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EMERGING PROPHYLAXIS FOR DENTAL PRACTITIONERS AGAINST COVID-19 INFECTION

Dental Science

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ABSTRACT

The current COVID-19 emergency warrants the urgent development of potential strategies to protect people at high risk of infection-particularly close contacts and health-care workers. In order to protect staff and preserve personal protective equipment and patient care supplies, as well as expand available hospital capacity during the COVID-19 pandemic, the Centers for Disease Control and Prevention (CDC) recommends that dental facilities postpone elective procedures, surgeries, and nonurgent dental visits, and prioritize urgent and emergency visits and procedures now and for the coming several weeks. Through this paper we would like to review the prophylaxis for dental practitioners.

KEYWORDS

19, Dental practitioners, Prophylaxis, infection

L. INTRODUCTION:

The current COVID-19 emergency warrants the urgent development of potential strategies to protect people at high risk of infection-particularly close contacts and health-care workers[l].

In order to protect staff and preserve personal protective equipment and patient care supplies, as well as expand available hospital capacity during the COVID-19 pandemic, the Centers for Disease Control and Prevention (CDC) recommends that dental facilities postpone elective procedures, surgeries, and nonurgent dental visits, and prioritize urgent and emergency visits and procedures now and for the coming several weeks[2].

WHO has accelerated research in diagnostics, vaccines and therapeutics for this novel coronavirus. The various strategies for prevention of transmission and infection of this respiratory pathogen includes[3]

1) Health Promotion - Non Pharmacological Interventions:

- Isolation at home
- Voluntary quarantine at home
- Social distancing of entire population
- Temporary closure of schools, universities and work places

2) Pharmacological Interventions- Specific protection through chemoprophylaxis or immunoprophylaxis

which includes:

- Antiviral agents
- Chloroquine-HydroxyChloroquine (HCQS) . Vaccination

II. Non pharmacological interventions at clinical setting:

Due to the characteristics of dental settings, the risk of cross infection can be very high between patients and dental practitioners. For dental practices and hospitals in areas that are (potentially) affected with COVID-19, strict and effective infection control protocols are urgently needed[4].

The person-to-person transmission routes of COVID-19 includes direct transmission, such as cough, sneeze, droplet inhalation transmission, and contact transmission, such as the contact with oral, nasal, and eye mucous membranes. COVID-2019 can also be transmitted through the saliva, and the fecal—oral routes may also be a potential person-to-person transmission route. The participants in dental practice expose to tremendous risk of COVID-2019 infection due to the face-to-face communication and the exposure to saliva, blood, and other body fluids, as well as the handling of sharp instruments. Dental professionals play great role in preventing the transmission of COVID-2019. The possible transmission routes of COVID-2019 in stomatology are airborne spread, contact spread, and contaminated surface spread.

Various practical strategies which can be implemented to block virus transmission during dental diagnosis and treatment includes patient evaluation, hand hygiene, personal protective measures for the dental professionals, mouthrinse before dental procedures, rubber dam isolation, anti-retraction handpiece, disinfection of the clinic settings and proper management of medical waste[5].

III. Pharmacological interventions

Pre-exposure prophylaxis and postexposure prophylaxis (PEP) with antimicrobial drugs are effective in preventing illness before potential exposure or after documented exposure to a variety of microbial pathogens, and in reducing the risk of secondary spread of infection. For example, PEP with Rifampicin is given to people exposed to index cases of invasive meningococcal infection, and oseltamivir has been recommended by WHO for people at high risk of infection before or after exposure to pandemic influenza[l].

a) Antiviral agents:

The implementation of antiviral treatment and prophylaxis has several requirements. The stockpile of drugs must be adequate, the safety of treatment must be very high, and costs should ideally be low. Antiviral drugs administered shortly after symptom onset can reduce infectiousness to others by reducing viral shedding in the respiratory secretions of patients (SARS-CoV-2 viral load in sputum peaks at around 5—6 days after symptom onset and lasts up to 14 days), and targeted prophylactic treatment of contacts could reduce their risk of becoming infected[1].

Protease inhibitors like Lopinavir have shown to be a strong inhibitor of the protease enzyme present in SARS-CoV which is important for the life cycle function of this virus. The largest study reported till date on use of Lopinavir plus Ritonavir for its efficacy in patients infected with COVID-19 conducted in China found no difference in the clinical outcome when compared to standard care alone. There is currently a trial NCT04304053 ongoing to look into the efficacy of Darunavir/Cobicistat plus chloroquine treatment in all who are found to be infected. Currently, there is no recommendation for use of antiviral agents for prophylaxis of COVID-19[3].

b) Chloroquine-Hydroxy Chloroquine (HCQS):
Chloroquine is a widely known for more than 70 years, is easily available and affordable antimalarial agent with proven chemoprophylaxis properties in malaria. Various mechanisms have shown it to have a role in SARS COV infection, too. The SARS-CoV2 is known to bind to human cells via the Angiotensin Converting Enzyme 2 (ACE 2) receptor. In vitro studies have shown that the glycosylation process of ACE-2 receptor gets affected thus causing the Vero cells pre-treated with chloroquine to be refractory to SARS-CoV infection, that may be the mechanism through which even human cells can become refractory to this infection. It has also been seen that treatment with chloroquine prevents the spread of SARS-CoV infection in the post infection period[3].

