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Original Article

Nano-treatment of HEPA filters in COVID-19 isolation rooms in an academic medical center in Saudi Arabia

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ABSTRACT

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), has spread globally. The major reservoir for SARS-CoV-2 transmission remains controversial, with the airborne route remaining a possible transmission vehicle for carrying the virus within indoor environments. This study aimed to detect contamination of SARS-CoV-2 in high-efficiency particulate air (HEPA) filters within hospital isolation rooms of confirmed COVID-19 patients, exploring the role of nano-treatment of these filters with silver and titanium dioxide nanoparticles (Ag/TiO_2 NPs).
Materials and methods: We investigated the effectiveness of Ag-NPs/TiO_2-treated HEPA filters in the air of rooms occupied by patients with confirmed COVID-19 in a university teaching hospital in the Eastern province of Saudi Arabia during the first wave of the pandemic. Ag/TiO_2 NPs were designed and coated on HEPA filters to examine the filtration efficiency and antiviral ability in the presence of aerosolized virus particles. A total of 20 viral swab samples were collected from five patients' rooms before and after treatment with nanoparticle-prepared solutions into the sterile virus-transporting media. Samples were evaluated for SARS-CoV-2 with a reverse transcription-polymerase chain reaction.
Results: Two samples taken from the HEPA filter air exhaust outlets prior to nano-treatment tested positive for SARS-CoV-2 RNA in the intensive care unit, which has stringent aerosolization control procedures, suggesting that small virus-laden droplets may be displaced by airflow. All air samples collected from the HEPA filters from the rooms of patients with confirmed COVID-19 following nano-treatment were negative.
Conclusion: We recommend further experimental exploration using a larger number of HEPA filters in areas with aerosol-generating procedures, along with viability studies on the HEPA filters to facilitate decision-making in high-risk facilities regarding the replacement, storage, and disposal of HEPA filters in wards occupied by cases diagnosed with a highly transmissible disease.

1. Introduction

COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has brought forth an urgent need for facility managers to better understand and implement the design, maintenance, and operations of high-efficiency particulate air (HEPA) filters and ventilation procedures that ensure the indoor air

*Abbreviations:*SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2

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quality in healthcare facilities [1,2]. HEPA filters cleanse the air of aerosols and droplets. They are, therefore, broadly used to eliminate spread of infections in high-risk healthcare settings as they can capture droplets along with aerosolized bacteria and viruses [3,4]. HEPA filters are capable of removing > 99 % of aerosolized particles, [5,6] can increase the effective air changes per hour (ACH), and remove particles, reducing the risk of transmission in general wards with insufficient isolation rooms, as is the case with the large, sequential waves of the COVID-19 pandemic [7].

Based on the Centers for Disease Control (CDC) recommendations, HEPA filtration can help prevent the spread of SARS-CoV-2 [8].

A combination of HEPA filtration supplemented with ultraviolet (UV) light has been suggested as a preferred solution for stopping viral spread [9]. Patients with potential risk of exposure to aerosolized infections are routinely placed on airborne precaution units where air is purified using in-duct HEPA filters before recirculation [10].

The diameter of SARS-CoV-2 is estimated to be approximately 0.1 µm [11]. Thus, facility managers are concerned about the ability of HEPA filters to trap SARS-CoV-2 to help prevent its spread through airborne transmission. Concomitantly, different nanomaterials are utilized as potential disinfectants by enhancing their physicochemical features. Other unique properties of nanoparticles (NPs), such as size, shape, and phases, contribute to viral inactivation.[16] Assessing the filtration potential of silver and titanium dioxide (Ag-TiO2)-coated NPs applied on air filters to improve air quality without affecting the efficiency of air filtration in the presence of infectious aerosols is necessary to use them as potential inactivators of respiratory pandemic viruses [12]. Ag-TiO_2 NPs possess extensively high antimicrobial activity compared to that of other nanomaterials, owing to their chemical stability, catalytic activity, elevated thermal and electrical conductivity, surface-enhanced Raman scattering, and nonlinear optical properties [13,14].

