration of Japanese cedar pollens in eyes and nasal cavities by using face-masks and eyeglasses, but no data were collected about symptoms.

Since in Campania region (Italy), during the COVID-19 lockdown, the use of protective masks outdoors has been mandatory since April 2020 and considering that April is a peak period of pollen release of some common herbaceous species, such as *Parietaria* (26,27), Liccardi et al.(28) compared, in patients with seasonal allergic rhinitis (SAR), the self-reported symptoms experienced in April 2020 (with face masks) with the ones of April 2019 (without face masks), and the correlation with time-of-use of masks, taking also into account the role of potential confounders (changes in pollen and pollution levels). Thirteen Allergy units or Centers belonging to the Italian Association of Hospital and Territorial Allergologists (AAIITO, Campania Region) participated in the study. The patients used non-standardized face masks mainly made of different washable fabrics, because of the well-known shortage of medical face masks during the first months of SARS-CoV-2 pandemic. Data showed similar and even higher environmental pollen levels in April 2020, compared to April 2019, stable values of PM_{2.5}, PM₁₀, slight increases of O₃, and a reduced trend of other pollutants. Based on this background, the results of the real-world study suggest that simple non-professional face masks can reduce the nasal symptoms of SAR induced by seasonal pollens, at least during seasonal pollen peaks. Certified and professional face masks (e.g. N95, FFP2) are likely to be even more effective, since they can filter also the ultra-fine components of pollen grains (28).

4- COVID-19 PPE, hygiene and allergy

The rapid and dramatic increase in the use of PPE (face masks, gloves, gowns, shoe covers, etc.) and sanitizing chemicals for hands and surface cleaning has led to an increasing amount of adverse events

especially in healthcare professionals (29) but also in the general population (30). Frequent use of hand sanitizers (containing antimicrobial agents, sensitizing compounds etc.) has increased the occurrence of contact dermatitis especially in healthcare professionals (31). The increase in reactive hand contact reactions was documented among surgeons and anaesthesiologists by comparing the frequency of these events before and during the months of the pandemic (32).

Although hands are the most frequent target of contact dermatitis case reports have documented significant facial contact dermatitis after prolonged use of surgical polypropylene face masks (33) probably due to formaldehyde and 2-bromo-2-nitropropane-1,3-diol (33).

Corazza et al. (34) have shown that surgical masks can induce even severe contact urticaria, even if the diagnostic tests were unable to highlight the sensitizing agent(s). Face masks can cause adverse events also in the ENT area.

An online survey conducted among healthcare professionals highlighted the benefits of using face masks due to the reduction of aerosol transmission protection from pollution and infections, reduction of nasal crusting, prevention of risky habits like nose picking or face touching (35). However, several drawbacks of using face masks have also been reported, like fogging of eyeglasses, ear pain due to elastic band, difficulty in breathing, excessive sweating, skin marks and scarring due to pressure etc.(35).

Primov-Fever et al.(36) reported deterioration of sinonasal quality of life in the COVID-19 pandemic period, possibly caused by mask-wearing, especially for a prolonged time, irrespective of the mask type. Irritant rhinitis (IR) is defined as an inflammatory and/or irritative response of the nasal mucosa due to non-allergic stimuli, e.g. a physical or chemical stimulus. IR has been found in 46 patients with nasal symptoms upon usage of FFP masks in private or professional environments, and this diagnosis was confirmed by the finding of polypropylene fibres in nasal lavage fluids (37).

The findings of the studies on face masks should encourage medical companies to produce more “airway-minded” PPE, considering also the high request for these devices in the future, due to COVID-19 pandemic or other possible pandemics.

It is also worth noting that the massive use of sanitizing agents (alcohol-based products) in spray formulations for the sterilization of surfaces and confined environments can induce an “ocular surface disease” in the absence of adequate protections (38). Serious undesirable effects may result by mixing different cleaning products, as this can generate hazardous fumes/gases (39). Chronic exposure to these gases can induce asthma and chronic bronchitis (40).

5- Lessons learnt from the “pandemic model”

The SARS-CoV-2 pandemic and the related lockdown can be considered a study model to evaluate the possible effects of these events in allergic patients, particularly in case of respiratory allergy.

During the interruption – or massive reduction- of many human activities, there has been a drastic decrease in pollution of external environments with positive effects in patients with respiratory allergies due to the reduction of the “adjuvant” and “direct ” effects on the airways. On the contrary, the compulsory indoor confinement has increased the reactivity of the airways to chemical agents and allergens of indoor environments. This study model confirmed the key role of pollution on airway inflammation and that, in the industrialized countries, a free-of-pollution environment does not really exist.

Furthermore, social distancing is likely to have reduced the circulation of seasonal viruses which commonly act as asthma exacerbating factors. In fact, the urban lifestyle is characterized by the frequent

gathering of people both in open (e.g. stadiums, public events in general, etc.) and confined environments (subways, theaters, cinemas, schools, etc.).

Another lesson learnt from the pandemic / lockdown is the usefulness of the face masks. This device, especially in the FFP2 or N95 version, is crucial in the prevention of viral and bacterial infections, but it has also proved good efficacy in reducing the symptoms of allergic rhinitis, being able to filter both allergens and pollutants. A more widespread use of masks by patients with respiratory allergy in the presence of high environmental levels of allergens, pollutants or micro-organisms would therefore be recommended, even after the pandemic emergency.

Concerning the hyper-hygiene state caused by the pandemic, although disinfectants and sanitizers have a key role in the prevention and control of COVID-19, important concerns must be considered about their large-scale use, including the side effects on human and animal health along with harmful impacts exerted on the environment and ecological balance (41).

6- Conclusions

This review of the available literature shows that the containment measures adopted around the world against the COVID-19 pandemic can induce both positive and negative effects in subjects with allergic diseases (figure 1). We believe that further studies should be undertaken to investigate the possible correlations between SARS-CoV-2 infection and allergy from a broader perspective. In particular, the risk factors for the development of adverse events should be investigated, especially in healthcare professionals forced to use PPE and sanitizing agents for a long time. However, since the COVID-19 pandemic probably will not be short-lived, the use of such protective aids will necessarily be widespread even in the general population. It has also been suggested that improper contacts and relationships between humans and animals (particularly birds), and other conditions related to the environment, could lead to the onset of other pandemics in the future (42).

Therefore, further studies on the materials used for the production of PPE and sanitizing agents would be necessary to reduce their sensitizing and, in some cases, toxic potential.

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Legend

Figure 1. Pros and cons of containment measures of SARS-CoV-2 infection.