

Post-Covid Prophylaxis in Adults: A Systematic Review

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Abstract

The COVID-19 pandemic has resulted in a growing population of individuals with a wide range of persistent symptoms after acute SARS-CoV-2 infection. This comprises patients with symptoms that develop during or after COVID-19, continue for ≥ 4 weeks, and are not explained by an alternative diagnosis. Several terms have been used to describe prolonged symptoms following COVID-19 illness, such as "post-COVID conditions," "long COVID," "post-acute sequelae of SARS-CoV-2 infection (PASC)," "post-acute COVID-19," "chronic COVID-19," and "post-COVID syndrome." Whether the constellation of symptoms represents a new syndrome unique to COVID-19 or if there is overlap with the recovery from similar illnesses has not been determined. While most patients with mild acute COVID-19 disease are expected to recover quickly (e.g., two weeks), a longer recovery should be expected in those with moderate to severe acute disease (e.g., two to three months, sometimes longer in those who survive critical illness). The wide variability in time to symptom resolution likely also depends upon premorbid risk factors as well as illness severity during acute COVID-19. During the initial follow-up evaluation, we obtain a comprehensive history of the patient's COVID-19 illness, including the illness timeline, duration and severity of symptoms, types and severity of complications, COVID-19 testing results, and any management strategies. The need for laboratory testing is determined by illness severity, prior abnormal testing during their illness, and current symptoms. We do not routinely re-test patients for active infection with SARS-CoV-2 at the time of follow-up outpatient evaluation. Instead, we follow a non-test-based approach to removing infectious precaution.

Keywords: Prophylaxis; Epidemic; Steam Inhalation.

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INTRODUCTION

In Dec 2019, a novel pathogen emerged, and within weeks, led to the emergence of the biggest global health crises seen to date. The virus called 'SARS-CoV-2', causes coronavirus disease which was named 'COVID-19' by the World Health Organization (WHO). The speedy spread of this infection globally became a source of public worry and several unknowns regarding this new pathogen created a state of panic. Mass media became

the major source of information about the novel coronavirus. Much like the previous pandemics of SARS (2003), H1N1 (2009), and MERS (2012), there were various prophylaxis found in the adults. In this review, we analyze the post Covid prophylaxis in adults, and make scientific inferences. The COVID-19 pandemic highlights multiple social, cultural, and economic issues arising from the media's arguable role.¹

From a healthcare perspective, infection due to the novel coronavirus SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) and the ensuing syndrome called COVID-19 (coronavirus disease 2019) represents the biggest challenge the world has faced in several decades. Particularly worrisome are the high contagiousness of the virus and the saturation of hospitals' capacity due to overwhelming caseloads. Non-pharmaceutical interventions such as quarantine and inter-personal distancing are crucial to limiting the spread of the virus in the general population, but more tailored interventions may be needed at an individual level on a case-by-case basis. In this perspective, the most insidious situation is when an individual has contact with a contagious subject without adequate protection. If rapidly recognized afterwards, this occurrence may be promptly addressed through a post-exposure chemoprophylaxis (PEP) with antiviral drugs. This strategy has been implemented for other respiratory viruses (influenza above all) and was successfully used in South Korea among healthcare workers against the Middle East respiratory syndrome (MERS) coronavirus, by providing people who were exposed to high-risk contacts with lopinavir-ritonavir plus ribavirin. Initial experiences with the use of hydroxychloroquine to prevent COVID-19 also seem promising. Post-exposure chemoprophylaxis might help mitigate the spread of SARS-CoV-2 in the current phase of the COVID-19 pandemic.²