Ag/TiO_2 NPs exhibit antimicrobial properties through reactive oxygen species (ROS) generation without affecting the airflow and static pressure characteristics of the filters [15,16].

For infection prevention and control policies, understanding the dissemination of infectious particles with varied size range and the pattern of environmental contamination by SARS-CoV-2 are critical.

Nevertheless, higher energy is required to push air through HEPA filters than that required for basic heating, ventilation, and air conditioning (HVAC) filters. Although HEPA filtration systems can efficiently eliminate infectious air droplets, microorganisms may remain viable and continue to replicate on the filter surface. Subsequently, the filters themselves serve as contamination reservoirs for airborne pathogens in healthcare environments [17].

COVID-19 pandemic has necessitated an urgent demand for novel antimicrobial approaches to aid in infection prevention. Even though the integration of Ag NPs into filters has been evaluated [18], the efficacy of the filters against coronaviruses was reportedly limited. Therefore, the reduced survival effect cannot fulfil the criterion of the required log reduction needed to be registered as a biocidal product [19,20].

Clinically, several trials have generated efficient antimicrobial HEPA filters that could aid in eliminating or inactivating infectious agents. However, high levels of microorganismal have been found on the filter material for extended periods of time, suggesting that contaminated filters could act as potential sources for pathogens that may further dislodge from the filter and pose infection risk.

To prevent the SARS-CoV-2 spread, developing HEPA filters with antimicrobial properties in the HVAC systems in healthcare settings is necessary.

Aerosols are generally available in sub- and super-micron ranges, 0.25–1.0 µm and > 2.5 µm, respectively. Nanotechnology plays a pivotal role in this regard. Ag and TiO_2 are the most commonly used antimicrobials in developing air filters. In particular, metallic NPs, including Ag and TiO_2 NPs with inhibitory properties and bactericidal potential, could be viable for preparing nanocomposites for HEPA filter nano-treatment. In HEPA filters, bactericidal/virucidal surfaces show tremendous potential. Photocatalytic material-based air filters, which produce ROS, and nano-TiO_2-based photocatalytic materials hopefully represent a solution for the aforementioned issues, with an efficiency exceeding > 99.99 %[20].

Accordingly, this study aimed to detect SARS-CoV-2 in HEPA filters from rooms with a risk of contamination, exploring the effect of nano-treatment of HEPA filters with Ag/TiO_2 in isolation rooms occupied by patients with confirmed COVID-19.

2. Materials and methods

2.1. Research setting

This study took place at the King Fahad Hospital of the University in Saudi Arabia (a 550-bed hospital). Environmental swab samples were taken from airborne isolation rooms occupied by patients diagnosed with COVID-19, and the intensive care unit (ICU). Only areas where COVID-19 (four rooms) patients resided for at least 24 h and not more than eight days were subject for air sampling. A room occupied by a non-COVID-19 patient in an adjacent ward was used as a negative control besides the assay's laboratory controls. As per the hospital policy, each patient room was cleaned and decontaminated at the beginning of each shift using sodium hypochlorite at 5 % concentration (50 g/liter), equivalent to 50,000 ppm of available chlorine, and 70 % alcohol spray.

2.2. Nanoparticle deposition method

The selected HEPA filter was HEPA AStroCel with an efficiency of 99.995 % @ 0.3 µm, size 575 × 575 × 112 (tested at 0.45 m/s), and resistance of 65 Pa.

The nanoparticles used were titanium dioxide (TiO_2 Anatase, 99.5 % 40 nm, Sigma) and silver (Ag, 99 %, 40 nm, Sigma). The combination of nanoparticles was mixed with methanol (Fisher-Scientific) to create a nanocomposite. HEPA filters were treated with 0.5 g/l of Ag/TiO_2 NPs in methanol as the carrier solvent (300 ml) to form nanocomposites.

