



Mini Review

Povidone Iodine (PVP-I) mouth gargle/nasal spray may be the simplest and cost effective therapeutic antidote for COVID-19 Frontier

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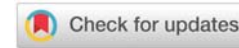
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Abstract

Need an effective protocol for health workers against dangerous and unpredictable SARS CoV-2, a RNA lipid bi-layer enveloped beta-coronaviruses which contains Hemagglutinin Esterase (HE) protein binds with human gene through Angiotensin-Converting-Enzyme 2 (ACE2) and CD147 receptor. Povidone-iodine (PVP-I) has effective virucidal activity by those receptors inhibition and direct kill the virus by membrane disruption. PVP-I gargle, nasal spray and eye drop in case of accidental exposure is well tolerated easy use and has 2-3 hours contamination protection properties. So, uses gargle and nasal spray every 3 hours during shifting duty of health care provider which will cover the total protection and reduced social contamination.

Introduction

Povidone Iodine is Polymer Polyvinylpyrrolidone (PVP-I) well tolerated than other conventional antiseptic agent and completely soluble in cold and mild warm water has pharmacological role of strong anti-viral effect against SARS-CoV, MERS-CoV and recent SARS-CoV-2 [1,2]. SARS-CoV-2 occupies host cells through two receptors: angiotensin-converting enzyme 2 (ACE2) and CD147 (also known as Basigin or EMMPRIN). CD147 is a transmembrane protein and highly glycosylated of the immunoglobulin super family which acts as the main upstream stimulator of Matrix Metalloproteinases (MMPs). Virus spike protein (SP) fixes to ACE2 or CD147 on the host cell, mediating viral invasion and spreading to other cells [3,4]. Like RBCs and type II alveolar cells (AT2) of lung, this CD147 also present in tear and ocular tissues, like conjunctiva, corneal epithelium, endothelium, keratocytes, and retinal

pigment epithelium but ACE 2 receptor absent in such healthy ocular tissues [5]. So, some shorts of upper respiratory tract infection due to binding of SARS CoV-2 with CD147 in ocular tissues then drain into nasal cavity via nasolacrimal duct [3,4]. Study demonstrate virus found in tear/conjunctival specimen is 1.949% of total COVID19 patients. These outcomes point out a possibility of local replication of the virus followed by systemic involvement, especially in cases of droplet or aerosol transmission through the ocular route [6,7]. Another recent study in China almost 31.6% of patients with COVID-19 had ocular involvement. It was also interesting to note that 91.7% of the patients with COVID-19-related conjunctivitis tested positive on a nasopharyngeal swab [8].

In case of SARS-CoV-2, initial interactions between its host receptor (either ACE2 or CD147) and the spike protein S1 domain are the initiating event in establishment of human host infection [9,10].



The inhibitory effect of PVP-I on Hemagglutinin(HA) protein mediated ACE2 and receptor binding host cell transmission decline the cross infection from patients to health care workers also true in opposite order [1,11,12]. The lipid bi-layer envelop The beta-coronaviruses contain several Hemagglutinin Esterase (HE) protein as fifth structural protein [13,14]. Abundant ACE2 receptor is identified in oral tissues, especially in epithelial cells of tongue, type II alveolar cells (AT2) of lung, esophagus upper, stratified epithelial cells, heart, lungs, kidneys, and gastrointestinal tract, thus facilitating viral entry into target cells [12,15]. High amount of ACE2 receptor is in lymphocytes of oral cavity [12], salivary glands which is an early target for SARS-CoV-2 [16]. Prophylactic mouth rinse/gargle and nasal spray inactivate the heamagglutin esterase activity as well as enhance absorption of ACE2 as receptor of host cell infection [17,18].

The process of SARS CoV-2 entering into the host cell begins through the attachment of the S glycoprotein to the ACE2 and CD147 receptor of host cells (such as in type II pneumocytes in the lungs) [19].

