

Iodine Oropharyngeal Solution for COVID19: A Cohort Study

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Resumen

Aunque se ha concedido autorización de uso de emergencia a varias vacunas, se han identificado cuatro inconvenientes. En primer lugar, la duración de la protección disminuye después de 3 a 6 meses y hacia el sexto mes la vacuna parece ofrecer poca protección (Tartof et al. 2021). En segundo lugar, se han informado varios efectos adversos directamente correlacionados de las diferentes vacunas (Sharifian-Dorche et al. 2021, Chan et al. 2022). En tercer lugar, las vacunas, incluso con la corta duración de la protección comprobada, no son antiinfecciosas y, aunque pueden proporcionar cierta protección contra infecciones graves, se ha demostrado que los individuos vacunados portan cantidades iguales de carga viral, lo que hace que la transmisión sea igualmente probable entre los vacunados y los no vacunados (Brosh-

Nissimov et al., 2021). Cuarto, se desconocen los efectos a largo plazo de la vacuna (González et al. 2022). Existe una lista cada vez mayor de medicamentos y nutracéuticos, así como de protocolos para protegerse contra la covid grave y aumentar la probabilidad de permanecer asintomáticos. Desafortunadamente, muchos miembros de la comunidad científica desconocen o son reacios a incorporar estos productos y protocolos preventivos y de tratamiento en la práctica médica convencional. Sin embargo, a medida que se disponga de nuevos datos de investigación, experiencia clínica y educación, debería ayudar a ampliar las prácticas clínicas y mejorar los resultados clínicos. Además de las vacunas, necesitamos otras terapias seguras, eficaces y rentables para salvar vidas y reducir la propagación de esta enfermedad infecciosa. El síndrome de dificultad respiratoria aguda

(SDRA) es un factor clave en la mortalidad por COVID-19. El estrés oxidativo significativamente aumentado debido a la rápida liberación de radicales libres y citocinas (tormenta de citocinas) es el sello distintivo del SDRA, que conduce a lesiones celulares, insuficiencia orgánica y posible muerte. Todo esto está relacionado con la carga viral. Presentamos un estudio de cohorte en Israel en el que más de 175 personas utilizaron una solución de enjuague de yodo patentada (faríngea oral y nasal) como método preventivo y de tratamiento. La implementación del protocolo es segura y parece contar con propiedades protectoras contra la infección por COVID-19.

Palabras claves: Sars-CoV2, COVID-19, yodo, antiviral, carga viral, nasofaríngeo, recuperación

Abstract

Though several vaccines have been granted emergency use authorization there are four drawbacks to the current vaccines; first, the duration of protection wanes after 3 to 6 months and by month six the vaccine appears to afford little protection (Tartof et al. 2021). Second, several direct correlated adverse effects of the different vaccines have been reported (Sharifian-Dorche et al. 2021, Chan et al. 2022). Third, vaccines, even with the short duration of proven protection are not anti-infective, and although they may provide certain protection against severe infection vaccinated individuals are shown to carry equal amounts of viral load making transmission just as likely amongst the vaccinated and unvaccinated (Brosh-Nissimov et al. 2021). Fourth, the long-term effects of the vaccine are unknown

(González et al. 2022). There is a growing list of medicines and nutraceuticals as well as protocols to protect against severe covid and to increase the likelihood of remaining asymptomatic. Unfortunately, many in the scientific community are unaware or reluctant to incorporate these preventive and treatment products and protocols into mainstream medical care practice. However, as new research data, clinical experience, and education is available, it should help amplify clinical practices and improve clinical outcomes. In addition to vaccines, we need other safe, effective, and cost-efficient therapies to save lives and curtail the spreading of this infectious disease. Acute respiratory distress syndrome (ARDS) is a key factor in the fatality outcome of COVID-19. Significantly increased oxidative stress due to rapid release of free radicals and cytokines (cytokine storm) is the hallmark of ARDS, which leads to cellular injury, organ failure, and possible death. All this is related to viral load. We report a cohort study in Israel in which over 175 persons used a proprietary iodine rinsing solution (oral and nasal pharyngeals) as a preventive and treatment method. The implementation of the protocol is safe and appears to have protective properties against Covid-19 infection.

