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Concise Communication

How well do N95 respirators protect healthcare providers against aerosolized influenza virus?

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Abstract

N95 respirator masks are recommended for protection against respiratory viruses. Despite passing fit-testing 10% of N95 respirator users encountered breakthroughs with exposure to influenza virus compared to full protection provided by a powered air purifying respirator. The current recommendation of N95 respirators should be evaluated for endemic and emerging scenarios.

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Relatively little is known about how best to protect ourselves and others against viral respiratory pathogens. This gap in knowledge is a major concern in light of endemic and emerging Influenza viruses. The World Health Organization and the Centers of Disease Control and Prevention (CDC) recommend the use of N95 respirators during exposure to novel influenza viruses or during aerosol generating procedures involving seasonal influenza.[1,2] However, how well N95 respirators actually protect healthcare providers remains unknown.[3] We assessed the efficacy of a commercially available N95 respirator mask against a novel half-mask powered air purifying respirator (PAPR) in a human exposure model.

Methods

Healthy employees and students at Wake Forest School of Medicine (WFSM) were randomized to an N95 (Kimberly-Clark N95 particulate filter respirator, Irving, TX) or aPAPR (Pioneer 300, Celios, Tampa, FL) exposure group. None of the participants had received the seasonal, live attenuated influenza vaccine strains (LAIV; 2015/16 FluMist Quadrivalent, Gaithersburg, MD; $2 \times 10^{6.5–7.5}$ fluorescent focus-forming units) before enrollment. Informed consent was obtained from all participants. The study was approved by the WFSM Institutional Review Board.

Participants completed qualitative fit-testing (Qualitative Fit Test Apparatus FT-10, 3M, St Paul, MN). Nasal swabs (FLOQSwabs, Copan Flock Technologies, Brescia, Italy) were obtained to establish absence of influenza virus before exposure. Study subjects were asked to dress in disposable attire and to don and fit-check the respective devices and airtight goggles. After placement of the individual in a test chamber and a 2-minute evacuation run of a HEPA air filtration unit, subjects were exposed to aerosolized LAIV (MQ5800 Airial, Medquip, Bluffon, SC) for 20 minutes (Fig. 1). During exposure, participants performed a standardized set of movement and reading exercises to mimic normal activity. Nasal swabs were collected following a test chamber evacuation run.

Virus RNA extraction was carried out using the QIAamp Viral RNA Mini Extraction Kit (catalog no. 52906, Qiagen, Valencia, CA). For quantitative reverse transcription polymerase chain reaction (qRT-PCR) detection of the influenza A strains, the M gene of the master donor virus strain A/Switzerland/9715293/2013 (H3N2)–like virus MP segment was the amplification target, using the following primer set (IDT, Integrated DNA Technologies, Skokie, IL):

- Flu A forward primer (FLUAM-1F): 5′-AAGACCAATCCTGT CACCTCTGA-3′ (IDT ref. no. 137171480)
- Flu A reverse primer (FLUAM-1R): 5′-CAAAGCGTCTA CGCTGCAGTCC-3′ (IDT ref. no. 137171481)

A DNA vector containing the M gene region for influenza A was synthesized by GeneArt (Burlingame, CA) in a pMA(ampR) vector. The influenza A standard curve (DNA vector) was used to quantify the amount of viral RNA present in the samples produced from the aerosolized runs (standard curve, 0.1–100,000 copies/μL). Quantitative real-time PCR was performed using the QuantiTect SYBR Green RT-PCR Kit (catalog no. 204245, Qiagen). Plates were assayed in the ABI Prism Fast RT-PCR system (ABI, Thermo Fisher Scientific, Waltham, MA) using thermocycler conditions described previously.[4]

Participants were randomized using block randomization of varying block sizes. Summary statistics, including means, ranges,