In case of unprotected and unattended eye an accidental ocular exposure to SARS-CoV-2 may occur due to accidental hand-eye contact during working in COVID-19 environment or by suspected or confirmed COVID-19 patients droplets, which also can result in accidental ocular exposure. This topic becomes multipart when news of some prevalence like intentional spitting on health worker. Post-exposure prophylaxis in case of accidental ocular exposure of SARS-CoV-2 still in dilemma [20].

Topical povidone iodine along with dexamethasone was found to be very effective in rabbit adenoviral conjunctivitis [21]. In clinical settings, PVP-I (1% and 5%) already showed clinical benefit in cases of adenoviral conjunctivitis. 1% topical PVP-I (eye drop) on stat dose has prophylactic or preventive role of during accidental ocular exposure to SARS CoV-2 [22,23].

Few well-designed studies have established the efficacy of PVP-I eye drops in viral conjunctivitis [21]. For a case of conjunctivitis with COVID-19, this preparation may help to reduce the viral load due to its action against a wide range of viruses. Burning and irritation is a significant side effect of the drug, which can be effectively reduced by diluting 1 mL of 5% PVP-I with 4 mL of BAK containing lubricant drops. This formulation will not only ensure patient comfort but also it will have the advantage of dual antiviral action with BAK and PVP-I [24].

PVP- I (1%) was effectively reducing the infectivity of both SARS-CoV and MERS-CoV in a invitro studies, SARS-CoV for one minute and 15-second for MERS-CoV, were associated with significant loss of viral infectivity to below detectable level [20].

Due to nature of job health workers are at risk group of being infected. According to statistical data analysis in China (December'19 to January'20) about 3.8% health care workers infected during their job. In Spain, an estimated 26% of

confirmed COVID-19 positive healthcare workers. In Italy the rate of infected health care workers was rising from March 2020 to April 2020 from 8% to 10.5%. In United Kingdom about 96% of doctors, 75% of nurses and 59% non-clinical staffs were got infected up to May 2020 [25]. For occupational exposure and scarcity of personal protective equipments (PPE) health care workers are also considered as professional risk group in South Asia. In Bangladesh about 1,172 doctors were confirmed cases, death rate 3.27%, India 1,028 health workers are confirmed cases, death rate 3.30%, Pakistan from 3,635 affected health workers 1.01% death and Afghanistan 346 confirmed cases and death rate is 3.30% till June 22,2020 [26].

After overwhelming devastating outbreak of COVID-19 with high morbidity and mortality rate with huge work load exaggerate the anxiety and Obsessive-Compulsive Disorder (OCD) among the health professionals. More over scarcity of PPE, critical situation handling within the dilemma of proper guideline which grab them into unwanted panic situation [27].

Rationale of study

Extensive risk of cross infection, long lasting pandemic outbreak of SARS-COV-2, critical patients in Intensive Care Unit (ICU) may be the trigger of mental health hazards of health workers worldwide. More over work load, adverse working environment, scarcity of Personal Protective Equipment (PPE), minimal availability of proper safety measures etc. become a challenge to serve the patients properly which turns into mental trauma for health professionals. This article will justify mental hazards and highlight the inexpensive, available and self applicable preventive measures by which health professional keeps confidence to minimize the control of COVID-19 spreading.

