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A new form of irritant rhinitis to filtering facepiece particle (FFP) masks (FFP2/N95/KN95 respirators) during COVID-19 pandemic

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ABSTRACT

Filtering facepiece particle (FFP) masks are important items of personal protective equipment in fighting COVID-19 pandemic. They shall protect the wearer of the mask from particles, droplets, and aerosols, but they also can prevent the spread of aerosol-transmitted viruses if the wearer becomes infected. Most often, FFP respirators consist of multiple layers of non-woven fabric made from polypropylene. Worldwide, FFP respirators are subject to various regulatory standards that specify physical properties and performance characteristics. During the SARS-CoV-2 pandemic, health authorities have temporarily repealed standards for respirators.

We report on 46 patients that presented with rhinitis-like symptoms strongly associated to the use of FFP masks. Some of them were obliged to use FFP masks in their work environment. Nasal endoscopy showed edemata of the nasal mucosa that significantly decreased after a period of non-use of FFP masks. Subjectively reported symptom levels decreased after cessation of FFP use for 3 or more days. The presence of polypropylene fibres isolated from nasal rinsing solution was significantly associated with the use of FFP masks in our patients. Material safety and performance deregulation of FFP masks can pose a health risk. Thus, especially health care professionals and other individuals with occupational need for FFP masks should be aware of possible hazards that come with COVID-19 pandemic protection measures.

Keywords: Filtering facepiece masks, Irritant rhinitis, Allergy, FFP2-Mask, N95-mask, KN95-Mask

DEAR EDITORS,

On March 11, 2020, the World Health Organization (WHO) declared "*corona virus disease 2019* (COVID-19)", transmitted by the severe acute respiratory syndrome coronavirus (SARS-CoV-2), a pandemic viral disease. Since the first reported infections in China,[1] the number of infected patients, as well as fatalities, is dramatically increasing worldwide.[2] COVID-19 patients can demonstrate symptoms of airway infection such as fever, coughing, shortness of breath, and sore throat, but also muscle and joint pain, headache, nausea or vomiting, and diarrhoea. Nasal symptoms are mostly limited to dysfunctions in smell and taste. While most of the registered cases show a mild and transient course of disease, in about 5% of patients admission to an intensive care unit (ICU) is necessary due to severe pneumonia with respiratory failure and for example coagulopathy,

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pulmonary embolism, and the involvement of other organs including kidney, heart, and the central nervous system.[3] SARS-CoV-2 infections are most often transmitted by direct mucosal contact to droplet-borne viruses originating from the nose or mouth of an infected individual.[4] Such exposure of droplets to the eyes, mouth, or nose, or inhalation of sneezed or coughed virus-containing particles from the air, as well as smear infection, are regarded as being common transmission mechanisms. Recommendations for health care-providers and patients include thorough hand washing with soap and water, frequent use of hand sanitizers and disinfectants, avoidance of touching face and eyes, avoidance of social contact to people with cold-like symptoms, and using the necessary personal protective equipment including face masks, eye protection, and others.[5-7] Filtering facepiece particle (FFP) masks are among the most frequently used items of personal protective equipment (PPE) in the medical field, and legislation and mandated protection measures in most public and business areas have made them an inherent feature to everyday life in many countries. Their purpose is to protect the wearer of the mask from particles, droplets, and aerosols, but they can also prevent the spread of aerosol-transmitted viruses if the wearer becomes infected. However, depending on the design of the FFP, the latter only applies to masks without exhalation valve, filtering both inhaled and exhaled air and therefore providing both self-protection and extrinsic protection. Models with exhalation valve do not filter the exhaled air. FFP respirators work by filtering out particles, thanks to the structure of their nonwoven material, as they get trapped and are forced to make twists and turns through the dense network of the material's fibres, which may be as thin as a single micron. In addition, masks may have electrostatically charged material to further attract particles. With increasing amounts of particles within the nonwoven mask material, it becomes an even more efficient filter. However, the build-up also makes the mask more difficult to breathe through, which is why the masks and filters are made to be disposable.

FILTERING FACEPIECE MASK REGULATIONS

FFP respirators are subject to various regulatory standards around the world. These regulations specify required physical properties and performance characteristics in order for FFP masks to comply with a certain protective standard. During the SARS-CoV-2 pandemic, health authorities often referenced these standards when making recommendations for minimal protective standard in different situations, depending on infection risk. A very commonly recommended standard for health professionals is FFP2; however, nomenclature of standards differs throughout the world. Table 1 summarizes important international standards for respirator masks. It may be reasonable to consider China KN95, AS/NZ P2, Korea 1st Class, and Japan DS2 FFRs as "equivalent" to US NIOSH N95 and European FFP2 respirators, for filtering at least 94% of non-oil-based particles such as virus bio-aerosols. Within these categories, masks are expected to function very similarly to one another, and conformity testing to physical standard is required for certification.

