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Hydroxy Chloroquine Prophylaxis Experience in Doctor Community with COVID-19 in West Bengal

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ABSTRACT

Background

The Indian Council of Medical Research (ICMR)National task Force for COVID-19 reviewed the data on in-vitro testing of Hydroxy Chloroquine (HCQ)for antiviral efficacy against SARS-CoV-2, safety profile and recommended it's use for prophylaxis among health care workers (HCWs). The efficacy of HCQ against Covid -19 has been the subject of contradictory results. Given the need for insights into the clinical outcomes and side effects among doctors on prophylaxis with hydroxychloroquine, we conducted a retrospective analysis of doctors treated at home or hospital with COVID-19 infection.

Methods

The data was collected by direct interview, electronic data transfer from COVID-19 positive doctors using real-time reverse transcription-polymerase chain reaction (RT-PCR) test from two medical colleges, friends and relatives of doctors who voluntarily provided their illness information during the period of August, 26 to Nov 25, 2020.

Results

A total of 117 doctors participated in study. Out of 117 covid positive doctors, 76 received no HCQ prophylaxis and 41 received prophylaxis till the onset of the symptom. Out of 117 positive doctors, 32(27%) developed moderate to severe (MS) illness. Nine doctors (22%) developed MS in HCQ group and none of them died. Out of no HCQ group 23(30%) developed MS illness and 7(9%) died. There was no statistically significant relation between use of HCQ and outcomes of disease. The most common (22%) side effect of HCQ prophylaxis was related to gastrointestinal system.

Conclusions

Hydroxy Chloroquine has a disease modifying effect on COVID-19 disease although it is not robust.

Keywords: COVID-19; doctor community; experience; HCQ; prophylaxis; side effects.

INTRODUCTION

The World Health Organization had declared COVID-19 as a public health emergency of international concern on 31 January 2020.[1] The clinical manifestations of SARS-CoV-2 infection ranges from asymptomatic infection to severe critical illness.[2] Apart from different anecdotal evidences, a meta-analysis suggests that glucocorticoids probably reduce mortality and mechanical ventilation in patients with severe COVID-19.[3] Among repurposing drugs, the antimalarial and immunomodulatory drug hydroxychloroquine (HCQ) captured great attention. It is preferred due to its higher water solubility, lower toxicity and also feasibility for prolonged use with increased tolerance.[4] The possible antiviral mechanism is multi-targeted, depending on the time

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point at which the drug is added.[5,6] The efficacy of HCQ against Covid -19 has been the subject of contradictory results. Given the great need for insights about hydroxychloroquine, we conducted a retrospective study on status of hydroxychloroquine prophylaxis, severity with outcome of COVID-19 in respect to recovery or death and its side effects in doctor community with COVID-19 in West Bengal.

METHODS

After ethical committee (RKC/38/20) approval, we conducted a retrospective analysis of doctors treated at home or hospital with COVID-19 infection. The data was collected by direct interview, electronic data transfer from COVID-19 positive doctors of two medical colleges, friends and relatives of doctors who voluntarily provided their illness information during the period of September to November, 2020. Each participant was informed about the study purpose, and verbal consent was obtained before proceeding with telephonic interview. All asymptomatic and symptomatic doctors testing positive on real-time reverse transcription-polymerase chain reaction (RT-PCR) for SARS-CoV-2 were included in the study. A brief 15-item interview schedule was developed to elicit the information on key issues, such as department, designation, HCQ prophylaxis with duration, clinical presentation, co-infection, co-morbidity, place of treatment with details and side effects of HCQ. The quantitative variables and qualitative measures were defined with mean and standard deviation and proportion respectively. Categorical measures were presented as percentages. The frequencies of categorical variables were compared using the chi-square and Fisher's Exact Test as appropriate. Statistical analyses were performed using SSPS software (version 25). The tests with p value of <0.05 were considered statistically significant.

RESULTS

A total of 117 doctors included in this study. Out of 117 COVID-19 positive doctors, 76(64.9%) received no HCQ prophylaxis and 41(35.1%) received prophylaxis till the onset of the symptom. Out of 76 non HCQ group, 8 doctors had taken hydroxychloroquine for initial 8 weeks then discontinued. Only 7.6% of the positive doctors were asymptomatic. Eighty-five per cent of doctors were males, although the reasons remain to be clarified. While the mean age of the doctors was 41.1 year (standard deviation ±12.97; interquartile range (IQR): 23-71). The demographic profile of doctors was depicted (Table 1).

