Original Article:

Doctors Perception of the Use of Hydroxychloroquine as Prophylaxis for COVID-19 Infection

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Article info:
Received: 13 Aug 2020
Accepted: 01 Feb 2021

Keywords:
COVID-19,
Hydroxychloroquine,
Prophylaxis

ABSTRACT

Background: The National Task force constituted by the Indian Council of Medical Research (ICMR) and various International agencies has recommended the use of Hydroxychloroquine (HCQ) as prophylaxis for Coronavirus Disease 2019 (COVID-19). This measure was taken because of the urgent need to protect high-risk individuals like Health Care Workers (HCW) from contracting COVID-19.

Objectives: This study aimed to assess the awareness, attitudes, and practices on using HCQ as prophylaxis to prevent COVID-19 infection.

Methods: A cross-sectional study was conducted among the doctors working in Dr RML Hospital, New Delhi, India, a tertiary care public hospital involved in the care of COVID-19 patients. The invitation to participate was electronically circulated, and the consenting participants were allowed to access an online survey. The survey had a total of 23 questions that were designed to understand the awareness, perception, and practices of doctors regarding the use of HCQ as prophylaxis in COVID-19.

Results: About 147 doctors participated in this survey. The major source of knowledge regarding HCQ prophylaxis was quoted as regulatory agencies (44%), particularly ICMR, and the main indication was reported as being a healthcare worker (60%). Most of the participants (91%) believed that the HCQ effect is not clear and felt more scientific data regarding the use of HCQ as prophylaxis for COVID-19. But many doctors (51%) still recommend using HCQ to their colleagues.

Conclusion: In this study, we observed that most doctors were aware of the recommendations regarding the HCQ prophylaxis in COVID-19 and had good adherence to therapy but felt the need for more concrete scientific evidence for using HCQ.

Citation Rana P, Ghadlinge M, Singh P, Chandane RD, Khanna A. Doctors Perception of the Use of Hydroxychloroquine as Prophylaxis for COVID-19 Infection. Pharmaceutical and Biomedical Research. 2021; 7(2):97-104. http://dx.doi.org/10.18502/pbr.v7i2.7362

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Introduction

The coronavirus disease 2019 (COVID-19) is an infectious disease caused by a newly discovered coronavirus. The disease is transmitted by droplets and presents with flu-like symptoms, i.e., fever, running nose, cough, and in severe cases breathlessness as the virus affects the respiratory system [1]. COVID-19 was detected as atypical pneumonia of unknown etiology in Wuhan City, China, and was formally brought to the notice of World Health Organization (WHO) on December 31, 2019. It was later declared as a pandemic on the March 11, 2020 [2]. For the containment of the COVID-19 epidemic, governments across the globe and health agencies took measures and issued guidelines [3].

During such a pandemic, it is common among Health-Care Workers (HCW), like doctors, to contract infection despite all precautions. There is a growing fear of contracting the infection and spreading the same to their close ones. On March 22, 2020, under the exceptional circumstances of the COVID-19 pandemic and the urgent need to protect the high-risk individuals, The National Task force constituted by the Indian Council of Medical Research (ICMR) recommended the use of Hydroxychloroquine (HCQ) for prophylaxis of COVID-19 infection. The eligible candidates for HCQ prophylaxis were asymptomatic HCWs involved in the care of suspected or confirmed COVID-19 cases and the asymptomatic household contacts of laboratory-confirmed cases. This recommendation was made based on the preclinical evidence of the efficacy of HCQ against coronavirus in laboratory studies and its overall favorable risk-benefit profile [4]. Also, few clinical studies from China showed that HCQ is superior to the control treatment to prevent the exacerbation of pneumonia associated with COVID-19 [5, 6].