Keywords: Sars-CoV2, COVID-19, iodine, antiviral, viral load, nasopharyngeal, recuperation.

Introduction

In December 2019, an outbreak of a respiratory illness caused by a novel coronavirus (SARS-CoV-2), officially named Coronavirus Disease 2019 (COVID-19), was first reported in Wuhan, China [Wu et al. 2008; Holshue et al. 2020, Lu et al 2020]. COVID-19 rapidly spread worldwide creating a global health emergency [Sohrabi, WHO]. Acute respiratory distress syndrome (ARDS) is a key factor in the fatality outcome of COVID-19. These patients are often depleted in vitamin C (Carr et al 2020) and other key immunomodulatory nutrients such as Vitamin D, Zinc, and Iodine which significantly increases oxidative stress due to the rapid release of free radicals and cytokines (cytokine storm). These events are a hallmark of ARDS, which leads to cellular injury, organ failure and possible death (Cheng, 2020).

The deployment of COVID-19 vaccines in specific regions appears to temporarily curtail widespread infection. In Israel, 80% of the qualified population have received two doses plus a booster jab, including 90% of individuals over the age of 60 years [Burki 2022]. However, the data shows that 6.2M Israelis took the first vaccine shot while 5.7M received the second shot and only 3.6M took the booster; nevertheless, there is close to a 40% decline in vaccine acceptance within just a matter of months (Israel Ministry of Health). It is unknown if this apparent increase in vaccine hesitance is due to the perception of ineffectiveness or fear of possible side effects upon vaccination.

Clinical studies of existing antiviral medications provide inconsistent results and have shown increased toxicity, as such, additional compounds with antiviral activity

should be considered for adjunctive therapeutic use. Iodine known as chemical element I-53 is a scientifically recognized biocide that eliminates fungi, bacteria, and viruses including enveloped viruses (Kariwa, Fujii and Takashima 2021; Wang et al. 2021; Chang et al. 2021). Iodine is an essential micro-nutrient that the body requires while converting iodine to iodide to support proper thyroid functioning and cellular metabolism (Velasco, Bath & Rayman 2018; Mansourian 2011).

However, iodine is different from other nutrients like vitamins C, D, and Zinc which have demonstrated antiviral activity improving clinical outcomes in Covid and other viral illness (González et al. 2014; González et al. 2016; González et al. 2018; González et al. 2020^{A, B}; Holford et al. 2020). They do so by supporting metabolic processes related in multiple mechanisms of both the innate and the adaptative immune system (Miranda-Massari et al. 2020; Miranda-Massari et al 2021).

Iodine is speculated to filter out the spike protein render the virus inactive; it also acts as a biocide. This means iodine plays an external and internal role in protecting our bodies by quite literally deactivating the virus on contact and limiting any viral replication thereby directly reducing viral load. This contrasts with other nutrients which support immunity and metabolic process in a more indirect manner.

Iodine preparations to prevent infection in wounds for over 150 years. Seaweed extracts and oysters were used in the American Civil War and during Napoleon's Egyptian campaign (Flynn, 2003). Later, during the 1950s, a less irritating iodine compound was developed using the combination of molecular iodine and polyvinylpyrrolidone to create a more

suitable compound known as polyvinylpyrrolidone-iodine (PVP-I or povidone-iodine) (Shelanski & Shelanski, 1956). Then, throughout the Asian flu in 1957 it was reported that the use of a compound of iodine compound (Mandl's paint) seemed to prevent the development of influenza. It was found that 14% in untreated group developed influenza, but only 2.8% in the treated group (Menon, 1957).

In addition to direct antiseptic properties, in-vitro studies have demonstrated that iodine can also support the **innate immune system** to protect from bacterial and viral infections Derscheid et al. 2014; Fischer et al. 2011).

In-vitro Iodine Studies

In-vitro studies of iodine, nasal and oral PVP-I antiseptic solutions at concentrations 1-5% were tested for inactivation of the SARS-Cov2 virus. All concentrations were found to be effective inactivating the SARS-CoV-2 after 60-second exposure times. This supports the idea that these types of formulations may help to reduce the viral load, the infection and the transmission of SARS-CoV-2 (Pelletier et al. 2021).