Table 1. Clinico-demographic profile of doctors with covid-19 (n=117)

Variables	Frequency (%)
Sex	
Male	100(85)
Female	17(15)
Age group (years)	
<40	62(53)
40-60	40(34)
>60	15(13)
Specialty	
Physician	93(79)
Surgeons	21(18)
Administrators	3(3)
HCQ	
Received	41(35)
Not Received	76(65)
Asymptomatic	
Present	9(8)
Absent	108(92)
Severity	
Mild	76(70)
Moderate	17(16)
Severe	15(14)
Outcome	
Recovery	110(95)
Death	7(5)
Co-morbidity	
Present	35(30)
Absent	82(70)
Co-morbidity	
Diabetes mellitus	15(13)
Hypertension	8(7)
Obesity	6(5)
Asthma	6(5)

Out of 117 positive doctors 32(27.3%) developed moderate to severe (MS) illness. Nine doctors (22%) developed MS in HCQ group. Out of no HCQ group 23(30%) developed MS illness (Table 2).

Table 2. Clinical outcome measures (severity ,mortality and hospitalisation).			
Covid Clinical Outcomes	Hydroxychloroquine		p-value
	Yes (N=41)	No (N=76)	
Severity			
Asymptomatic/ mild disease	32(78)	53(70)	0.39
Moderate	9(22)	23(30)	
Severe disease			
Mortality	0(0)	7(9)	0.09
Treatment			
Hospitalization	14(34)	31(41)	0.55
Home care	27(66)	45 (59)	

The most common (22%) side effect of HCQ prophylaxis was related with gastrointestinal system (Table3).

Table 3. Adverse events of doctors on HCQ prophylaxis. (n=49)	
Adverse events	**Frequency (%)**
Anorexia	6(12%)
Nausea	5(10%)
Abdominal pain	2(4%)
Diarrhea	1(2%)
Gasstro-Esophagial Reflux	3(6%)
Transient Headache	0
Fatigue	2(4%)
Rash	1(2%)

DISCUSSION

Over a period of time, we have seen immense growth on the protective front against the COVID-19 pandemic. Be it novel antiviral, antibody cocktails to ultimate options as vaccines, we have come a long way from the very beginning of HCQ. Prevention is always better than cure and the current pandemic has only emphasized this from sanitizers to face-mask. A potential repurposing drug HCQ for prevention of disease has received little attention, and it has been studied throughout the world and dismissed based on flawed studies and political controversy that obscured the value of this treatment as pre-exposure prophylaxis for SARS-CoV-2 infection.[7] In this study only 7.6% of the study cohort were asymptomatic. A possible reason for the same is believed to be selection bias of the cohort of doctors who got infected. Gao et al noted that chloroquine had a significant effect both in terms of clinical outcome and viral clearance compared to control groups. They found that chloroquine was useful in inhibiting the exacerbation of pneumonia, improving lung imaging, and bringing about virus-negative results, therefore shortening the disease's course.[8] The in-vitro testing of HCQ for antiviral efficacy showed reduction of infectivity /log reduction in viral RNA copy of SARs-CoV2 at National Institute of Virology, Pune, India. The Indian Council of Medical Research (ICMR) approved the use of HCQ for the treatment as well as prophylaxis of COVID-19 in asymptomatic healthcare workers (HCW) involved in the care of suspected or confirmed cases of Covid19 and asymptomatic house hold contacts of confirmed cases. [9]The National task Force for Covid 19 reviewed the data on in-vitro testing of HCQ for antiviral efficacy against SARS-CoV-2, safety profile of HCQ reported to the pharmaco-vigilance program of India, and data on the use of HCQ for the prophylaxis of SARS-CoV-2 infection among health care workers (HCWs).[10] In view of recent randomized trials and meta-analysis showing contradictory results regarding any positive impact of HCQ on SARS-COV-2 infection and related outcomes both as pre and post-exposure strategy, a real-life data on doctor community would help complement the existing database. Most of the studies on pre-exposure prophylaxis from India had a focus on prevention of disease, but severity or clinical outcomes were not so much reported in a high risk community. However, in spite of existing guidelines from government, 35 percent of doctors seemed to be taking HCQ regularly as evident from our study. The doses schedule of HCQ is recommended ,400 mg twice a day on Day 1, followed by 400 mg once weekly for next 7 weeks; to be taken with meals, even beyond 8 weeks on weekly dosage with strict monitoring of clinical and ECG parameters which would also ensure that the therapy is given under supervision[10] . There were significant differences in the distribution of COVID-19 patients within variables. The incidence of COVID 19 was higher in medical specialties (79%) as surgical specialties had less exposure to infected patients due to cancellation of routine surgeries. The severity of COVID-19 is

