

1. Saline in COVID-19 – WHO:

To note, saline irrigation in COVID-19 has been removed from the list of myth busters by the WHO.

2. Saline nebulization and risk of transmission

A number of countries, such as Belgium, advise against use of nebulization of saline because of an enhanced risk of viral spread by the produced aerosol. A new study assessing the effect of nebulization on SARS-CoV-2 in bio-aerosol in severe COVID-19 patients does not find such effect.

Thibon C, Vecellio L, Dubus JC, Kabamba B, Reyckler G. Nebulization and COVID-19: Is the risk of spread actual? Respir Med. 2022 Jun;197:106854. doi: 10.1016/j.rmed.2022.106854. Epub 2022 Apr 20. PMID: 35472716; PMCID: PMC9020501

This study assessed SARS-CoV-2 in the released bio-aerosol during saline nebulization (alone or after other drug nebulization) in 10 severe COVID-19 patients.

- Patients had tachypnea, hypoxemia, more than 50% lung involved on imaging.
- They were treated with nebulization with a standard single-use jet nebulizer operating at 8 L/min with a T piece connected to a mouthpiece (Opti-Mist Plus®, ConvaTec, Bridgewater, NJ) and a filter.
- Immediately after the first nebulization, the residual solution of each nebulizer was sampled.
- Then, the nebulizers were refilled with 3 mL isotonic saline solution (0.9%) to complete the residual volume (1mL).
- The filter was replaced by a BioSampler® (SKC 20-mL) loaded with 20 mL phosphate-buffered saline (PBS) and 0.5% bovine serum albumin
- The nebulizer was driven by a compressed air supply, and a 10min-nebulization was performed again on the bench. The emitted aerosol was continuously collected during the nebulization.
- The nominal and emitted dose were sampled. The SARS-CoV-2 viral load was quantified in all samples by RT-PCR (negative threshold <10 copies/mL).
- The experimental set up was previously validated with a positive control of SARS-CoV-2 directly loaded into the nebulizer's reservoir.
- Result:
" The median viral load of the patients was 5.6x10 copies/mL (range 1.5x10 to 189x10). **No SARS-CoV-2 RNA was found in any sample for all nebulizations.**" " ...result of this study shows "**no SARS-CoV-2 nebulizers contamination by COVID-19 patients at hospital and does not support the role of nebulizers in terms of aerosol virus dissemination in air.** Nevertheless, exhaled virus by the patient itself remains and must be considered independently to the nebulizer."

Striking is the full absence of SARS-CoV-2 contaminated bio-aerosol in the collected material upon saline nebulization in this study. The results are in line with the published properties of NaCl on bio-aerosol, as we formerly reviewed (

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7998085/pdf/228_2021_Article_3102.pdf), and now for the first time confirmed in COVID-19 patients. Hydration of the airways and stimulation of the mucociliary clearance by saline nebulization may be of benefit to patients with COVID-19, as many patients at

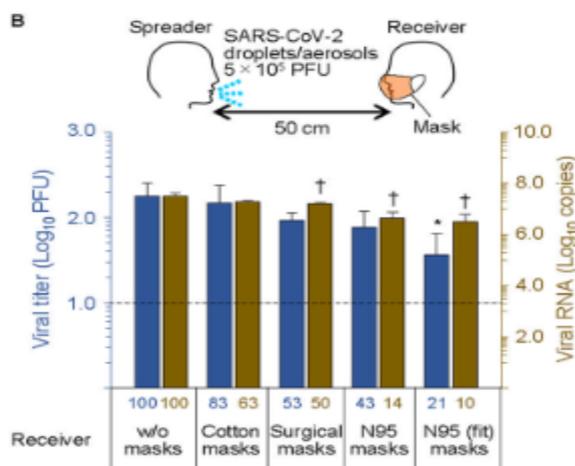
risk (such as with hypertension, high BMI, diabetes, polypharmacy) have a reduced mucociliary clearance. Also mask wearing is dehydrating to the nasal and airway mucosa.

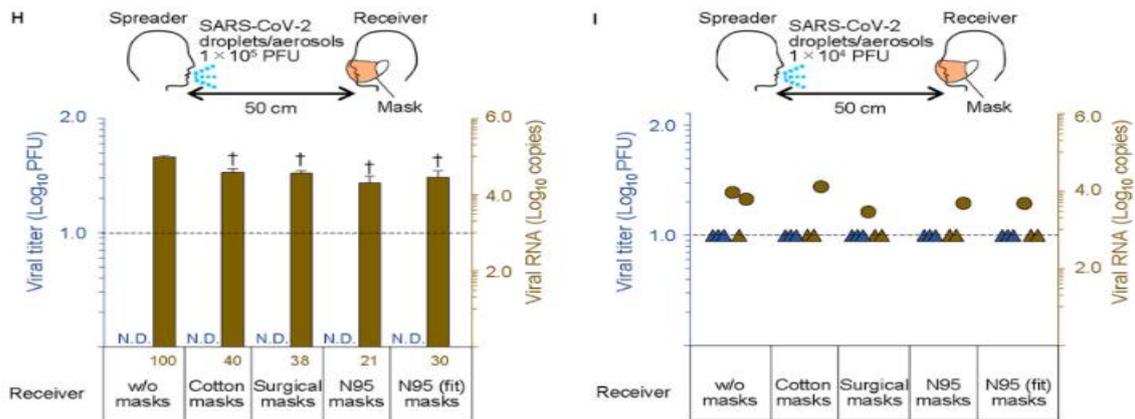
3. Saline and mask wear (unless I wrongly interpret...)