DEFINITION

The World Health Organization (WHO) defined the coronavirus disease 2019 (COVID-19), which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), as a public health emergency of international concern.¹ The spread of COVID-19 is reaching alarming figures in many countries. As of 2 May, 2020, 3,267,184 cases of COVID-19 have been confirmed worldwide. Overall, more than 229,971 deaths have been reported thus far, with a case fatality rate of about 7%. In such a situation, it is essential to forecast the epidemic trend in order to take adequate healthcare

measures.³ The attack rate (AR) (i.e., the percentage of exposed patients who will eventually become infected) is a metric that may help to estimate this trend. The AR of SARS-CoV2 is still a matter of debate. The WHO reported an AR of about 3%–10% in household contacts of SARS-CoV-2 patients in the Guangdong Province of China, which is similar to that of influenza viruses (about 10%). In the absence of a specific vaccine, the strategy of epidemic containment lays mainly in the isolation of both cases and contacts and in social distancing of the entire population. Many countries have taken a series of exceptional containment measures, including locking down entire cities. These measures have high social and economic costs but are necessary to avoid the potential collapse of national health systems.⁴

In this context, a post-exposure prophylaxis (PEP) approach may help to reduce the spread of the COVID-19 epidemic. This procedure consists of the administration of drugs to a subject who has been exposed to an infected patient, in the attempt to reduce the risk of becoming infected. The drugs administered are often the same drugs used to treat patients. This strategy is not novel. Indeed, it is well established in the setting of acute viral respiratory infections. For example, oseltamivir and zanamivir, two antivirals used to treat flu symptoms, are administered to exposed subjects to reduce the risk of secondary cases.⁵ In a meta-analysis, oseltamivir and zanamivir prevented flu symptoms recurrence in 67%–89% of subjects who underwent PEP. With respect to the coronavirus responsible for the SARS epidemic, no pharmacological prevention strategies were implemented beyond non-specific measures as active symptom monitoring or home quarantine in some countries in 2002–2004. On the other hand, in the setting of the coronavirus responsible for the Middle East respiratory syndrome (MERS), a study conducted in South Korea evaluated whether PEP was effective in preventing MERS in healthcare workers (HCWs) after unprotected exposure to infected patients. The study enrolled 22 HCWs receiving ribavirin plus lopinavir/ritonavir within 80 h (median 36 h) of unprotected exposure in the previous 14 days. No HCW in the PEP arm contracted MERS versus 6/21 cases in the control (non-PEP) arm (0% vs. 28.6%, $p = 0.009$). Overall, 21/22 HCWs undergoing PEP experienced adverse effects, but all were mild. Moreover, there were no discontinuations, and the risk/benefit ratio was considered reasonable.⁶

Regarding COVID-19, a study from South Korea evaluated the efficacy and tolerability of a PEP strategy using hydroxychloroquine, which was

administered to 211 persons (189 patients and 22 HCWs) who were potential contacts of the index patient, a hospital social worker. The drug was administered at a dose of 400 mg/die for the period of quarantine (14 days) within a median of 58 h after the detection of the index case. The type of exposure was classified as high-risk exposure in nine cases. PEP was completed in 97% of subjects without serious events. The most common symptoms associated with the drug were diarrhea and skin rash. No subject tested positive at the end of quarantine period. However, no definitive conclusions may be drawn from this study without a control arm.⁷

To date, there is no approved treatment for COVID-19. Several trials are now evaluating the effects of various types of COVID-19 treatment but, to our knowledge, only a few studies have been designed to evaluate a prophylactic approach in COVID-19.⁸

Given the worldwide spread of the COVID-19 epidemic, the lack of treatment and the very promising results of the MERS study, it seems reasonable to evaluate whether a PEP approach could reduce the spread of the infection. However, several aspects remain to be established before conducting such a trial, including the drug to administer, the interval between exposure and PEP onset, as well as the dosage and the duration of administration. The drug to use should be one of those currently under study, namely lopinavir/ritonavir, chloroquine, remdesivir, darunavir/ritonavir, ribavirin, arbidol, neuraminidase inhibitors, peptide (EK1), and RNA synthesis inhibitors. Although these drugs were developed for a vast array of treatments, they are now being repurposed to counter COVID-19 based on potential in vitro efficacy.⁹

SCOPE

This document provides an integrated holistic approach for managing patients who have recovered enough from COVID for care at home. It is not meant to be used as preventive / curative therapy. The recovery period is likely to be longer for patients who suffered from more severe form of the disease and those with pre-existing illness.