This nanocomposite was then aerosolized using a pressurized sprayer system. The aerosolized spray with a pressure of 4 bars was directed toward the HEPA filter while maintaining a spray distance of about 20 cm for 10 min to ensure adhesion of the NPs to the HEPA filter surface (Fig. 1). The selection of nanoparticles was based on their safety profiles and non-toxicity; the dislodged nanoparticles were verified to fit within acceptable standards.

2.3. Filter system sampling

Multiple swab samples (moistened with the viral transport media immediately before sampling) were collected from the HVAC HEPA filter systems at all isolation sites in the hospital before and after treating filters with the nanocomposite Ag/TiO_2 NPs to detect any trapped SARS-CoV-2 on the filters and before room fumigations (room disinfection with aerosolized hydrogen peroxide (AHP) [21] and patient transfer. Swabs were placed into viral transport media (Vircell, Granada, Spain), transfered on ice packs to the laboratory, and stored at −80 °C until testing.

2.4. Viral genome detection

Reverse transcription-polymerase chain reaction (RT-PCR) was used to detect SARS-CoV-2 in environmental samples before and after the nano-treatment [22,23]. Viral nucleic acid was extracted using Bioneer extraction system (Bioneer Corporation, Republic of Korea), and RT-PCR was conducted using a Powerchek 2019-nCoV

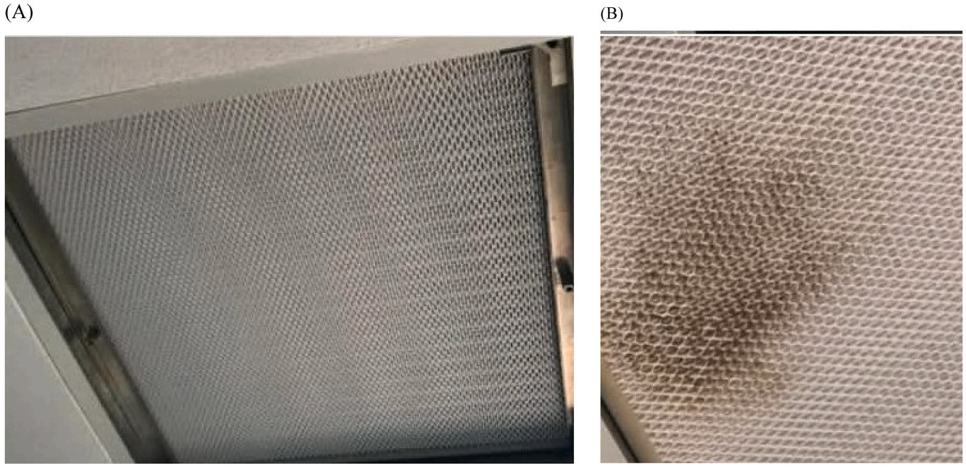

Fig. 1. (A) Normal HEPA filter and (B) nanocoated sprayed HEPA filter.

Real Time PCR kit (Analis, Namur, Belgium) to detect the E gene of betacoronavirus and the RdRp gene sequence specific to SARS-CoV-2. Samples tested positive were further assessed using an Xpert® Xpress SARS-CoV-2 system (Cepheid, Sunnyvale, CA, USA) that targets the E and N2 genes of SARS-CoV-2 following the manufacturers' recommendations and using positive and negative controls in each run. The lowest cycle threshold (Ct) values (cycles needed for the fluorescent signal to cross the threshold in RT-PCR) were used to evaluate viral load. Samples were processed under a biosafety cabinet Class IIB in a Biosafety Level 2 laboratory to minimize occupational risk since no viral propagation or aerosol-generating procedures were performed [24].

A "no template" control, consisting of RNase-free water, was used in every run to monitor the contamination during sample extraction and processing. In addition, negative and positive controls were processed in parallel to all samples to monitor if the instrument and kit worked properly. Additionally, an internal control targeting human RNaseP mRNA, used to detect the presence of potential PCR inhibitors in the specimens, was used through the entire sample processing procedure.[25].