Discussion

Povidone-Iodine (PVP-I) is effective virucidal but well tolerable mouth gargle, nasal spray and eye drop than other antiseptics which working against severe acute respiratory syndrome and Middle East respiratory syndrome coronaviruses (SARS-CoV and MERS-CoV) is already proven [1,28]. After dilution in aqueous solution PVP-I complex releases free iodine which oxidizes fatty acid of viral cell wall and deactivates cytosolic enzymes of respiratory chain and inhibits the inflammation of host tissue [13,14,29]. Viral loads are high in the nasal cavity, nasopharynx and oropharynx, lymphocyte of oral tissues, goblet and ciliated cells within the respiratory epithelium of nose have the highest expression of ACE2 the main receptor of SARS-CoV-2 and sometimes accidental ocular exposure CD147 receptor involvement contaminate tear then drain into nasal cavity through nasolacrimal duct. Saliva contains high SARS-CoV-2 viral load up to 1.2×10^8 infective copies/mL [30]. A clinical trial resulted the virucidal efficiency of PVP-I against the SARSCoV-2 virus after incubation time 60 seconds at $22 \pm 2^\circ\text{C}$ in different concentration like 5.0%, 2.5%, 0.5% nasal Antiseptic after 1:1 dilution 2.5%, 1.25%, 0.25% and as oral antiseptic 3.0%, 1.5%, 1.0% after 1:1 dilution minimizing $>4 \log_{10}$ CCID₅₀ infectious virus, from $5.3 \log_{10}$ CCID₅₀/0.1 mL to $1 \log_{10}$ CCID₅₀/0.1 mL or less [30].



Some authors suggested in hospital settings in case of suspected or confirmed COVID-19 patients 0.5% PVP-I solution (0.55 mg/mL available iodine) be applied to the oral, oropharyngeal and nasopharyngeal mucosa of patients with the healthcare personnel in close contact to prevent cross infection [1]. 1 mL of 5% PVP I with 4 mL of BAK containing lubricant drops stat dose during accidental eye exposure or contact decrease the risk for contamination at remarkable level. 0.2% povidone iodine may reduce the risk of ventilator pneumonia [2,20].

Below 0.5% PVP-I gargle once or twice a day up to six-months showed no alteration in thyroid hormone levels (serum T3/T4 and free T4) but small increase in TSH levels within normal range [31]. In case of pediatric patient below 6 years not recommended, 6years or above may use single episode of PVP-I if mandatory [1,32].

Recommendation

According to evaluation of study we found, use of 0.4 % Povidone iodine(PVP-I) gargle, 1% 1:5 prepared solution as eye drop for post exposure stat dose if accidental exposure happened and 0.23% nasal spray doctor's (Anesthesia, oral Dental surgeon and ENT) can get at least 20 minutes working time regarding patient treatment. PVP-I inactivated oropharyngeal cells and salivary gland's ACE2 receptor for SARS CoV 2 and reducing viral load (99.99%) from oronasopharyngeal region for 2-3 hours. Research suggests 1% Povidone iodine (PVP-I) with water/0.9% Normal saline in 1:1.5 ratio mixing and 10% PVP-I with water/normal saline in 1: 30 ratio make 0.4% dilute PVP-I can use as Mouth gargle and Nasal spray. PVP-I with normal saline it beneficial to clean thick mucous secretion, reduce inflammation and allergic reaction [1,33-35].

It would be very cost effective defending front line health workers. On the basis of stable evidence, live clinical trial of USA, UK, Japan, New Zealand, we can recommend every health worker, COVID-19 patient, suspected patient with family or any nursing personnel including patients will be protected from risk of SARS-CoV-2 transmission by using prepared saline diluted 0.4% to 0.23 % gargle and nasal spray (1:1.5 dilution of 1% and 1:30 for 10% PVP-I) [1,11,36].

Nurse, Doctor or health worker use such PVP-I gargle and nasal spray immediate before the starting the duty and just completing the shift. Two spray in each nasal cavity and feel it in throat, hold it for 30 seconds followed by gargle for 30 seconds and should avoid eat or drink till 30 minutes. Person who staying or related to COVID-19 patient including asymptomatic COVID-19 patients or has transmission risk, all should continue the PVP-I gargle and nasal spray in every 3 hour or 4 times a day. There is evidence of 0.4% to 0.23% has no side effect even continuous use of 3 month to 2 years [15,33,34-39]. More over, gag reflex and unconscious cases may be recommended 0.4%-0.5% throat spray.

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