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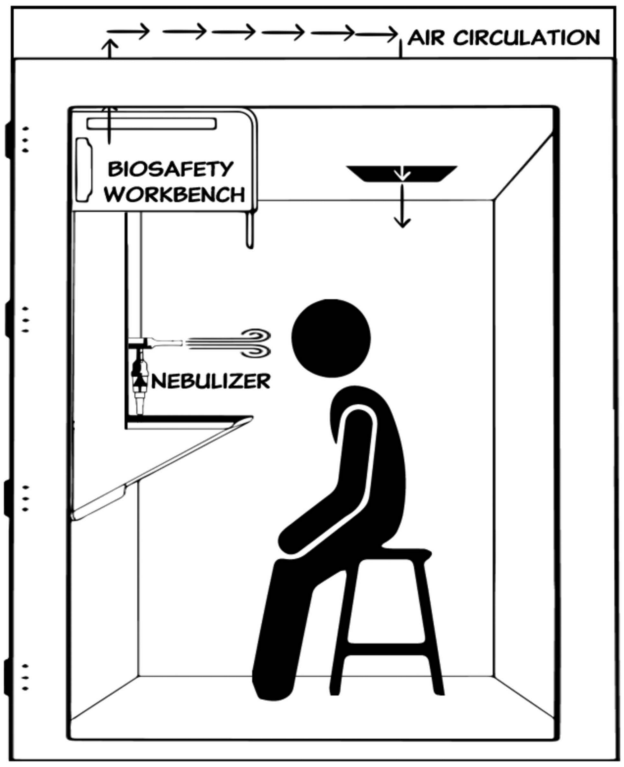

Fig. 1. Exposure test chamber set-up.

and proportions, were calculated for the demographic data of the subjects. To estimate the exact 95% confidence interval (CI) around the proportion observed, the Clopper-Pearson method was used for calculation of that range. SAS version 9.4 software (SAS Institute, Cary, NC) was used for all analyses.

Results

In total, 58 participants were exposed to LAIV (mean age, 31 years; range, 21–49 years; male, 33%). Influenza virus was newly detected on the nasal swabs of 3 subjects after exposure wearing N95 respirators (10%; n = 29; 95% confidence interval [CI], 0.02–0.27) (Fig. 1). Total RNA recovered from the 3 subjects were 4,745 copies, 5,471 copies, and 65,206 copies (mean, 25,141 copies). No virus was found in subjects wearing the PAPR (n = 29; 95% CI, 0–0.12). The 3 subjects with virus detection included 2 white males (ages 31 and 40 years) and 1 black female (age 23 years).

Discussion

There has been considerable controversy regarding the infection control recommendations for influenza.[5] Seasonal influenza is thought to be transmitted via droplets, defined as large, heavier particles compared to smaller aerosols (droplet nuclei $\leq 5\,\mu m$). The CDC recommends surgical masks to block large droplet transmission.[1] N95 respirators should be worn during aerosol-generating procedures such as extubation and intubation, airway suction, and positive pressure ventilation, or when novel influenza strains are suspected.

However, a growing body of evidence indicates that influenza, seasonal or novel, is spread not only by large droplets but also via droplet nuclei able to travel long distances and remain airborne for extended periods of time. Surgical masks have been shown to provide inadequate protection against droplet nuclei with failure rates ranging from 10% to 90%.[6] N95 respirators require certification by the National Institute for Occupational Safety and Health based on filter efficiencies with an assigned protection factor (APF) of 10.[7] The APF indicates a reduction of aerosol concentration to one-tenth of the outside concentration, which equates to blocking 90% of biological hazards including viruses. Investigators have attempted to assess the protective impact of N95 respirators and surgical masks.[3] Although respiratory protection reduced respiratory infections, no definitive differences were detected between N95 respirators and surgical masks.

We previously undertook a pilot study testing surgical masks against N95 respirators using a human exposure model.[4] With goggles, surgical masks failed to protect 3 of 4 participants. N95 respirators blocked influenza in 4 of 5 participants. Building upon these findings, we set out to assess the efficacy of N95 respirators. A novel half-mask PAPR was selected as a control providing an APF of at least 50 (ie, 98% biohazard blockage).

