Aerosolization of COVID-19 and Contamination Risks During Respiratory Treatments

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Background: Aerosolized medications are frequently administered across the health care continuum to acutely ill patients. During viral pandemics, the World Health Organization and the Centers for Disease Control and Prevention advise the application of airborne precautions when performing aerosol-generating medical procedures, such as aerosolized medications.

Observations: Appropriate personal protective equipment (PPE), including fit-tested particulate respirators should be worn when administering nebulized medications to patients. These PPEs have been in short supply in the US during early phases of the COVID-19 pandemic, which is increasing the risk faced by health care workers (HCWs) who are treating patients using aerosolized medications. Despite taking appropriate precautions, HCWs are becoming infected with COVID-19. This may be related to secondary exposure related to viral longevity in fugitive emissions and viability on fomites.

Conclusions: We have expanded on non-US public health recommendations to provide guidance to frontline HCWs to enhance collaboration between clinicians, who are often siloed in their clinical practices, and ultimately to protect the federal workforce, which cannot sustain a significant loss of frontline HCWs.

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Beyond asthma and chronic obstructive pulmonary disease (COPD), inhalation therapy is a mainstay in the management of bronchiectasis, cystic fibrosis, and pulmonary artery hypertension. Several US Food and Drug Administration off-label indications for inhalational medications include hypoxia secondary to acute respiratory distress syndrome (ARDS) and intraoperative and postoperative pulmonary hypertension during and following cardiac surgery, respectively.[1-11] Therapeutic delivery of aerosols to the lung may be provided via nebulization, pressurized metered-dose inhalers (pMDI), and other devices (eg, dry powder inhalers, soft-mist inhalers, and smart inhalers).[12] The most common aerosolized medications given in the clinical setting are bronchodilators.[12]

Product selection is often guided by practice guidelines (Table 1), consideration of the formulation's advantages and disadvantages (Table 2), and/or formulary considerations. For example, current guidelines for COPD state that there is no evidence for superiority of nebulized bronchodilator therapy over handheld devices in patients who can use them properly.[2] Due to equivalence, nebulized formulations are commonly used in hospitals, emergency departments (EDs) and ambulatory clinics based on the drug's unit cost. In contrast, a pMDI is often more cost-effective for use in ambulatory patients who are administering multiple doses from the same canister.

The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) recommend droplet and contact precautions for all patients suspected or diagnosed with novel coronavirus-19 (COVID-19).[13,14] Airborne precautions must be applied when performing aerosol-generating medical procedures (AGMPs), including but not limited to, open suctioning of the respiratory tract, intubation, bronchoscopy, and cardiopulmonary resuscitation (CPR). Data from the severe acute respiratory syndrome (SARS-CoV) epidemic suggest that nebulization of medication is also an AGMP.[15-17]

Institutions must ensure that their health care workers (HCWs) are wearing appropriate personal protective equipment (PPE) including gloves, long-sleeved gowns, eye protection, and fit-tested particulate respirators (N95 mask) for airborne procedures and are carefully discarding PPE after use.[13,14] Due to severe shortages in available respirators in the US supply chain, the CDC has temporarily modified WHO recommendations. Face masks are now an acceptable alternative to protect HCWs from splashes and sprays from procedures not likely to generate aerosols and for cleaning of rooms, although there is no evidence to support this decision.

Internationally, HCWs are falling ill with

TABLE 1 Practice Guidance for Aerosolized Medications Use in Health Care Settings[1,2,4,8,9]

Organizations	Publication, y	Conditions	Recommendations
Global Initiative for Chronic Obstructive Lung Disease	2020	Chronic obstructive pulmonary disease	There is no evidence for superiority of nebulized therapy over handheld devices in patients who are able to use them properly. When using the bronchodilator pMDI for acute management, administer 1-2 puffs every h for 2-3 doses then every 2-4 h based on clinical response.
Faculty of Intensive Care Medicine and Intensive Care Society Guideline Development Group	2019	Acute respiratory distress	Do not suggest using the vasodilator iNO in adult patients based on low quality, consistent evidence suggesting a lack of mortality benefit and an association with renal dysfunction. Vasodilator use in severe right ventricular dysfunction or extreme hypoexemia fall outside the scope of this guidance.
Global Initiative for Asthma	2019	Asthma	Avoid overuse of ambulatory nebulized therapy as risk of death is higher with nebulized short-acting β-agonist compared to the pMDI equivalent. When using albuterol pMDI for exacerbations, administer 6 puffs initially with subsequent dosing in 1 hour guided by clinical response (adults). Alternative: may administer 2-4 inhalations every 20 min for 3 doses; if good response, can lengthen dosing interval to every 3-4 h.
American Association for Respiratory Care	2015		There is little published evidence demonstrating the effectiveness of aerosolized medications in secretion clearance in hospitalized adult and pediatric patients without cystic fibrosis (ie, no role for β-2 agonists, anticholinergics, N-acetylcysteine, dornase α, or hypertonic saline).
American College of Chest Physicians	2014	PHTN	Indicated for PHTN patients in WHO functional class III who have evidence of progression of their disease, and/or markers of poor clinical prognosis despite treatment with 1 or 2 classes of oral agents and for WHO functional class IV. Preference is for IV therapy. Options include epoprostenol, treprostinil, or iloprost. Major adverse effect is cough.

Abbreviations: iNO, inhaled nitric oxide; PHTN, pulmonary artery hypertension syndrome; pMDI, pressurized metered-dose inhalers; WHO, World Health Organization.