Name	Country/Region
FFP2	European Union
N95	United States
KN95	China
P2	Australia/New Zealand
Korea 1st class	South Korea
DS	Japan

Table 1. International equivalent standards for FFP2- masks

In Germany, where they are facing a severe shortage of FFP masks in many areas, such regulation has been temporarily suspended early during the COVID-19 pandemic. This concerns regulation on FFP mask performance as well as wearer safety, which is usually guaranteed by the *conformité européenne* (CE) label certification. According to these exceptions, … in order to cope with the current crisis situation regarding the containment of COVID-19 (…), medical face masks and FFP masks which are marketable in the United States of America, Canada, Australia or Japan, are also considered marketable in Germany, even if they do not bear a CE/NE marking".

MATERIAL AND METHODS

The Ethics Committee of the local authorities gave approval to this study. Study subjects gave permission to participate in the form of written informed consent. Patients had no history of sinonasal diseases based on anamnesis or chart history. Visual Analogue Scales (VAS) were used to document patient-reported symptoms of rhinitis such as sneezing, itching, nasal blockage, and rhinorrhea immediately after wearing an FFP2 respirator masks and after a minimum 3 days of absence from using the mask (eg, after a weekend in occupational users). Mucosal irritation, secretion, and edema in nasal endoscopy was graded using VAS.[8]

Possible type-1 inhalation allergies were ruled out using an extended version of the GA^{2}LEN skin prick test set.[9,10] Moreover, patients were examined for possible type-4 allergies using the standard patch test set of the German Contact Dermatitis Research Group (DKG) complemented by the fabric material of the used FFP respirators,[11-13] and no contact allergies to standard path test or face mask fabric were found. Bilateral nasal lavage with 5ml of isotonic saline solution was performed as described earlier.[14] Lavage fluid was centrifuged and analysed for eosinophilic

Patient reported nasal symptoms (VAS):	wearing FFP2	absence of FFP2	$n = 46$
sneezing VAS (0–10 cm)[a], mean (SD)	8.04 (1.41)	4.83 (1.12)	$\mathbf{p < 0.01}$
itching VAS (0–10 cm)[a], mean (SD)	9.16 (1.05)	3.27 (2.24)	$\mathbf{p < 0.01}$
nasal blockage VAS (0–10 cm)[a], mean (SD)	7.86 (2.31)	4.72 (3.02)	$\mathbf{p < 0.01}$
rhinorrhea VAS (0–10 cm)[a], mean (SD)	8.13 (2.09)	2.85 (2.74)	$\mathbf{p < 0.01}$
Endoscopic nasal findings (VAS)			
Mucosal edema VAS (0–10 cm)[a], mean (SD)	6.88 (1.57)	2.79 (1.06)	$p < 0.01$
irritation VAS (0–10 cm)[a], mean (SD)	5.74 (1.17)	5.03 (1.46)	$p > 0.05$
secretion VAS (0–10 cm)[a], mean (SD)	8.76 (1.94)	3.22 (1.72)	$\mathbf{p < 0.01}$
Cell mediators in nasal lavage			
Tryptase (ng/ml)#, mean (SD)	41.7 (18.3)	15.4 (16.9)	$p < 0.01$
ECP (ng/ml)#, mean (SD)	78.3 (46.7)	87.1 (50.8)	$p > 0.05$
total IgE (kU/l)	<0.1	<0.1	NA
polypropylene fibres in nasal lavage			
number, median (SEM)	3.8 (7.9)	0.4 (0.7)	$p < 0.01$
length, median in mm (SEM)	3.4 (13.7)	3.1 (11.6)	$p > 0.05$

Table 2. Symptoms, nasal endoscopy, and lavage findings in irritative rhinitis patients *SD, standard deviation; SEM, standard error of the mean; VAS, visual analogue scale. a.* Higher scores indicate worse status.//#established norm values for nasal tryptase range from 12.0 to 18.7 ng/ml (95% confidence interval) and for ECP from 84.4 to 102.6 ng/ml (16, 19)

cationic protein (ECP), Tryptase, total IgE, and in addition for any solid material under the microscope.

RESULTS

Between March and May 2020, a total of n = 46 patients (24 females, age 34,2 ± 12.7yrs; mean ± SD) were seeking advice in our centres for suspected "allergy to FFP respirators". Seventeen health care workers were included in this study. Patients reported on new-onset symptoms of rhinitis, such as sneezing, itching, nasal blockage, and/or watery nasal discharge after wearing their FFP for a minimum of 2 hours or longer (Table 2). Longer periods of FFP use were regularly associated with more severe symptoms. Endoscopic signs of irritation and edema with mucosal swelling and watery secretions were mainly found in the area of the inferior and middle turbinates and quantified using VAS (Table 2). Endoscopic signs of secretion and edema were significantly lower after 3 days of absence from mask use (both $p < 0.01$), but not irritation ($p > 0.05$) (Table 2).

After wearing FFP2 respirators for a minimum of 3 hours, a mean number of 3.8 ± 7.9 (mean ± SD) polypropylene fibres were found in nasal lavage fluid per nasal side with a maximum of n = 47 fibres in the lavage fluid of one patient, while the number decreased to 0.4 ± 0.7 (mean ± SD) after 3 mask-free days ($p < 0.01$). At a "wearing day", polypropylene fibres had a length of 3.4 ± 13.7mm (mean ± SD) with a maximum length of 42mm in the lavage fluid of 1 patient, while with absence from FFP2 respirators for >3 days the fibre length was 3.1 ± 11.6mm (mean ± SD) ($p > 0.05$) with a maximum length of 37mm in the lavage fluid of 1 patient.

