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Editorial

Nebulization: A potential source of SARS-CoV-2 transmission

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The risk of airborne transmission of SARS-CoV-2 by patients with Coronavirus disease 2019 (Covid-19) is unclear [1]. However, the Aerosoltherapy workgroup (GAT) of the Société de Pneumologie de Langue Française decided at SARS-CoV2 pandemic preparedness to suggest avoiding a drug delivery via nebulization to reduce the risk of spreading the virus by this way.

Indeed, some arguments suggested that the aerosol generated from the patient during the nebulization or from the nebulizer can directly exposes mucosae and eyes of the health care workers and contaminate surfaces with potentially infective droplets.

1. The nebulizers are a source of contamination

Many publications demonstrated in the past that the nebulizers from patients can be contaminated by different germs. These studies were performed mainly in patients with cystic fibrosis. However, positive microbiological samples were also found from devices of patients with asthma and in intensive care units. Then a risk of nebulizer's contamination by SARS-CoV2 can be extrapolated. This hypothesis is reinforced by the demonstrated stability of SARS-CoV-2 on plastic up to 72 hours [2]. Thus, at the time of the nebulization session, the particles generated by the contaminated nebulizers could be charged by the patient with the virus which could be transmitted to people in the close circle of this patient, particularly healthcare workers.

2. The aerosolized droplet are dispersed

As some healthcare workers are in close contact to the patients infected with the SARS-CoV2, if these patients or their devices emit particles containing the virus, there is a risk of transmission through the healthcare workers. In 2003, the administration of aerosolized salbutamol in the index patient was suggested to have probably participated to the spread of SARS-CoV1, leading to a major nosocomial outbreak in a hospital in Hong-Kong [3].

Nebulization (as other respiratory modalities such oxygen delivery, high flow nasal cannula, and non-invasive ventilation) has been largely demonstrated to disperse particles in the environment. The nebulizer reservoir can be contaminated by hand contact or patient saliva during nebulization treatments. Consequently, it can operate like a generator of SARS-CoV2 aerosol with a perfect particle size to travel long distances and to penetrate into health-care worker upper and lower airways. The first air contamination step consists in the aerosol generation at a relative short distance with a high concentration. Dispersion distances of exhaled air and aerosolized droplets in the sagittal and coronal planes during jet nebulization were quantified using a human patient simulator. The leakage jet plume was highlighted by the laser light sheet and captured by a high-definition video recorder. The results showed that the exhaled air leakage through the side vents of the jet nebulizer increased from 0.45 m to 0.8 m with worsening lung injury [4]. Cough induced by nebulization is an additional source of spreading. Although it produces large droplets with a high velocity falling to the floor or onto other surfaces, it is also associated with fine particles smaller than 5 μm with a lower velocity. The second step of airborne contamination is the dispersion in the air. The velocity of particle is reduced and the concentration decreased from the nebulizer distance. An additional step is the deposition on surfaces depending on particle size and ventilation. One can suppose that the particles generated by the nebulizer and those exhaled by the patient will have optimal sizes to transmit the SARS-CoV2 to the healthcare workers.

The risk of exposure of the healthcare workers is also confirmed by the pentamidine detected in their urine after the nebulization of this medication as prophylaxis against *Pneumocystis carinii* in immunosuppressed patients [5] and by the bronchial hyper-responsiveness observed following administration of some aerosolized irritant medications.

The kind of nebulizer and the interface play certainly an important role in the dispersion of particles. Indeed, the unvented nebulizers and the nebulizers generating continuously the aerosol produces greater drug losses during the expiratory phase compared to vented, breath-enhanced or breath-actuated nebulizers. Some mesh or dosimetric nebulizers delivers little or no exhaled dose in the environment. For these reasons, it is recommended to apply a filter on the expiratory port of the nebulizers when there is a risk

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of second hand exposure to contaminated substances. By this way, the dispersion of particles can be reduced.

3. The SARS-CoV2 is stable in aerosols

At the beginning of the SARS-CoV2 pandemic, an in vitro study demonstrated the stability of the SARS-CoV2 in aerosols. Indeed, an aerosolized environment containing SARS-CoV2 was generated with a jet nebulizer and the sample demonstrated that the SARS-CoV-2 remained viable in aerosols throughout 3 hours after the nebulization. A reduction in viral concentration from $10^{3.5}$ to $10^{2.7}$ $TCID_{50}$ per litre of air was observed during this duration. The same experiment was performed in parallel with SARS-CoV1 and the results were similar. SARS-CoV1 has already been suggested to be airborne. The same conclusion can be extrapolated to the SARS-CoV2 based on these results [2]. Moreover, recent studies suggested that small SARS-CoV2-laden droplets may be displaced by airflows and ventilation from air conditioner [6–8].

Based on these three elements, we think reasonable to avoid delivery of drugs via nebulization to SARS CoV2 patients for reducing the risk of exposure of the healthcare workers. A drug delivery from pressurized metered dose inhaler or dry powder inhaler should be preferred or, if the drug cannot be delivered other than nebulization, the use of a nebulizer equipped with an expiratory filter and/or a disposable nebulizer is recommended. Moreover, the maximal protection of the healthcare workers (FFP2 mask, disposable gown, protective glasses, and hat covering completely the hair) is required during the three hours following the nebulization session. Caution should also be taken about the risk of surface contamination with nebulized aerosol.

Disclosure of interest

The authors declare that they have no competing interest.

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