categorized as mild, moderate, severe and critical illness depending upon presence of mild symptoms without dyspnea ; presence of clinical or radiographic evidence of lower respiratory tract disease with oxygen saturation ≥94% ;oxygen saturation <94% respiratory rate >30 , lung infiltrate >50%; and respiratory failure, shock, and multiorgan dysfunction or failure respectively.[11] Forty-five doctors were hospitalized, out of them 32 for moderate to severe illness and four for only co-morbidity, 2 doctors for associated hepatitis (A and B) and 7 doctors admitted mainly for isolation. Among HCQ group 14 (34%) doctors were hospitalized. Hospitalized patients were more likely to have coexisting medical conditions including asthma, hypertension, diabetes mellitus and obesity. The majority of hospitalized patients received dexamethasone, low-mol heparin and remdesivir. A definite change in treatment protocol has been observed. All patients were initially treated with hydroxychloroquine and azithromycin. However, later on all were advised to take doxycycline and ivermectin. Some of them received other medications such as, flavipiravir , tocilizumab, or plasma therapy. A wide variation in treatment protocol was observed from hospital to hospital. Out of 32 moderate to severe illness group 7 doctors died and none of them received any HCQ prophylaxis. But there was no significant relation between use of HCQ and outcome of disease as death by Fisher's Exact Test (P =0.09). It is important to note that our study exclusively analyzed HCQ Pre-exposure prophylaxis and excluded HCQ post-exposure prophylaxis (PEP). Although clinical outcome measures like severity and mortality of disease were not reported for infected subjects in most of the Indian pre-exposure prophylaxis studies, this study helps to find out clinical outcomes in treated doctors. Non-survivors were older and male. Non-survivors were more likely to have coexisting medical conditions including hypertension, DM, and obesity. It is apparently showing that HCQ has some protective role as most of the moderate to severe disease patients and all of non-survivor never received any prophylaxis. The important contributing factors for poor outcome were older age and associated co-morbidity. It is appearing that HCQ has a "disease modifying effect" on COVID-19 infection. The results from our study is consistent with two randomized clinical trials[12,13] of hydroxychloroquine for pre-exposure prophylaxis in health-care workers at risk of SARS-CoV-2 infection. But statistically our findings do not provide any strong support for a major protective effect from ongoing routine hydroxychloroquine use, as has been previously hypothesized [8,14,15]. The HCQ could not prevent mortality due to COVID-19 as evidence by a large population based cohort study done upon patients with systemic lupus erythematosus or rheumatoid arthritis who were already taking hydroxychloroquine for 6 months.[16] Several randomized controlled trials on HCQ were conducted throughout the world. Treatment is more effective when used early. Very late stage treatment is not effective and may be harmful, especially when using excessive dosages. A meta-analysis done on Indian studies suggests that weekly HCQ Pre Exposure is safe and effective in preventing COVID-19 in a high-risk group of HCWs.[7] The common side effects due to HCQ use in different study were mild gastrointestinal problems like nausea, vomiting, diarrhea, abdominal cramps, headache, rashes, retinopathy and QT prolongation.[5,17,18] None in this study group experienced grade 3 or 4 adverse events on the CommonTerminology Criteria for Adverse Events scale, hospitalizations, or death. However, there was at least one non serious adverse events reported by 40%(n=20) doctors on HCQ prophylaxis(n=49). None of them had any cardiac complications (e.g, chest discomfort, syncope, arrhythmia). Our study findings were similar to others COVID-19 clinical trials which showed minimal adverse events with good safety profile.[19] The limitations of our study are weak power, retrospective in nature and subject homogeneity.

CONCLUSIONS

This study gives an overview of HCQ prophylaxis experience regarding different clinical outcome measures and adverse effects in a high-risk medical community with different co-morbidity. No

treatment, vaccine, or intervention is 100% available and effective for all current and future variants. All prescribed public health measures, effective and safe means should be used. But they are not sufficient for protecting the HCW; some form of pharmacological intervention for prevention may be used in addition to vaccine.

Conflict of interest: None

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