A group of dentists and oral pathologist evaluated the data related iodine rinsing to reduce risk transmission of SARS-Cov2. They found in-vitro studies confirmed that 0.5% PVP-I is effective in reducing SARS-CoV-2 in the nasal cavity, nasopharynx, oral cavity, and oropharynx. Since of oropharyngeal PVP-I is safe, simple, and inexpensive this group recommends its use to reduce the risk of transmission of SARS-CoV-2 viral particles among all patients infected with SARS-CoV-2 to reduce the viral load. In addition, they recommend healthcare professionals and frequent

travelers to use PVP-I mouth rinse to minimize the risk of cross-infection (Chopra et al. 2021).

The threshold for the infectious dose in SARS-COV2 is believed to be quite low while the viral load to trigger severe covid is quite high. The infection period is defined as the incubation period (US National Library of Medicine, NIH) which occurs in the nasal and oral passages. It is here that the virus attaches to the ACE 2 receptors cells with the goal of self-replication. The replication increases the viral load then aerosolized and consequently inhaled into the respiratory tract and potentially further into the respiratory system.

The incubation time in the oral and nasal passages is time zero and ground zero for the start of the immune response. This initial response is the dispatch of T-Cells and Natural Killer (NK) Cells. If viral replication and thus the load is minimized, the patient will likely remain asymptomatic. It has been demonstrated that the lower the viral load the lower the risk is for severe covid (Fajnzylber et al. 2020). Rinsing the oral and nasal passages with an iodine-based rinse which deactivates the virus almost on contact also reduces the virus's ability to replicate and aerosolize into the respiratory tract. The pharmacodynamics of Iodine allows for quick penetration of the cell wall of microorganisms and disrupts protein-nucleic acid structure and synthesis, causing them to become denatured and deactivated (Edis et al. 2019).

Iodine antiseptic uses

Oral and nasal iodine spray rinse has no approved claim in Europe, however, Povidone-iodine or iodopovidone (Betadine) is a Registered E.U. Approved Biocide for external use and a proven antiviral element against "enveloped viruses", i.e Coronavirus

(The European Chemicals Agency (ECHA) Europa Listing on Povidone-iodine). Standard over-the-counter (OTC) iodine sold in retail pharmacies and medical settings is known as Povidone-iodine or Betadine. The use of iodine tinctures has been replaced by the widespread use of povidone-iodine, a water-soluble compound with a well-documented broad spectrum of antimicrobial and its efficacious against several resistant pathogenic microorganisms [Durani and Leaper 2008].

It is these products that the current protocols recommend diluting, however, they require proper dilution for use in the sensitive oral and nasal passages. An extensive review regarding the use of iodine-povidone Povidone-iodine revealed that it can safely be used in the nasal cavity at concentrations up to 1.25% and in the mouth at concentrations up to 2.5% for up to 5 months (Frank et al., 2020).

Clinical trials and In-vivo testing

Based on mechanism of action and data on its effectiveness and safety and clinical experience, several clinical studies were conducted that resulted in similar outcomes. Iodine is one of the most efficient OTC products available for preventing early onset coronavirus immediately reducing viral load at the origin in incubation.

A small randomized clinical study compared reduction in the viral load of patients with COVID-19 when using nasopharyngeal iodine solution. 57 study patients and 33 controls were compared. It was found that nasopharyngeal decolonization may reduce the carriage of infectious SARS-CoV-2 in adults with mild to moderate COVID-19.5 Thyroid dysfunction occurred in 42% of the patients exposed to PI (Guenezan et al. 2021).

In vivo testing with 4 patients demonstrated clear reduction in viral load in 3 of 4 subjects (Martinez Lamas et al. 2020). One study in which 189 people participated used iodine-based nasal irrigation and or spray versus a control group using only water. A statistically significant percentage of nasopharyngeal clearance with all strengths (0.4, 0.5 & 0.6%) of PVP-I nasally compared to the corresponding controls. (Arefin et al. 2022). Oral and nasal iodine rinses demonstrate unequivocal efficacy in Covid-19 patients by reducing viral load and eliminating the virus altogether in just days as proven in these studies and validated by negative PCR test results.

