



Nasal Rinsing Efficacious Curing Covid-19, Low Temperature May Be Crucial Of Priming Intranasal Administration for Viral Sterilization

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Keywords: Nasal lavage; Nasal rinsing; SARS-cov-2 Sterilization; Mucosal administration; Long Covid; Low temperature.

Abstract

Background: The global pandemic of Coronavirus Disease 2019 (covid-19) is ongoing and, SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) is the causative organism which or its variant is still to menace everybody in the world. An efficacious protocol against this disease in up respiratory tract is still urgent demand from folk.

Method: A group of outpatients (n=14) accepted nasal lavage including improved versions these conferred to regulate intranasal administration against illness, whom we followed up at 12 months beginning from onset of symptoms mainly causative strain was Omicron; during these months cure also covered the Long Covid that correlates to virus load of that harbored in cytoplasm of host cell.

Results: Besides rapidly suppressing mild clinical manifestation by cure locating nasal cavity this way likewise efficacious on treating acute viral bronchitis that can be manifested on senior citizen and wrecks death everywhere in the world cited in clinical reports the last 4 years. Intranasal administration is acquired to realize it can effectively sterilize virus inside host cells therefore Long Covid is acquired curable.

Conclusion: The covid-19 is not so intractable including viral mutation. From temperature technology to prime intranasal administration on mucosa it offers a promising vision for people health not only limited in up respiratory tract.

Introduction

The causative organism of Coronavirus Disease 2019 (covid-19) is the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) also responsible for the global crisis of health in 2019. Until today, people have invested countless resources in exploration for how to stop it and, the situation may be near to 80% of patients suffered mild symptoms in up respiratory airway and about 14% severe clinical manifestation; 6% of cases

developing to critical the hyperinflammatory [1]; besides, the ensuing Long Covid presents a set of chronic syndromes that credible more than 200 symptoms involved and multiple organ systems expose to risk of failure. And the contracting population is surprised up to more than 65 million [2], a long-term growing crisis of health.

Well, in those measures attempting to contain pandemic, vaccination has long been expected as being the primary weap-



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on to inhibit viral invasion or neutralize the virulence. Yet, following up 446 hospitalized adults for covid-19 at 12 months [3] persistent in measuring two immunoglobulins, IgA and IgG, respectively from nasal tissue and serum in order to assess the vaccinating long-term effect. The conclusion depressingly refers to lack of long-lasting topic defense in nasal cavity nevertheless through 9 months of serum elevating patients thus have to expose to risk of reinfection. The crux comes down to the nasal-associated lymphoid tissue unable to mirror serum immune responds in the case of intramuscular inoculation.

Meanwhile vaccinal itself specificity is commonly identified should be responsible to compromised effect of antagonizing virus in present of viral rapid mutation, depending on which SARS-CoV-2 evades vaccinal striking. Among our outpatients (n=14), there is 9 of vaccinated with three doses though; while exposed to Omicron strain as was the mainly concerned overrunning the last 2022 in China when government abolished the mandate of quarantine, all suffered high fever for their body temperature climbing over 39°C in half hour basically stands the appraisal that is vaccinations essentially short-lived [3] for prevent Omicron or its subtypes; apparently, the intranasal vaccinating is key. Alternatively, in the official guideline from NCBI upon novel therapies against variant of SARS-CoV-2 [5], the mild manifestation can be the indication for having drugs; such as the paxlovid [4] that has a week to control the progression of disease by inhibiting the viral replication thus prevent conditions exacerbating to manifest with low respiratory symptoms. But on whom contracted Long Covid with asymptomatic in respiratory tract, can pharmacotherapy be a long-term solution?

Our contribution: Is to confer nasal lavage not only an adjuvant measure of clearance as well as hand washing or face mask [6] but to mediate agents into endoplasm of intranasal ciliated cell albeit solution can be 0.9% (w/v) isotonic saline or hypertonic saline in 1.5% made of tap water and table salt on which based we formulated the *cocktail* by mixing other agents but also from over-the-counter.

Why must we have to locate nasal cavity as being treating site yet less consideration on others? Except that site is the portal of infection, even more is it the best to benefit viral entry with rich of required enzymes or proteases which representatively include Angiotensin-converting-enzyme-2 (ACE2) as the receptor [7] in motile cilia [8], which host cells ciliated cover ~ 90% surface of nasal cavity of human [9] also commonly distributing in lumen of airway, whom SARS-CoV-2 would locate and hijack with viral Spike protein (S) to prime entry; moreover, the proprotein convertase Furin, which cleavage should responsible to amplify the affinity of ACE2 to S protein to accelerate the fusion among virus and plasmatic membrane; does so the Transmembrane Serine Protease 2 (TMPRSS2) [10].