POST-COVID FOLLOW UP PROPHYLAXIS

- At individual level
- Continue COVID appropriate behaviour

(use of mask, hand & respiratory hygiene, physical distancing). • Drink adequate amount of warm water (if not contra-indicated).

- Take immunity promoting AYUSH medicine (details of medicines and their dosage is at Annexure I) - To be practiced and prescribed by at qualified practitioner of AYUSH. If health permits, regular household work to be done. Professional work to be resumed in graded manner.
- Mild/ moderate exercise & Daily practice of Yogasana, Pranayama and Meditation, as much as health permits or as prescribed.
- Breathing exercises as prescribed by treating physician. tolerated.
- Daily morning or evening walk at a comfortable pace
- Balanced nutritious diet, preferably easy to digest freshly cooked soft diet.
- Have adequate sleep and rest.
- Avoid smoking and consumption of alcohol.
- Take regular medications as advised for COVID and also for managing comorbidities, if any. Doctor to be always informed about all medicines that the individual is taking (allopathic/AYUSH) so as to avoid prescription
- Self-health monitoring at home temperature, blood pressure, blood sugar (especially, if diabetic), pulse oximetry etc. (if medically advised)
- If there is persistent dry cough/ sore throat, do saline gargles and take steam inhalation. The addition of herbs/spices for gargling/steam inhalation. Cough medications, should be taken on advice of medical doctor or qualified practitioner of Ayush.

Look for early warning signs like high grade fever, breathlessness, SpO₂ < 95%, unexplained chest pain, new onset of confusion, focal weakness.¹⁰

AT THE LEVEL OF COMMUNITY

- Recovered individuals to share their positive experiences with their friends and relatives using social media, community leaders, opinion leaders, religious leaders for creating awareness, dispelling myths

and stigma.

- Take support of community based self-help groups, civil society organizations, and qualified professionals for recovery and rehabilitation process (medical, social, occupational, livelihood)
- Seek psycho-social support from peers, community health workers counsellor. If required seek mental health support service. Participate in group sessions of Yoga, Meditation etc. while taking all due precautions like physical distancing.¹¹

IN HEALTHCARE FACILITY SETTING

- The first follow-up visit (physical/ telephonic) should be within 7 days after discharge, preferably at the hospital where he/she underwent treatment.
- Subsequent treatment/follow up visits may be with the nearest qualified allopathic/ AYUSH practitioner/medical facility of other systems of medicine. Poly-therapy is to be avoided due to potential for unknown drug-drug interaction, which may lead to Serious Adverse Events (SAE) or Adverse Effects (AE).
- The patients who had undergone home isolation, if they complain of persisting symptoms, will visit the nearest health facility.
- Severe cases requiring critical care support will require more stringent follow up.

Another issue is the design of the study. A high-quality randomized controlled trial (RCT) would

reveal whether the PEP strategy is effective or not in containing COVID-19. A potential example is an ongoing RCT from Spain. However, such a design might be prone to distortions, such as contamination and attrition bias; moreover, a large sample size is required, and results cannot be obtained in a timely fashion. As an alternative, in countries with a high burden of cases, a study comparing the attack rate before and after PEP onset in the area under study may provide initial proof of efficacy more rapidly. Potential enrollees would be people who are in contact with COVID-19 patients, individuals already identified by health authorities, or HCWs after unprotected exposure to COVID-19 patients. In ordinary times, such a study should follow proof of in vitro and in vivo activity of the drug and its therapeutic efficacy. In the present exceptional times, any promising approach should be urgently exploited to contain the epidemic.¹²

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