COVID-19. Data from Italy and Spain show that about 9% to 13% of these countries' cases are HCWs.[18,19] Within the US, the Ohio health department reports approximately 16% of cases are HCWs.[20] It is possible that 20% of frontline HCWs will become infected.[21] Evolving laboratory research shows that COVID-19 remains viable in aerosols for up to 3 hours postaerosolization, thus making aerosol transmission plausible.[22] Nebulizers convert liquids into aerosols and during dispersal may potentially cause secondary inhalation of fugitive emissions.[23] Since interim CDC infection control guidance is to allow only essential personnel to enter the room of patients with COVID-19, many facilities will rely on their frontline nursing staff to clean and disinfect high-touch surfaces following routine care activities.[24]

Achieving adequate fomite disinfection following viral aerosolization may pose a significant problem for any patient receiving

TABLE 2 Advantages and Limitations of Drug Aerosols in Health Care Settings[12]

Aerosol Devices	Products	Advantages	Limitations/Barriers to Use
Pressurized metered-dose inhalers	• Albuterol • Ipratropium	• Suitable for emergencies (rapid onset) • Most patients can achieve the targeted inspiratory flow rate of 30 L/min via slow inhalation • High local concentration in the lung with a reduction in systemic adverse effects	• Patient-specific characteristics may be a barrier to administration (eg, cognition, physical impediments, and clinical acuity may prohibit coordination of inspiration and inhaler actuation) • Inhaler education requirement and/or reassessment for correct administration technique is necessary • Optimal use, particularly for those with coordination issues, requires valved holding chambers or spacers to overcome pressurized metered-dose inhalers limitations (eg, these hold the aerosol until inhalation and reduce high oropharyngeal deposition) • Patient or caregiver preference due to prior poor experience
Nebulization (eg, jet, ultrasonic, mesh)	• Albuterol • Ipratropium • Corticosteroids (eg, budesonide) • Antibiotics (eg, aztreonam, aminoglycosides) • Dornase α (for cystic fibrosis only; no evidence for other indications) • Prostanoids (eg, epoprostenol (off label in cardiac surgery), iloprost, and treprostinil	• Suitable for emergencies/critically ill patients • Patient or clinician preference due to prior positive experience (eg, asthma symptom scoring) • Provider administered (eg, no patient-specific characteristics are a barrier to administration) • High local concentration in the lung with a reduction in systemic adverse effects	• Length of treatment and staffing time requirement • Contamination possible • Drug degradation possible

scheduled doses of nebulized medications. Additionally, for personnel who clean rooms following intermittent drug nebulization while wearing PPE that includes a face mask, protection from aerosolized virus may be inadequate. Subsequently, fugitive emissions from nebulized medications may potentially contribute to both nosocomial COVID-19 transmission and viral infections in the medical staff until proven otherwise by studies conducted outside of the laboratory. Prevention of infection in the medical staff is imperative since federal health care systems cannot sustain a significant loss of its workforce.

RECOMMENDATIONS

We recommend that health care systems stop business as usual and adopt public health recommendations issued by Canadian and Hong Kong health care authorities for the management of suspected or confirmed COVID-19 disease.[25-28] We have further clarified and expanded on these interventions. During viral pandemics, prescribers and health care systems should:

1. Deprescribe nebulized therapies on medical wards and intensive care units as an infection control measure. Also avoid use in any outpatient health care setting (eg, community-based clinics, EDs, triage).
2. Avoid initiation of nebulized unproven therapies (eg, n-acetylcysteine, hypertonic saline).[1]
3. Use alternative bronchodilator formulations as appropriate (eg, oral β-2 agonist, recognizing its slower onset) before prescribing nebulized agents to patients who are uncooperative or unable to follow directions needed to use a pMDI with a spacer or have experienced a prior poor response to a pMDI with spacer (eg, OptiChamber Diamond, Philips).[25,27]

4. Limit nebulized drug utilization (eg, bronchodilators, epoprostenol) to patients who are on mechanical ventilation and will receive nebulized therapies via a closed system or to patients housed in negative pressure hospital rooms.[22] Use a viral filter (eg, Salter Labs system) to decrease the spread of infection for those receiving epoprostenol via face mask.[25]
5. Adjust procurement practices (eg, pharmacy, logistics) to address the transition from nebulized drugs to alternatives.
6. Add a safety net to the drug-ordering process by restricting new orders for nebulized therapies to the prior authorization process.[27] Apply the exclusion criterion of suspected or definite COVID-19.
7. Add a safety net to environmental service practices. Nursing staff should track patients who received ≥ 1 nebulizations via open (before diagnosis) or closed systems so that staff wear suitable PPE to include a N-95 mask while cleaning the room.

CONCLUSIONS

To implement the aggressive infection control guidance promulgated here, we recommend collaboration with infection control, pharmacy service (eg, prior authorization team, clinical pharmacy team, and procurement team), respiratory therapy, pulmonary and other critical care physicians, EDs, CPR committee, and other stakeholders. When making significant transitions in clinical care during a viral pandemic, guidelines must be timely, use imperative wording, and consist of easily identifiable education and/or instructions for the affected frontline staff in order to change attitudes.[29] Additionally, when transitioning from nebulized bronchodilators to pMDI, educational in-services should be provided to frontline staff to avoid misconceptions regarding pMDI treatment efficacy and patients' ability to use their pMDI with spacer.[30]

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