3. Results

RNA was successfully extracted from all samples. Among the five treated HEPA filters sampled from different hospital sites (including ten swabs before and ten swabs after nano-treatment of the filters) from five patients' rooms, one filter (2 of 10; 20 %) was positive for SARS-CoV-2 RNA (Table 1).

Samples collected using a high-flow nasal cannula (two swabs) from HEPA filters in room 4 (ICU with aerosol-generating procedures) 2.5 h after the last decontamination were positive for SARS-CoV-2 (Ct value, 38.3) before nano-treatment (Tables 1 and 2).

Swabs collected from isolation rooms (rooms 1–3) occupied by confirmed COVID-19 cases with aerosol-generating procedures showed no evidence of viral load before and after treatment (Table 2). HEPA filters of room 5, occupied by a non-COVID case, remained negative for viral presence before and after NP application (Tables 1 and 2).

4. Discussion

The ability of SARS-CoV-2 virions to persist in the air for extended periods is evident as SARS-CoV-2 genome in aerosol particles larger than 1 μm in diameter were detected in rooms occupied by COVID-positive patients [26]. Institutions have employed several advanced environmental disinfection procedures for areas with confirmed or suspected COVID-19 cases to inhibit secondary transmission. In this study, we performed nano-treatment of HEPA filters, swabbing, and viral testing to assess the efficiency of HEPA filter decontamination in a COVID-19 facility. Frequent screening and monitoring of respirators and HEPA filter settings are crucial, as caution has been recently raised that mechanical air movement across filters may occur, resulting in the spread of contaminated air, particularly in the presence of dust [26,27].

Our small study generated prior to-and-after decontamination data demonstrating a low initial positivity level of 20 % in the filters. This detection rate of environmental viral RNA is consistent with a previous study involving a novel portable air treatment unit designed to eliminate airborne particles and destroy microorganisms using electrostatic capture and nonthermal plasma reactors [28]. Although early studies highlighted the potential risk of airborne transmission of SARS-CoV-2, the overall transmission and secondary attack rates support a primary mode of droplet transmission in the absence of aerosol-generating procedures, notwithstanding the potential of these viruses for long-distance airborne transmission in places with poor ventilation [29,30].

Filters enhanced with antimicrobial coating are in demand and have attracted increasing attention in the past few years. In one

Table 1
Frequency of SARS-CoV-2 viral genome detection before and after nano-treatment of HEPA filters in a COVID-19 hospital ward.

Type of room	Pre-nano-treatment		Post-nano-treatment		CT values
	RNA detected	RNA not detected	RNA detected	RNA not detected	
Rooms 1–3 **Isolation ward**	0	6	0	6	NEG
Room 4 (ICU/AGP) * High-flow nasal cannula	2	0	0	2	38.3
Non-COVID room	0	2	0	2	NEG
Total	2	8	0	10	–

*Intensive care unit with aerosol-generating procedures.

Table 2
Characterization of COVID-19 patients occupying HEPA filtered sampled rooms.

Room no		Patient age	Triage score	AGP*	Time after admission	Time after last decontamination
Room 1	Isolation ward	59 years	8	Yes	3 days	4 h
Room 2	Isolation ward	71 years	10	Yes	2 days	2 h
Room 3	Isolation ward	67 years	15	Yes	5 days	1 h
Room 4	ICU	73 years	18	Yes	7 days	2.5 h

