

POST COVID MUCORMYCOSIS PREVENTION WITH ORO-NASAL APPLICATION OF POVIDONE IODINE (PVP-I)

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Abstract

In March 2020 WHO declared COVID-19 as pandemic while April 2021 Indian authority concede to declare a significantly increased incidence of “Black Fungus” among the COVID-19 patients.

The primary route of infection for Mucormycosis or fungal infection following COVID-19 is inhalation or ingestion resulting accumulation of the agents in nose, para-nasal sinuses and mouth. The spores of black fungus intrude neural and vascular structure, which cause mucosal necrosis due to thrombosis in vasculature. The extension of the disease then increases through further destruction of bones of para-nasal sinus as well as neural and vascular route dissemination.

We thought about removing, neutralizing or destroying the culprit fungi from its route of entry zone, i.e. nose and mouth. Povidone Iodine (PVP-I) is a microbicidal agent having effective fungicidal as well as virucidal and bactericidal property. PVP-I can be used in both oral and nasal cavity safely. Efficacy and safety of PVP-I is proved in nose in case of COVID-19. PVP-I is proved effective against different fungi at different concentration at different site.

So, we recommend Povidone Iodine nasal spray or irrigation and mouthwash for gargling for these vulnerable group of patients in large scale to prevent post-COVID mucormycosis or fungal infection.

Key Words: Povidone Iodine, Mucormycosis, COVID-19

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Introduction

On the eve of the new year 30th December 2019, Chinese authority notified World Health Organization (WHO) about an unknown pathogen, causing fatal Pneumonia among the patients. Within a few months, WHO declared the newly named disease COVID-19 as pandemic. On April 2021, the Indian authority discovered an increased incidence of Mucormycosis among the patients suffering from COVID-19, dubbed as “Black Fungus”.¹

Mucormycosis is an opportunistic infection, mostly infecting the people with compromised immunity like patients suffering from diabetes for a long time, people who are taking immune-compromising agent or suffering from diseases that affect their immunity significantly.^{1,2} Manifestation of infection for Mucormycosis tends to be starting from para-nasal sinuses leading to the spread to orbit and brain, hence it is termed Rhino-Orbital-Cerebral infection.^{3,4} Mucormycosis infection frequently cause complete ophthalmoplegia with rapid vision loss, result of affecting cranial nerves II, III, IV, V, and VI 5 which need prompt intervention with anti-fungal agents, surgery and reduction of morbidity risk factor through different measures.⁶ The alarming rise in the prevalence of Mucormycosis among the COVID-19 patients may be the consequence of COVID-19’s ability to alter the immunity of the patient or due to the administration of steroid.⁷

The primary route of infection for Mucormycosis is inhalation, resulting accumulation of the agents in mouth and nose for COVID-19 and para-nasal sinuses for Mucormycosis. The spores of black fungus intrude neural and vascular structure, which cause mucosal necrosis due to thrombosis in vasculature. The extension of the disease then increases through further destruction of bones of para-nasal sinus as well as neural and vascular route dissemination.⁸

We thought about neutralizing or destroying these fungi from its route of entry zone, i.e. nose and mouth.

Povidone Iodine (PVP-I) is an established microbicidal agent having excellent/ effective fungicidal as well as virucidal and bactericidal

property.⁹ PVP-I can be used in both oral and nasal cavity safely. Efficacy against SARS-CoV-2 is already proved.^{10,11} Again, Povidone-iodine has shown rapid activity against *Candida* species in vitro, ranging between 10 and 120 s from contact to kill time.¹² PVP-I has been shown to be highly effective against *Candida albicans*, *Aspergillus species* and *Mucormycosis species* and its use has been reported to reduce medical costs associated with fungal infection.¹² In the study of Ajay Philip et al, effectiveness of Povidone Iodine was proved against otomycosis or fungal otitis externa, which is mostly caused by *Aspergillus species*.¹³

If PVP-I is applied in nasal and oral cavity rationally /properly, the fungi will not be able to settle, invade or grow. Moreover, force of water in nasal irrigation or nasal spray have potentiality to remove fungal particles.

So, use of Povidone Iodine as mouthwash and nasal spray or irrigation will be beneficial as preventive measure for mucormycosis for the vulnerable group of patients, i.e. immunocompromised COVID or non COVID patients.