ECP in nasal lavage fluid was within normal range independent on the wearing of FFP2 respirators ($p > 0.05$) and total IgE was below detection limit, while Tryptase significantly increased at "wearing days" in comparison to days with absence from FFP2 respirators ($p < 0.01$) (Table 2).

All positive skin prick and patch test results were unrelated to either seasonal or occupational allergen exposure of the patients and thus, no type-1 and/or type-4 sensitization was suspicious for causing the rhinitis-like symptoms.

DISCUSSION

In this study, 46 patients with nasal symptoms upon usage of FFP masks in a private or professional environment most likely encountered irritant rhinitis. Missing increase of ECP and local IgE levels under detection limit with elevated Tryptase in nasal secretion after exposure to FFP respirators demonstrates activation of nasal mast cells without activation of eosinophils and IgE production. Substantial accumulation of polypropylene fibres was found in nasal lavage fluid after FFP utilization with adequate symptoms and endoscopic findings. Most importantly, rhinitis symptoms as well as FFP material “fallout” decreased significantly after a period of non-usage of FFP masks.

Irritant rhinitis (IR) is defined as an inflammatory and/or irritative response of the nasal mucosa due to causes attributable to non-allergic stimuli, eg, a physical or chemical stimulus.[15] If symptoms can be matched to a particular work environment, the pathology can be classified as "work-exacerbated" rhinitis. Irritant rhinitis belongs to a subgroup of non-allergic rhinitis (NAR) and several agents are reported to be associated.[15] The induction of nasal hyperreactivity (NHR) with one or more nasal symptoms upon encounter of unspecific environmental stimuli such as smoke, temperature/humidity changes, strong odors, and physical or other irritants is a key clinical feature.[15] Given their length of several millimetres, here-found polypropylene fibres are capable to cause such IR in patients with or without NHR. Particles of this size are too large to penetrate epithelial borders and are therefore treated similarly to other foreign bodies on nasal mucosa, causing classical symptoms of rhinitis. The cellular and inflammatory mechanisms causing IR in our study subjects are still under investigation; however, here-assessed parameters in nasal secretions emphasize a central role of mast cell degranulation. Mast cells are thought to be attracted by foreign body reactions and may attract macrophages through degranulation, maintaining and priming the inflammatory response in previous animal models.[16] Further studies are needed to

investigate these mechanisms in patients with face mask-related IR.

The here-presented mask-associated IR is unusual with regards to the broad use of FFP masks even before the pandemic. Reports on IR in health care workers and other mask-requiring professionals are rare, even though time of wearing was likely similar to the currently observed long periods due to COVID-19 outbreak. Hence, the deregulation of mask fabrication and material safety requirements, resulting in the widespread distribution of non-CE marked products, has to be discussed as a potential hazard to user safety. Our hypothesis is that the fabric of certain non-CE masks are more likely to seed parts of their fabric polypropylene into the inspiratory air flow, leading to accumulation on nasal mucosa and potentially throughout the airways. Due to the lack of branding information on the FFP masks used by the here-presented patients, a thorough investigation regarding CE certification and fulfilment of claimed physical standards was not possible for us, which presents a limitation to this study. In conclusion, with COVID-19 numbers decreasing in some countries and recovering of medical supply stocks, user safety has to become an equal priority for regulation authorities again. The development and validation of a patient questionnaire, eg, for health care professionals could be helpful to improve monitoring and detection of mask-related symptoms. Avoiding hazards in the work environment remains a challenge from different perspectives during the COVID-19 pandemic.

Abbreviations

COVID-19: coronavirus disease from the year 2019; FFP: filtering facepiece particle; N95 / KN95: technical / physical standard for filtering face masks (not penetrated by particles larger 0.3 µm, *N/KN* indicating that aqueous, but not oily aerosols are filtered; SD / SEM: standard deviation / standard error of the mean; CE: *conformité européenne* label indicating conformity to the EU-regulation 765/2008; PPE: personal protective equipment; VAS: visual analogue scale; ECP: eosinophilic cationic protein; WHO: World Health Organization

Author contribution

All authors made substantial contribution to study design, data acquisition or interpretation of data. LK, TH, AA, MS drafted the manuscript. KH, CM and JH revised it critically. LK,TH, AA, MS, KH, CM and JH gave final approval of the here-submitted version of the manuscript.

Ethics statement

The journals guidelines to ethics in publishing and research were respected. Ethics committee of the local authorities, the Landesaerztekammer of Rhineland-Palatinate gave approval to this study (No. 2020–15123).

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Consent for publication

All authors approved the publication of this work.

Availability of data and materials

Authors confirm to comply with the open data requirements of the journal. Datasets are presented in the manuscript.

Potential competing interests

LK,TH, AA, MS, KH, CM and JH declare no competing interests.

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