Certainly, through measuring the three expressions at several depth of respiratory tract we can learn where avails viral entry. From proximal nasal cavity to distal alveolus, Ji Hoon Ahn et al [11] depict a descent gradient thus they conclude viral pneumonia is caused by viral shedding from nasal cavity where naturally becomes crucial of treating covid-19.

Accordingly, it is reasonable to reckon rinsing gives rise to double effects: reduce viral load that has been demonstrated responsible to severity of clinical manifestation [12] and dilute concentration of enzymes or proteases in order to attenuate viral entry when virus spreads. But is the challenge what volume of rinsing solution is safe to a person. This worry in [6] is com-

monly offered to lesion on mucosa, while, this impair is actually decided on mucus that is rather tough and monolithic to protect mucosa though enriched of 98% water [13].

It can be viewed consisting of two layers in 100 nm height [14]: The up one exposing to air is watery (here calls W-layer) facilitate flowing for liquid clearance from nostrils down tract to nasopharynx, which impulse from cilia beating and at length dried by air into sputum; the *mucoiliary clearance* thus acquired to accomplish. Beneath W-layer is sediment made of mucin polymers [15] and comparatively static lining cytomembrane, called M-layer, which usage is to inhibit noxious agents or microbes, both harbored in W-layer and try accessing to the apical side of epithelium [16]; i.e. impossible exposure to W-layer defends cytomembrane.

Consequently, saline flowing in nasal cavity is merely to influence W-layer should scarcely sweep a pinch from M-layer away; in this regard, we are able to extrapolate the dosage of solution in a proper osmolality should amount to unlimited; therefore, our aggressive application proves this hypothesis with adverse event absent in rinsing. Maybe that is why applying hypertonic saline to control infection [17] incurs controversy upon efficacy they report, however, it is sure for lavage impossible to mediate agents into endoplasm to sterilize virus that harbored in host cells so longer as the existence of M-layer of mucus. That likewise yields the big distance between *in vivo* and *in vitro*.

Nevertheless, the dosage parameter is with an extend to decide rinsing efficacy. To our outpatients who effectively subdued their onset of mild clinic manifestation within a few minutes after rinsing with 1,000 mL isotonic saline: The hyperthermal progression would be turned upside down from 39°C or beyond to low the 37.5°C and return to normal within 12 hours contrasting with those in [18], whose fever persisting for 7.32±5.56 days; furthermore, the acute pharyngitis caused by viral shedding and to nasopharynx where such invasion acquires mucoiliary-clearance [11] carrying, but just occurs of itchy symptom instead of soreness, that reflects the viral load very low [19] through lavage; also is dyspnea duration within 18 hours and then recover, compares to 8 days in general case [20] of those patients who get through the mild onset without lavage.

Noted that, according to our observation pure nasal rinsing does not affect virus life cycle the part inside host cell, certainly unable to shorten the duration of illness still is *fortnight* that may have been already decided on cytokine level [21]. Additionally, our Long Covid has myalgia, cough, or acute/chronic constipation [22,23] manifested, likewise less signs and diagnosis mainly depending on what patients complain [24].

However, these clinical manifestations can further be used to signal the outcome of our viral sterilization for which, we formulated *cocktail* with hypertonic saline that can be available for hinder viral replication [25] and ethanol as being surfactant conferred to destruct viral lipid shell [26] but this intranasal administration at length depends on low temperature priming.

Another interested outcome of this therapy to induce reinfection may implicate SARS-CoV-2 untimely egress from morbid microvillus contrasting to past observation from *in vitro* assays that shows only out from mature cilia [27].

Materials and Methods

We followed up 14 patients at 12 months who accepted our advice to use nasal rinsing as being their personal hygiene

against covid-19. They all contracted Omicron the last 2022, therein including three senior citizens for up to 75 ~ 85 years, and all are female with underlying conditions including type II diabetes, cardiovascular disease, or obesity.

In addition, two between 60 ~ 70 years; five are at least 50 years; a gravida with her husband both for ~ 30 years; a teenage for 16 years. Totally are 4 male subjects.

Isotonic rinsing

The strategy is incessantly rinsing until asymptomatic or feel well. And, during fortnight of onset of acute symptom, the dosage should keep 3,000 mL isotonic saline rinsing per day as being essential treatment. Note that, discharge the mucus out of nostrils as much as possible over rinsing course.