Using saline hydration by irrigation and nebulization may not just be relevant to mask wear for patients from an airway hydrating point of view, but also – as with nebulization – from a transmission point of view. I like to point to the former findings by Ueki et al. using SARS-CoV-2 cultures and dilutions and breathing mask wearing mannequins, a study that was set up to test the efficacy of mask wear against (live) SARS-CoV-2 transmission:

- While not set to prove an effect of saline, the 0.9% saline dilution in this mask model (illustration H, 1×10^5 PFU) showed no longer life virus and appears to do better than the same original life viral dilution (culture 5×10^5 PFU; no saline as vehicle)
 - illustration B (life culture) showed life virus and titers of about one log higher in about 50% of the receivers wearing cotton and surgical masks when compared to the only half-diluted PBS (=saline containing)-dilution;
 - with life culture exhaled behind a mask, life virus was still detected in 43% of the receivers with professional N95 masks if not fitting well, 21% if well fitting, and this just after 20 minutes of pulse breathing cultured virus.
 - Yet, the log-values became about 1 log unit lower, while life virus was apparently no longer well detectable following the dilution with saline to 1×10^5 PFU in illustration H.
- The further, 10x more diluted SARS-CoV-2 sample with 0.9% NaCl in the vehicle (illustration I) further reduced detection of virus (both by culture and by PCR), in fact in line with effects observed with saline gargling (see point 4); the effect of dilution with saline is larger than can be obtained by a masks itself.
- Unfortunately, no data after 3-4 hours – just after 20 minutes of breathing only.

Better filtering of ionic loaded aerosols of by ionic/salt loaded masks have been described independently in the literature. The results in the study by Ueki – while not set up to prove an effect of 0.9% NaCl on bioaerosol – are in line with the properties of NaCl/saline on (virus-containing) bioaerosol.

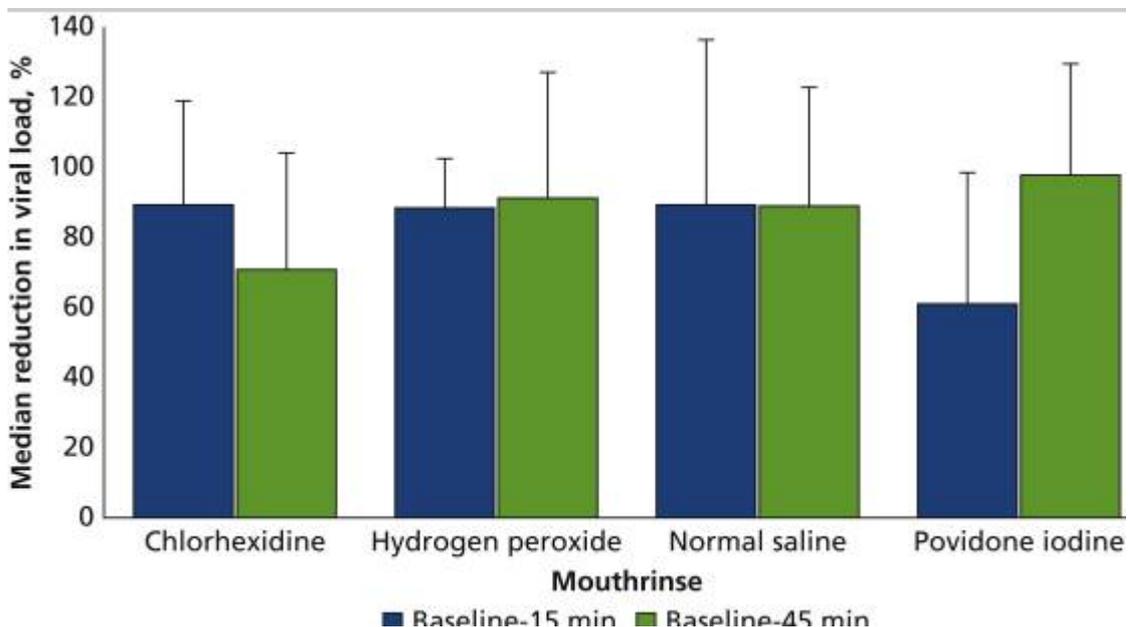




4. Saline gargling:

The effect of dilution by gargling with saline to reduce the viral load has recently also been shown by Chaudhary

(<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8193024/pdf/main.pdf>): gargling with 15 mL of normal saline reduced the viral load by ~90% 15 minutes after gargling, an effect sustained at 45 min; the effect was at least as good as with oral antiseptic gargles. To note, there was a significant correlation between baseline viral load and reduction at 15 minutes ($P = .0073$, Spearman rank correlation) and persistence at 45 minutes ($P = .0087$, Spearman rank correlation), while participants with a baseline viral load less than 10^4 copies per mL of saliva ($n = 6$), there was 100% reduction at 15 and 45 minutes.



In conclusion, although this traditional remedy used against common colds may not be the magic solution, studies increasingly motivate the use of saline irrigation and nebulization as an extra-hygiene measure in COVID-19; regular repeated use of saline gargling, irrigation and/or nebulization may help to reduce the burden of COVID-19, as also increasingly suggested by clinical studies evaluating the effects of saline on clinical parameters (Baxter 2021, Chatterjee 2021, Spinato 2021, Jadhav 2022....).

The fact that saline irrigation is now removed from the myth buster list by the WHO hopefully opens the opportunity for larger systematic evaluation and use.

I look forward to your feedback. Please, feel free to communicate if of interest to your readers,

[A common concern against use saline has been the proposition by some that saline use would enhance postnasal drip and aspiration to the lungs. Also that objection can now be dismissed. Interest in this objection handling?]

Regards,

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