Based on the antimicrobial and safety profile of iodopovidone, BioSimplx LLC designed and produced a patent pending precise iodine formula called AQUARA. It uses a natural elicitor technology and mucosa adhesion to eliminate toxicity, irritation and staining which are the three main concerns that arise from attempting to dilute traditional external iodine applications such as Betadine and Povidone-iodine. The Company has not been granted permission to make anti-covid claims, however, iodine gargle mouthwash was included in the Frontline Covid Critical Care (FLCCC) I-MASK+ Prevention & Early Outpatient Treatment Protocol for COVID-19 version 18. It is also included in our updated Orthomolecular Covid19 protocol (Submitted for publication in Townsend Letter). Since the inclusion of iodine gargle mouthwash in the FLCCC protocol, it was adopted by a group of home respiratory specialists and health care providers in Israel. Consent was obtained from participants.

Prospective Cohort Report

Rabbi Yehoshua Gazi, a community leader, and Rabbi to one of the largest synagogues in his town located in Beit Shemesh, Israel, is a physical therapist and nutritionist that has volunteered his time over the last two years educating in health promotion and preventative care (Prevention Advisor). The educational program included breathing techniques, a healthy diet, and recommendations consistent with the FLCCC protocol including the use of dietary supplements and off-label pharmaceuticals such as ivermectin. From the onset of the pandemic until August 2021, he had seen over 700 COVID patients and their families. Patients ranged in age from their mid-thirties through their mid-eighties and were nearly equally divided between men and women. Prior to implementing the use of topical nasopharyngeal spray iodine solution, he observed the time to recovery was 7 to 11 days (avg = 9 days) with only one person requiring hospitalization. From August 2021 through October 2021 Rabbi Yehoshua Gerzi saw another 160 patients and members of their household and added the iodine-based oral and nasal sprays from BioSimplx LLC. He noted that the time to recovery greatly improved to 3 - 5 days (avg = 4 days) and with zero hospitalizations. The average time to recovery was reduced by 66.6% in the iodine spray group in comparison to the control group.

The reduction in recovery time is consistent with in vitro studies reporting the potent viral inactivation by iodine which as a result produces reduction in viral load. In addition, clinical studies referenced hereto in which iodine hygiene rinsing is found to reduce viral load substantially. Within three days of initiating the protocol nearly all symptoms had resolved themselves.

Another Prevention Advisor for ambulatory home care in Beit Shemesh, Israel, Mr. Chaim Sidman introduced the same proprietary iodine nasopharyngeal spray in response to the update in version 18 of the FLCCC protocol which added iodine gargle mouthwash. Mr. Sidman counselled and advised more than 56 persons from March of 2021 through September of 2021. In most cases where he performed routine follow up care, he noted that other members of the same household did not appear to contract the virus even when in contact with infected individuals.

Discussion

At the outset of the Pandemic the Centers for Disease Control (CDC) The World Health Organization (WHO), The American Dental Association (ADA) and The Australian Dental Association issued guidance for dentists to use a Preprocedural Mouth Rinse (PPMR) to lower viral load of SARS-CoV (Kariwa et al. 2006) and MERS (Eggers et al. 2015) in oral cavities and the oropharynx and consequently, reduce viral load aerosolization. This was also supported by some clinicians and researchers (Ribeiro Reis et al. 2020; Induri et al. 2021; Parhar et al. 2020). The PPMR recommendation consisted of iodine, commonly known as povidone iodine. The organizations did disclaim that at the time of the guidance more testing was necessary. However, vital in vitro research was already known to deactivate the virus in the prior SARS outbreaks (Eggers et al. 2018; Eggers 2019) which demonstrated 99.99% deactivation in seconds using iodine. An in vitro study demonstrated that A PPMR with 100 ppm molecular iodine will play a vital role in combating COVID-19 pandemic by preventing the spread of infection (Moskowitz & Mendenhall 2020).