Povidone Iodine (PVP-I)

Mechanism of action

It is this free iodine that mediates the basic mechanism of action (oxidation of amino acids and nucleic acids in biological structures), which is difficult, if not impossible, to counteract. This basic mechanism of action leads to strong microbicidal activity expressed by multiple modes of action that include the disruption of microbial metabolic pathways, as well as destabilisation of the structural components of cell membranes, causing irreversible damage to the pathogen. PVP I exposure leads to destruction of cytosolic and nuclear structures in bacteria, damage to the cell wall in fungi and degeneration of the nucleoproteins of viral particles. 8,9,12,14,15

Nasal irrigation or spray- How do they work?

In case of nasal irrigation or douching, forceful introduction/application of water causes dislodgement or detachment of fungus (and viruses). Removal of fungus (by any means) is one of the most important issue for treating fungal infection. Even plain water or saline water can serve this purpose partially for this

property 16. Nasal irrigation with saline water is an established treatment option for different types of sinusitis for long time, even PVP-I was used for same purpose in several studies. The topical application of iodine (in low concentration) intranasally for the treatment of recalcitrant chronic rhinosinusitis has been described by the St. Paul's Sinus Centre team in Vancouver. They found it was beneficial for the management of this condition, but also did not lead to any significant effect on thyroid function, mucociliary clearance or olfaction 17.

In case of nasal spray, though the force of water or drug will do the same, but amount of solution, used in nasal spray is minimum, which is suboptimal for removal of fungi, in some extent. To remove or dislodge fungal debris, hyphae or particle- irrigation or douching is much better. Nasal spray is easy to carry, easy to use, no need to have a basin or washroom facility 18. So working/ ambulatory patients can use it. But if the patient is in hospital or home, he / she should use nasal irrigation or douching for better efficacy.

Our novel experience with nasal irrigation (and spray) in COVID-19 patient:

Interestingly, nasal irrigation with PVP-I is soothing for the COVID patient, which is rarely discussed in any literature (still now). During the clinical trial for "Virucidal efficacy of PVP-I in nasopharynx In COVID patient- in vivo" PVP-I nasal irrigation (PNI) is applied to 81 patient and nasal irrigation with Distilled water, i.e. control (CNI) was applied in 27 patient 10. In that trial, patients gave outstanding feedback regarding their feelings following nasal irrigation, especially for PNI (supplementary file – video, consent from patient was taken) . Nasal irrigation with PVP-I was so soothing and refreshing that, some of them insisted our team members of that said clinical trial to apply on them repeatedly.

Recommendation for all confirmed or suspected COVID Patients, especially for immunocompromised patients

A. For nasal application of PVP-I: Any of 2 forms is more or less effective, i.e. i) nasal irrigation or ii) nasal spray .

i. Nasal irrigation :

With 100-150 ml of 0.5% PVP-I solution and with Higginson's syringe or 50 cc Disposable syringe, each nasal cavity should be irrigated 2-4 times daily for 1 month.

ii. Nasal spray:

0.6% PVP-I nasal spray 2-3 puff in each nostril 3-4 times daily for 1 month is recommended.

(a) For fully conscious patients- nasal irrigation (preferable) or nasal spray (alternatively)

(b) For patient with altered consciousness – nasal spray

B. For oral application of PVP-I: Any of 3 forms is effective, i.e.

i. Mouth rinsing and gargling with PVP-I 1% solution (undiluted) 10 ml for 30 second or PVP-I 0.5% solution 20 ml for 1minute (here, PVP-I 1% solution 10 ml should be mixed with 10 ml water) for 1–2 min for 1month is proposed. In case of 10% PVP-I solution, 1 ml should be mixed with 19 ml water to get the same concentration.

ii. PVP-I Throat spray is an alternative (if available) of gargling.

iii. A sponge swab or similar is soaked in 2–5 ml of 1% PVP-I solution and this is carefully wiped around all oral mucosal surface and tongue

(a) For fully conscious patients- gargling, mouth rinsing or throat spray

(b) For patient with altered consciousness—throat spray or PVP-I soaked sponge swab 19,20,21,22.

Conclusion

PVP-I is proved effective against all types of virus and fungi, irrespective of their species due to its extraordinary mechanism of action. Use of this compound is quite safe for human body and already is being used in different form in different site of human body since 1955. This strategy benefits from broad availability of materials, excellent safety profile and associated low costs. Introduction of PVP-I may reduce the incidence of Mucormycosis and thus reducing the disease burden of the immunocompromised patients along with the minimization of prolonged anti-fungal drug administration and surgical intervention. It will not only make the

patients suffer less, but also it will ease the additional logistics requirement for the treatment of the patients. As the death toll and number of patients is still on the rise, intervention as such will have tremendous effect on the disease transmission and outcome of the disease.

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