

Role of Nasal concentrations of Cl^- ions by Jala Neti in COVID-19 Infection

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Abstract

Of all the sites in the body, the lung is perhaps the most common target of the microbial pathogens, many times, which proves to be lethal if unopposed. One such relevant example in the current time is the COVID-19 pandemic that emerged in Wuhan, China caused by SARS-CoV-2 virus and now has entered into almost every part of the world. Respiratory droplets and close contacts mainly spread COVID-19 infection. The droplets generated during coughing and sneezing by symptomatic patients transmit the virus. SARS-CoV-2 binds to the Angiotensin Converting Enzyme 2 (ACE2) receptor. An essential prerequisite for the innate immune response of the infected person mediated by phagocytes and neutrophils is the Chloride ion. Within phagosomes, myeloperoxidase mediates the conversion of Cl^- and hydrogen peroxide to hypochlorous acid (HOCl). Non-myeloid cells such as respiratory epithelial cells utilize available Cl^- ions to produce HOCl, which in turn has antiviral activity and reduces viral replication. Hence, HOCl production is an innate antiviral mechanism that works against RNA enveloped viruses which requires a continuous supply of chloride for HOCl generation. Nasal irrigation techniques such as Jala neti helps in mechanical removal of mucus, infective pathogens, and inflammatory mediators, promotes ciliary beat frequency and strengthens the antimicrobial and antiviral barrier function. Jala Neti with the help of lukewarm NaCl solution provides a continuous supply of Cl^- ions, which may have a role in inhibiting viral replication. Since SARS-CoV-2 Receptor Binding Domain attaches loosely to ACE 2 receptor, Jala neti could have a role in limiting the shedding of virus in the infected patients by detachment of the virus from the receptor. Further research in the form of Randomized control trials are required to study the effect of Jala neti against COVID-19 infection in humans.

Keywords: COVID-19, SARS-CoV-2, Jala Neti, Viral Replication, NaCl

Introduction

Lungs are the most common target of the airborne pathogens, many times which proves to be lethal if unopposed [1]. One such relevant example in the current time is the COVID-19 pandemic that emerged in Wuhan, China caused by SARS-CoV-2 virus and now has entered into almost every part of the world [2]. The first point of entry of the novel coronavirus causing COVID-19 infection is the nasal passage. If the barriers in the nasal passages fail, the virus travels through the respiratory system and affects the type-2 alveolar cells of the lungs causing acute respiratory distress syndrome [3]. Therefore, the immune response to respiratory infection must be rapid and efficient.

Respiratory droplets and close contacts mainly spread COVID-19 infection. The droplets generated during coughing and sneezing by symptomatic patients transmit the virus. Even asymptomatic patients and those before the onset of symptoms generates droplets and can spread the infection. These droplets, which contain virus, can spread up to 1-2 m and deposit on surfaces where they can remain viable for days [4]. These droplets may fall on the ground and remain infectious to an onward host as contaminated fomites for a period. Viability of virus on surface depends on favorable atmospheric conditions like temperature, airflow streams and humidity. A healthy person acquires infection either by inhalation of these droplets or by touching surfaces contaminated by droplets and then touching the nose, mouth and eyes [5].

After inhalation, as microorganisms enter the respiratory tract, the first obstacles to entry are from mechanical

barriers. Mucins of the mucociliary blanket lining the surface of the airways trap the microorganisms, which further cleared by the ciliary movement. Particles which pass this barrier are then met by mediators such as lactoferrin, lysozyme, collectins and defensins when activated can lead to lysis of pathogens or their destruction with the help of inflammatory cells [6]. SARS-CoV-2 possesses glycoprotein spikes on the outer surface, which helps in attachment and entry of the virus to host cells, which are respiratory epithelial cells in the nasal cavity. SARS-CoV-2 binds to the Angiotensin Converting Enzyme 2 (ACE2) receptor. The receptor-binding domain (RBD) of the SARS-CoV-2 has 394-glutamine residue, which is recognized, by lysine 31 residue on the human ACE2 receptor. This RBD loosely attaches the virus; therefore, the virus may infect multiple hosts [7].

Virus particles that pass this mechanical barrier of mucin and cilia are then encounter by a range of soluble mediators produced by cells of the respiratory tract. The airway surface fluid contains several proteins which has antimicrobial activity and which are highly sensitive to local salt concentrations. This constitutes the innate immune response of the host against the invasion by the virus [6]. An essential prerequisite for the innate immune response mediated by phagocytes and neutrophils is the Chloride ion. Resting neutrophils have a four to five-fold higher intracellular Cl^- concentration than activated neutrophil. Within phagosomes, myeloperoxidase mediates the conversion of Cl^- and hydrogen peroxide to hypochlorous acid (HOCl). Both H_2O_2 and HOCl have antimicrobial

activity, out of which HOCl is the most potent. An activated neutrophil produces 2.6×10^6 molecules of HOCl per second. Within phagosomes, an estimated 70% of the oxygen consumed is converted to HOCl. Hence, a continuous supply of chloride is required for HOCl generation^[8].