Participants wearing N95 respirators encountered breakthrough events to LAIV in 3 of 29 cases (10%), confirming our previous findings. This matches the 90% blocking of biohazards indicated by the APF of 10. The PAPR completely blocked transmission of LAIV. The findings represent the protective efficacy of the devices since wearers covered their eyes disrupting trans-ocular transmission.[4]

This study has several limitations. We used vaccine strains diluted in saline solution to simulate exposure to influenza. Wild-type viruses naturally aerosolized by sneezing, coughing, or breathing may display different transmission characteristics. However, successful transmission was assessed directly after exposure, making it less likely to be influenced by the need for virus replication or signs of infectivity. RT-PCR is more sensitive than virus cell culture, but it does not provide proof of viability. Previous studies have correlated the amount of decay of influenza virus aerosols to RNA copies, establishing a ratio of 150–650 RNA copies to 1 tissue culture infectious dosage ($TCID_{50}$).[8] Given a human infectious dosage (HID_{50}) of 0.6–3 $TCID_{50}$, an RNA load of 90–1,950 copies is necessary to infect an individual.[9] In a previous study, all influenza emitters met the above threshold during routine care.[10] RNA copies recovered from the respiratory tracts of the 3 participants ranged from 4,500 to >65,000, superseding the HID_{50} and making inoculation likely.

Our knowledge regarding the efficacy of respiratory equipment against virus transmission is mainly based on material testing and field studies in outbreak situations. Using a controlled human exposure model this study demonstrated successful blockage in 90% of influenza virus transmissions for N95 respirators with eye protection. However, a 10% failure rate compared to the complete protection provided by a PAPR raises the question of acceptable limits for virus exposure especially to resistant or novel pathogens.

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References

1. Prevention strategies for seasonal influenza in healthcare settings. Centers for Disease Control and Prevention website. http://www.cdc.gov/flu/

https://doi.org/10.1017/ice.2018.326 Published online by Cambridge University Press

professionals/infectioncontrol/healthcaresettings.htm. Published 2018. Accessed September 6, 2018.
2. Epidemic- and pandemic-prone acute respiratory diseases: infection prevention and control for acute respiratory diseases in health-care facilities. World Health Organization website. http://www.who.int/csr/resources/publications/EPR_AM3_E3.pdf. Published 2008. Accessed September 6, 2018.
3. Offeddu V, Yung CF, Low MSF, Tam CC. Effectiveness of masks and respirators against respiratory infections in healthcare workers: a systematic review and meta-analysis. *Clin Infect Dis* 2017;65:1934–1942.
4. Bischoff WE, Reid T, Russell GB, Peters TR. Transocular entry of seasonal Influenza-attenuated virus aerosols and the efficacy of n95 respirators, surgical masks, and eye protection in humans. *J Infect Dis* 2011;204:193–199.
5. Chao YS, Spry C. *The Use of N95 Respirators for Protection against Droplet Borne Illness: A Review of the Clinical Effectiveness and Guidelines*. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2017.
6. Oberg T, Brosseau LM. Surgical mask filter and fit performance. *Am J Infect Control* 2008;36:276–282.
7. Assigned protection factors for the revised respiratory protection standard, 2009. Occupational Safety and Health Administration (OHSA) website. https://www.osha.gov/Publications/3352-APF-respirators.pdf. Published 2009. Accessed September 6, 2018.
8. Tellier R. Aerosol transmission of influenza A virus: a review of new studies. *J R Soc Interface* 2009;6 Suppl 6:S783–S790.
9. Alford RH, Kasel JA, Gerone PJ, Knight V. Human influenza resulting from aerosol inhalation. *Proc Soc Exp Biol Med* 1966;122:800–804.
10. Bischoff WE, Swett K, Leng I, Peters TR. Exposure to influenza virus aerosols during routine patient care. *J Infect Dis* 2013;207:1037–1046.

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