*Aerosol-generating procedures

study, filters coated with tannic acid, known for its antiviral properties, have shown efficient microbial-capturing properties using the influenza virus as a model [31]. The utilization of Ag NPs has been previously assessed on filter settings against aerosolized bacteriophage MS2 virus particles with promising results [27,32]. Although HEPA filters may block particles with a diameter > 0.3 µm, viral particles with a smaller diameter, such as influenzae virus (approximately 100 nm), can pass through them. This prompted the development of filters equipped with improved virus capturing potential. Filters designed with antiviral coats such as sodium chloride, zinc oxide, sialyl lactose, and poly ethylenimine have been found efficient despite the variable cost, narrow-spectrum activity, and potential substance toxicity [31,33]. On the other hand, Ag/Tn NPs represent the potential for a wide-spectrum antiviral coat that is inexpensive and environmentally friendly. These properties are particularly useful during pandemics as Ag/Tn NPs could serve as an affordable option for low-resource clinical settings [31]. The CDC, the National Institute for Occupational Safety and Health, and the American Society of Heating, Refrigerating and Air-Conditioning Engineers have recommended approaches that combine filtration and disinfection to clean the air-conditioning systems of rooms [34,35]. Although intensified UV light and ozone gas have been used as an alternative approach to eliminate SARS-CoV-2 from contaminated surfaces [36,37], data are still emerging about the efficiency of their widespread and standardized use to replace existing technologies and therefore, should be evaluated for their reliability and cost. Viral resurgence is possible with potential virus variants of clinical significance; therefore, healthcare settings should be equipped with reliable systems capable of efficiently eliminating viruses.

An intensive care-based study showed a higher positivity rate of SARS-CoV-2 after routine disinfection using hydrogen peroxide wipes and ammonium chloride-based detergents [36]. The current study was investigated in an airborne isolation facility with an ACH of 15; therefore, with a relatively lower risk of viral droplet accumulation. This area of research focusing on the use of antimicrobial agents, nano-treatment, and HEPA filter coating is still in its infancy. Thus, more applied, extensive studies are warranted to characterize the viral viability and reproduction on the filters, particularly in rooms where aerosol-generating procedures are performed. Such data are significant when determining procedures for disposing, sorting, or HEPA filters used in high-risk healthcare institutions. Nano-treatment of the filters could inhibit viral accumulation on filters that otherwise serve as a potential source of environmental contamination and might increase the filter durability. Thus, whenever HEPA filters are used, they should be disposed and disinfected with caution to eliminate potential risk of secondary contamination [3].

Filter durability is another important factor. During COVID-19 pandemic, various new air-purifying technologies, such as installing UV light-containing equipment and HEPA filters, have been designed and tested. However, majority of these models could not ideally fit with most of the existing HVAC systems as considerable infrastructural upgradation was needed. Comparatively, the novel nanoparticles described in the present study can be reliably used to coat the filters of the existing HVAC systems with no further adjustments.

This groundwork finding suggests the need for hospitals to consider testing HEPA filters used in isolation suits with a high turnover of patients, to establish the possible need for disinfection strategies, besides contact- and droplet-based precautions particularly during viral resurgence. Including other droplet and airborne pathogens in future research could help attain a more comprehensive antimicrobial outlook for nanoparticle-based decontamination of isolation hospital units.

5. Conclusion

We demonstrated the ability of Ag/TnO_2 NPs to eliminate SARS-CoV-2 RNA in a subset of HEPA filters placed in rooms occupied by patients with confirmed COVID-19 and the practicality of applying this strategy. Our preliminary data suggest that air ventilation systems within hospitals may represent a potential reservoir where SARS-CoV-2 virions can be trapped in epidemic settings. Nevertheless, further exploration of the efficacy of Ag and TiO_2-based nano-decontamination systems in healthcare settings using a larger sample and in multiple centers is warranted. Nano-treatment of HEPA filters can possibly serve as an effective adjunct strategy to conventional methods of terminal decontamination. Investigating the mode of interaction between infectious aerosol particles of SARS-CoV-2 and HEPA filters is important to establish and adopt best practices for controlling the potential dissemination of COVID-19.

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Authors' contributions

All authors made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Data availability statement

All data required to understand this article are presented in the study any raw data further requested will be provided from the corresponding authors

Conflicts of interest

The authors declare no conflicts of interest.

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Ethical approval

The study was approved by the Institutional Review Board of Imam Abdulrahman Bin Faisal University (IRB no 2020-01-144).

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jiph.2022.07.004.

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