The concept of therapeutic rinsing was originated in Japan. The population in this country for a long time had consumed the highest amount of daily iodine in the world and for more than 40 years Japan's Ministry of Health, Labour, and Welfare strongly recommended the use iodine mouth rinses for healthcare workers and patients to reduce airborne illness and it remains a standing practice. It would be logical to assume that given what we do know about severe Coronavirus infection and transmission that Japan would be a hot spot. This presumption is due three critical factors; Japan with a population of approximately 130M has (1) amongst the highest average age in the developed world (2) vitamin D levels are just around the average (3) Japan is amongst the most crowded region on a square meter (sqm) basis. It is more crowded than the smaller Country of Israel on a sqm basis. However, according to the data set from World O'Meter (October 31st), Japan's three-day moving average of New Covid Cases is 335 versus Israel at 564. In Japan there has been a total of 1.7M cases {Population 130M} compared to Israel 1.3M {population of 9M} and the U.S. 44M {population of 330M}. The statistics demand a closer look at correlative factors. The epidemiological data show that during the COVID-19 pandemic, in Japan, despite having the eldest population in the world (Population Reference Bureau 2023) and the modest national lockdown measures, have a very low number of COVID-19 deaths compared to other countries. Peru was ranked with highest covid mortality with deaths per 665 deaths per 100K of population, United States ranked 14 with 341 deaths per 100K, UK ranked 20 with 325 deaths per 100K, Israel ranked 70 with 142 deaths per 100K, and

Japan ranked 108 with 57 deaths per 100K. (John Hopkins Coronavirus Resource Center, 2023)

Japan and iodine might have one more hidden story to tell. Covid-19 attacks the most vulnerable of our population; seniors, those with pre-existing conditions, and immunocompromised systems amongst others. Vitamin D is known to help offset severe symptoms of Influenza while Zinc fortifies us against the common cold. Other vitamins also play a vital role in boosting our immune health, especially Vitamin C (González et al. 2020 A, B, Miranda et al. 2021). This process starts from birth and so the deficiency naturally needs to be supplemented constantly. Pregnant women are advised to increase their iodine intake. Correlating this to the data we have seen thus far, the pandemic has seen extremely low childhood mortality (especially amongst children in developed countries where iodine dietary recommendations are followed, and iodine is added to salts). Also in Japan, there is high consumption of high iodine-containing algae. This has very strong implications for iodine consumption and may further explain Japan's success in combating SARS-COV2 without lockdowns and other indirect protocols. The average Japanese diet includes 3000 mcg of daily iodine while the recommended daily allowance is a mere 150mcg.

Initial guidance from leading global health organizations called for the institution of a safe sanitary protocol consisting of rinsing the oral and nasal mucosa to reduce viral load. This protocol serves two main purposes. It prevents severe Covid-19 in patients and reduces transmission of the highly contagious virus. The guidance has since been validated by in vitro testing and subsequently confirmed by

several clinical trials (Seet et al. 2021; Elzein et al. 2021; Seneviratne et al. 2021; Chaudhary et al. 2021). More recently, a systematic review of controlled clinical trials concluded that the current evidence supports povidone iodine as effective against SARS-CoV-2 in saliva and could be implemented as a mouth wash before interventions to reduce the risk of cross-infection in healthcare sites (Garcia-Sanchez et al. 2022).

Conclusion

Iodine has a track record as antiseptic with a broad range of antimicrobial effects for over 150 years. In-vitro, in-vivo and clinical trials have shown that it has antiviral effects against SARS-CoV-2 and can safely reduce viral load when applied to orally and intranasally (oropharyngeal). Initial guidance from leading global health organizations called for the institution of a safe sanitary protocol consisting of rinsing the oral and nasal mucosa to reduce viral load and transmission of the highly contagious virus.

The cohort study in Israel discussed herein using a proprietary iodine formulation establishes a strong case to institute a daily hygiene iodine rinsing protocol. The iodine formula used in Israel utilizes natural elicitors to maintain the virucidal efficacy as that used in Japan. As the first rule of medicine is to do no harm, it would be beneficial to use this essential micronutrient which is proven safe and effective, and incorporate it into a daily hygiene routine when necessary.

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