Ramalingam *et al* in their study in Edinburgh, observed that non-myeloid cells which were considered incapable of producing HOCl, when these cells were supplied Cl^- ion they showed antiviral effect by generation of HOCl using enzyme myeloperoxidase. They cultured both enveloped and non-enveloped RNA viruses (e.g. HCoV-229E) in non-myeloid cells such as respiratory epithelial cells and observed inhibition of viral particles in the presence of NaCl. SARS-CoV-2 is an enveloped RNA virus^[9]. Further, viral inhibition was not a direct effect of NaCl on the virus particles but was an intracellular process augmented by the presence of NaCl. In addition, viral inhibition was reverse prevented Chloride ions from entering cells. This viral inhibition was associated with an increase in the production of intracellular HOCl acid, which was corroborated by the reversal of viral inhibition in the presence of a known myeloperoxidase inhibitor. For this, a continuous influx of Cl^- was essential. They concluded that non-myeloid cells utilize available Cl ions to produce HOCl, which in turn has antiviral activity and reduces viral replication. Hence, HOCl production is an innate antiviral mechanism which works against RNA enveloped viruses^[8].

Coronaviruses are extremely fastidious viruses, which grows only in differentiated respiratory epithelial cells. The infected cells become vacuolated, cilia damaged and syncytia formed. Inflammatory mediators released due to cell damage, which leads to increase nasal secretion causing local inflammation and swelling, which in turn stimulates sneezing, obstruct the airways, causing cough and raise the mucosal temperature^[10].

Sandeep Ramalingam and colleagues performed an open labelled RCT in adults of Edinburg within 48 hours of upper respiratory tract infection caused by rhinovirus and coronavirus. They reported that hypertonic saline nasal irrigation does reduced viral shedding. Nasal irrigation physically wash off the virus from the nasal cavity^[11].

Nasal irrigation, since ages, is a common procedure used to unblock the nose by gently rinsing the nasal and sinus cavities^[12]. It helps in mechanical removal of mucus, infective pathogens, and inflammatory mediators, promotes ciliary beat frequency and strengthens the antimicrobial and antiviral barrier function. Nasal irrigation device can be categorized according to the volume of the saline solution used. A high-volume device uses more than 100 ml of saline solution. Which can be subdivided again based on the pressure of the solution when introducing into the nose. A low-pressure device uses gravitational pressure or the solution is expelled from the nose when the pressure is high. Examples of low-volume low-pressure device are nasal drops, low-volume high-pressure are nasal sprays, high-volume low-pressure are Neti pot and high-volume high-pressure are syringe with adaptor. Salib *et al* reported that high-volume low-pressure devices such as Neti pot have a significant effect on the clearing of the nasal disease. A study by Tano *et al.* on healthy adults found that those who practice daily saline nasal irrigation had lesser attacks of upper respiratory tract infections. In another study by Rabago *et al.*, daily nasal irrigation with hypertonic saline solution reduces the severity of symptoms and occurrence of

acute exacerbations of sinusitis^[13].

The use of nasal saline is deeply rooted in history. It has been practice for thousands of years as part of Hatha Yoga, where it is referred as JalaNeti. Yogis use nasal cleansing, as well as cleansing of other areas, to attain a higher state of meditation, but practitioners also note advantages related to bodily health^[14]. Jala neti is the process of cleansing the nasal passages using lukewarm NaCl water by means of Neti pot device. It is one of the Shatkarmas of Hatha yoga. It helps in removing dirt and bacteria filled mucus from within the nose. It drains the sinus cavities, which in turn reprograms the body's natural mechanisms against nasal infections such as hay fever, allergies, sinusitis and other ARTIs. It has a cooling and soothing effect on the brain by drawing out excessive heat and thus is beneficial to reduce depression and mental tension. Jala Neti improves sensitivity of the olfactory nerves and helps in restoring lost sense of smell^[15]. In addition, the Neti pot can be easily sterilized using 70% Isopropyl alcohol or with soap & water and can be used daily as a cost-effective measure.

Jala neti is beneficial in a number of ways such as helps in mechanical removal of mucus, infective pathogens, and inflammatory mediators, promotes ciliary beat frequency and strengthens the antimicrobial and antiviral barrier function. Jala Neti with the help of lukewarm NaCl solution provides a continuous supply of Cl^- ions, which has a role in inhibiting viral replication^[15].

COVID-19 is highly contagious infectious as asymptomatic patients can shed the virus and spread the infection. In a study done in Vietnam by Le *et al* regarding SARS-CoV-2 shedding by travelers found that virus shedding was detected from day 1 after illness onset continuing through day 19. They also observed that virus shedding was present in asymptomatic patient for up to 9 days. This may explain the high magnitude of the current covid19 outbreak^[16]. If those infected with COVID-19 infection practiced nasal irrigation by jala neti, there may be some chances of reduction of viral shedding as evident by the loose attachment of the RBD part of virus with the receptor area in the nasal cavity^[16].

As of now, there are very limited evidence on role of Jala neti in upper respiratory tract infection. Since coronavirus RBD attached loosely to ACE 2 receptor, Jala neti could have a role in limiting the shedding of virus in the infected patients. Further research in the form of Randomized control trials are required to study the effect of Jala neti against COVID-19 infection in humans.

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