i. Theories of mechanism of action:
The anti-viral and anti-inflammatory activities of chloroquine may have a role in the treatment of patients with novel COVID-19. Chloroquine increases endosomal pH and interferes with the glycosylation of cellular receptor of SARSCoV and thereby it has the potential to block viral infection[4]. Chloroquine also inhibits the quinone reductase-2, that makes this agent a broad antiviral agent. It is believed that chloroquine can also interfere with ACE2 receptor glycosylation thus prevents SARS-CoV- 2 attachment to the target cells. Since the structure and mechanism of action of chloroquine and hydroxychloroquine (HCQ) are exactly same except an additional hydroxy moiety in one terminal in HCQ, both act as a weak base that can change the pH of acidic intracellular organelles including endosomes /lysosomes, essential for the membrane fusion.Data show HCQ effectively inhibited both the entry, transport and the post-entry stages of SARS-CoV2. In addition, HCQ acts effectively on other intracellular bacterial infections such as Coxiella burnetii (Q fever) and Tropheryma whipplei . Addition of hydroxyl molecule makes HCQ less permeable to blood-retinal barrier and allows faster clearance from retinal pigment cell, thereby suggesting a lesser risk of retinal toxicity, as compared to chloroquine. Furthermore, the narrow therapeutic and safety index margin with chloroquine makes HCQ a safer option than chloroquine, specially in severely sick patients where a cytokine storm may be associated with disease severity of SARS-CoV-2. The significant decrease in the production of pro-inflammatory markers and cytokines with HCQ has made this agent a successful disease modifying anti-inflammatory agent in the treatment of various autoimmune diseases including rheumatoid arthritis, systemic lupus erythematosus and Sjogren's syndrome. Long-term clinical safety profile of HCQ is better than that of chloroquine, that allows higher daily dose of I-ICQ with less drug-drug interactions [6]

In other human trial Hydroxychloroquine along with azithromycin was studied in Marseille, France.[5] HCQ plus azithromycin appeared to lead to faster reduction in viral carriage.

Results are not adequate to support clinical use of this combination.

Combining azithromycin along with HCQ has shown to increase the risk of QTc prolongation. Dose : 500 OD for 5 days. (Monitor Qtc interval especially when combined with HCQ).

Both these drugs have also shown to have immunomodulatory effects and can suppress the increase immune factors, which may play a role in reducing the severity of coronavirus disease.

The first ever human trial of chloroquine against COVID19 was conducted by Chinese investigators. The study conducted in more than 100 patients found chloroquine to be superior in reducing symptom duration, exacerbation of pneumonia, radiological improvement and lead to virus-negative seroconversion. The National Health Commission of the People's Republic of China recommended inclusion of chloroquine in the Guidelines for the Prevention, Diagnosis, and Treatment of Pneumonia Caused by COVID-19. In this study, chloroquine was given in dose of 500 mg of chloroquine twice daily in mild to severe COVID- 19 pneumonia[6].

Analysis revealed that chloroquine could prevent ORFIab, ORF3a, and ORFIO from attacking the heme to form the porphyrin, and inhibit the binding of ORF8 and surface glycoproteins to porphyrins to a certain extent, effectively relieve the symptoms of respiratory distress[7]

Currently many trials are still underway to study the effect both for prophylaxis and treatment.

ii. The National Taskforce constituted by Indian Council for Medical Research for COVID-19 recommends the use of hydroxy-chloroquine for prophylaxis of SARS-CoV-2 infection for selected individuals as follows[7]:

Eligible individuals:
Asymptomatic healthcare workers involved in the care of suspected or confirmed cases of COVID-19

Asymptomatic household contacts of laboratory confirmed cases

2. Dose:
Asymptomatic healthcare workers involved In the care of suspected or confirmed cases of COVID-19: 400 mg twice a day on Day 1 , followed by 400 mg once weekly for next 7 weeks; to be taken with meals

Asymptomatic household contacts of laboratory confirmed cases: 400 mg twice a day on Day I followed by 400 mg once weekly for next 3 weeks; to be taken with meals

3. Exclusion/contraindications:
The drug is not recommended for prophylaxis in children under 15 years of age.

The drug is contraindicated in persons with hypersensitivity to these agents, retinopathy, porphyria, epilepsy, pre-existing maculopathy, G6PD deficiency, recent myocardial infarction and Q Tc >500 msec. Chloroquine is not contraindicated in pregnancy. iii. Precautions Patients taking these drugs should be frequently monitored for hematological parameters, serum electrolytes, blood glucose, hepatic and renal functions. As these drugs are known to cause QTc prolongation, routine ECG is essential prior to starting these drugs [3]. Co-administration of other drugs known to prolong the QTc interval (such as anti-arrhythmic, anti-depressants, anti-psychotics, anti-histaminic, teneligliptin, ondansetron and moxifloxacin etc.) must be avoided [6]. iv. Key considerations:

The drug has to be given only on the prescription of a registered medical practitioner.

Advised to consult with a physician for any adverse event or potential drug interaction before initiation of medication

The prophylactic use of hydroxychloroquine to be coupled with the pharmacovigilance for adverse drug reactions through self-reporting using the Pharmacovigilance Program of India (PvPl) helpline/app.

If anyone becomes symptomatic while on prophylaxis he/she should immediately contact the health facility, get tested as per national guidelines and follow the standard treatment protocol.

All asymptomatic contacts of laboratory confirmed cases should remain in home quarantine as per the national guidelines, even if they are on prophylactic therapy.

S i m u ltaneously, proof of concept and pharmacokinetics studies be taken up expeditiously. Findings from these studies and other new evidence will guide any change in the recommendation.

C) Vaccines:
There is considerable global investment and effort towards development of a vaccine. Various clinical trials are going on around the world and we hope that the results of the ongoing trials give us more insight on prophylaxis and help in better prevention and thus decreasing the transmission of this widely spreading disease[3].

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