Administration for sterilization

The hypertonic saline for sterilization may be 1.5% NaCl (w/v). The temperature of solution should be set less than 15°C (not freezing). The process generally should follow the rinsing sequence of *warm-cold-warm*: the first rinsing should utilize warm isotonic, maybe 500 mL, to do clearance for prime administration; the cold solution may be 250-500 mL but the inflowing should be comparatively slowly amounts to dousing mucosa; the last warm saline rinsing is sweeping out possible debris. We call this operation Warm-Cold Method (WCM). As the case may be, the WCM can be plus to several times pre day; besides, the enhance version may have four aspects of improvement on cold solution: Adding ethanol into cold solution which concentration reminds up to 5%; setting temperature around 0°C and 125-500 mL; thus called *Ice-cold Beer Method* (IcBM); forth is rubbing menthol in cavity during cold or the last warm rinsing.

Results

Benefited from subduing onset of illness, all subjects successfully got through the onset–fortnight without adverse event thus without necessity of hospitalization. The only moderate case was whom of 82 years old. Such age–factor overlaps to underlying condition of type II diabetes and comorbidities diabetes causes is pretty high mortality [28] needing into intensive curing unit. But this is atypic for asymptomatic yet it develops to bronchitis manifested with roar-cough that is the sort of loud, bass, and longer resounding as out of an empty lumen.

Within 48 hours, depleting 30,000 mL isotonic saline per day, survived her. That corroborates the opinion of viral shedding not correlated to severity of illness [29].

In post-onset-fortnight, sequela including myalgia or cough now termed Long Covid on 2 subjects of ours approaching to 14% was effectively dissipated and a deal of mucus presented in three types or white debris discharged while applying WCM not more than 3 times per day and a standard course for 7 days; while, 3 subjects suffered chronic constipation [1] from July, 2023; and therein 2 began ameliorated after 7 days for accepting IcBM therein pigment on face signaling the systemic toxication but the time has come to Jan, 2024 for tentative testing succeeding; one merely agreed to accept enema to alleviate syndrome of systemic toxication for 6 months. Whereas sterilization can bring tissue lysis, the large area necrosis also harbors danger. The typical sign is fever up to 39°C at 24 hours accompanies with comparative serious chill and shivering and corresponding sweaty. Yet, the mental condition may present excitement like done with exercise instead of generally morbid fatigue. And, the top of 39°C merely kept for few minutes, the

body temperature ran down quickly even to touch the bottom of 33°C; at length, fluctuate around 35°C for 0.5 amplitude through 5 days.

Consequently, the possible imbalance of water and electrolyte for fever and attenuate digestion for body lower temperature or lower metabolism are mainly comorbidity.

A case of contracting unknown strain

One senior citizen with up to 78 years old in 2024 who has been around 5 years of implantation for coronary artery stenosis and post-operation or chemotherapy against rectum cancer, serious hypertension; infected on 10, Feb, 2024 in China where she has already announced no longer to report prevailing strains in public.

A mild syndrome presents low fever approaching to 38.5°C; myalgia and malaise thus indifferent to milieu; aphonia; irritating larynx; cough aggravating headache; but without sputum or hypertension aggravation. After 4 hours accepting IcBM for 500 mL cold *cocktail*, the all symptoms except body temperature fluctuating between 37°C and 38°C for 4 days, were acquired in amelioration. Yet, however, drinking water could pull down temperature; maybe, this outcome comes down to Myelosuppression for her ever chemotherapy. Note that, IcBM may be her every day cure for three rounds.

Remark: Solution coverage may be critical key for a comparatively thoroughly sterilization. Bowing body to let forehead facing ground for lavage can be acquired a posture of relatively sufficient washing or dousing in cavity. Especially to olfactory area the top of cavity in the case of common posture of head can be covered less for gravity of rinsing solution.

Note that, constipation can engender systemic toxication: Headache, malaise, pigment on face, leaden lips, or muscle insistent on neck. The body temperature may be drawn down for 0.5°C.



Figure 1: The Modality of Our Nasal Rinsing.

Discussion

The interesting is sodium or ethanol for their intranasally administration in WCM or IcBM. Firstly, Rafael R G Machado, et al [25] have their assays to proven 1.5% hypertonic dousing host cells can 100% inhibit SARS-CoV-2 replication since a high concentration of cation Na^+ that inside cytosol can depolarize cytomembrane so as to locate Na^+/K^+ ATPase pumps that thus act to expel surplus Na^+ for balance osmolality of cytoplasm. This intrinsic mechanism running can effectively deplete the ATP in

cytoplasm thus motivates endoplasmic reticulum loses enough energy to saccharify or fold proteins among which also include SARS-CoV-2's envelope.

This consequence can upregulate endoplasmic reticulum probability to send apoptosis or autophagy [30] message. This can explain the 30% infected cells death a rather higher ratio than that of less than 9% in control group, which effect equivalent to do viral clearance *in vivo*.

The surfactant such as ethanol follows another pathway of viral sterilization. These ethanol molecules may be assembled into viral lipid envelope [26] as being composition; just because of such harboring defect in structure will give rise to content leakage, and inactivation accomplishes.

Well, the actual barrier for administration is M-layer, except its clinging to cytomembrane exterior surface that facing lumen of tract like film, which viscosity is conferred to defend the cytomembrane [31] with three lines in the monomer of mucin [32]: Colloidal nebula full of cations Ca^+ and H^+ at outmost among W-M layer, commits the electrostatic repulse; physical porous size; inside which is likewise electrostatic repulse correspondingly generated by anions from multivalence of sulfate or sialic acid.

On macro level, a multitude of monomers may commonly compose a matrix standing on cytomembrane like huge-shield, moreover, between their overlapping each other into a monolithic whole; while, monomers are polymeric which form can be tethered rod-like [14] in 190-1500 nm and, may exhibit a plasticity character by immediately stretching body from been folded when secreted away cytoplasm [33]. In this regard, lower temperature may be hypothesized to curl this plastic body thus fissures emerge on originally robust molecular matrix. By this momentary *window*, cytomembrane partly direct exposes to W-layer.

This physical way other than the two [32] which spots a capsule mimicking viral shell that attempts to penetrate M-layer for further entry; another is to develop agents available to briefly compromise mucin viscosity.

Reinfection

Note that, after IcBM, it can be observed that myalgia more or less appears, generally within 2 hours. That can be hypothesized the cold solution dousing may facilitate viral egress from host cells to cause reinfection. Due to Jackson's model of SARS-CoV-2 egress [27] out of host cells, those pathogenic vesicles would gather in microvillus of host cell for budding. At this moment microvillus is extruded into a drum-like profile though, yet the real releasing is via morbid cilia that has been mature in high branched.

This strange behavior of releasing limited at higher altitude may be related to strong viscosity of M-layer yielding a spontaneous high stress to inhibit these pellets erupting; on contrary, lower stress may be responsible for egress at lower site, untimely. The interesting is two distinct events appear on a same spot thus implicates that viscosity can be compromised by low temperature.

Our method against this minor reinfection is increasing viscosity of W-layer attempts to restrain viral activity amounts to enhance mucociliary clearance like spraying *Carrageenan* [34]; but here we rub menthol which avail can be subduing cough or itchy in nasopharynx.

Summary

The covid-19 may be not so intractable but maybe a long-term influence upon people health. The three methods we designed of nasal lavage may be well cost-efficiency and pertain to a broad application scenario including the most coverage on patients for less adverse events and easy being performed for agents from over-counter.

Alternatively, we seldomly exert lab instrumentalities such as Cycle threshold (Ct) value in our diagnose or prognosis and assessment on treating outcome. In a sense, nasal lavage may distort the truth of condition what is such the sort of testing intended to reflect for probability of always negative [41,42] this signals a minimal clinical significance but likely to mislead patients believe it none pathogen resides in their body.

To address mutation of SARS-CoV-2, which common mutating site is at viral spike protein [43] contrast with the sterilization this locates viral body further to affect its life cycle; thus decides viral mutation with scarce impact on sterilization and we acquire a long-term measure to treat Long Covid.

The cool finding in this paper is low temperature available to prime agents through mucus further accessing to cytomembrane is important for people who are dedicated on formulating cocktail. Until now, there are a sort of agents proven efficacious in viral sterilization by *in vitro* assays, including: Hydrogen peroxide [35], Nitric Oxide [36,37]; and traditional agents including alkaline[38], Povidone Iodine [39,40].

Meanwhile means a genuine intranasal vaccination [44] may be done. So, the future works not only include establishing the topic defense in up respiratory tract but an extensive application upon other tracts that expose to exomilieu in anatomy.

Conflict of interest: None declared.

Our limitation: Certainly, our report is short on quantity contrasting to that with more and more convincing data to represent a more general significance. Nevertheless, the realistic is tentative is strictly limited by ethics or moral, so our exploration is not more than reporting cases with a few of people. The cool hypothesis of low temperature regulating intranasal administration still calls for crucial evidence to justify though is critical to future.

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