In addition, many experts across the world believe that recommendation made by the US Food and Drug Administration (FDA) and ICMR for the use of HCQ in COVID-19 is based on inadequate clinical data [7]. Also, there is a need for properly strong, randomized clinical trials on HCQ to strengthen this recommendation [8]. The adherence to any therapy is based on existing knowledge and understanding of the person's undergoing therapy. During the initial days of the pandemic, new guidelines and recommendations were released to guide the HCW working in COVID hospitals. Since the drug was recently recommended, it was also required to follow up its safety profile. Because of this new recommendation for HCQ in the COVID-19 pandemic, a study was planned to assess the knowledge, attitude, and practices among doctors regarding the use of HCQ as prophylaxis for COVID-19. This study aimed to understand how doctors who are trained to practice evidence-based medicine can make an informed choice for themselves in this exceptional situation. In this case, the recommendation to use HCQ is based on insufficient clinical data, and there is conflicting scientific evidence for its efficacy in COVID-19.

Materials and Methods

This research was a cross-sectional study conducted in Dr RML Hospital, New Delhi, India, tertiary care, 1420 bedded. This is a referral hospital involved in the care of COVID-19 patients. An online survey was electronically circulated among all the doctors working in this hospital. The survey had a total of 23 questions that were designed to understand the awareness, perception, and practices of doctors regarding the use of HCQ as prophylaxis in COVID-19. The questionnaire was divided into three parts; the first part was designed to determine the knowledge pertaining to the use of HCQ prophylaxis in COVID-19 as per the recommendation made by the National Task Force of ICMR [4]; the second part was designed to assess the attitude towards HCQ use and final part was designed to gain information about practices adopted by doctors.

Multiple options were provided with each question. Few questions had multiple answers, and appropriate directions were given to answer the multiple choices. Initially, the questionnaire was distributed among the co-authors and few resident doctors for face validation, content validation, and content reliability.

All doctors working in Dr RML Hospital involved in patient care were included in this study. A sample of 145 doctors was chosen out of the total 980 doctors involved in patient care at this hospital. The sample size was estimated using Ransoft sample size calculator (2004) [9] by assuming a response rate of 75%, with a 90% Confidence Interval (CI), Z of 1.96, and 5% margin of error.

The study was approved by the Institutional Ethics Committee of ABVIMS and Dr RML Hospital comprehensive letter No. 394.43/2020.IEC/ABVIMS/RMLH), dated May 22, 2020. The invitation to participate was circulated through email and multiple groups on social media. The consenting participants were allowed to access the questionnaire. The survey was commenced on May 26, 2020, and the required sample size was achieved on July 5, 2020. The survey was anonymous, and the information of the participants was excluded during the analysis. All the data were tabulated in Microsoft Excel.

Descriptive statistics were used, and all categorical variables were presented as percentages.

Results

A total of 147 doctors participated in this survey. The majority (80%) of the doctors were males with postgraduate degrees and aged between 30 and 45 years. The primary source of knowledge as regards HCQ prophylaxis was quoted from regulatory agencies (44%), particularly ICMR, followed by media (35%), journals (35%), and colleagues (30%).

The major indication for HCQ prophylaxis was reported as "all Health Care Workers (HCW)" (60%) followed by "contacts of COVID-19 positive patient" (28%). About 38% of participants believed that HCQ provided some protection from contracting COVID-19 infection, but most (60%) believed that its role is unclear and is still under investigation (Table 1). The correct prophylactic dose of HCQ was known to 86% of participants, and the maximum recommended duration (7 weeks) was known to 78% of the study participants. Overall, 70% of the participants knew the major contraindications of HCQ and were also aware that screening test (like ECG) needs to be done before initiating or during HCQ prophylaxis.

A 5-point Likert-type scale [10] was used, and responses were recorded over a range of strongly agree to strongly disagree (Table 2). The responses were scored as 5 = strongly agree, 4 = agree, 3 = not sure/don't know, 2 = disagree, and 1 = strongly disagree. All options were given a score, as shown in Table 2. Mean and median were calculated to know the most frequent answers. About 41% of the participants thought that HCQ prophylaxis was an important measure for HCWs in addition to the standard measures of using a face mask, hand sanitization, and social distancing. One-third of the participants also believed that HCQ decreases the likelihood of contracting COVID-19. About 16% of the doctors disagree that HCQ prophylaxis was an important preventive measure or decreases the chances of contracting COVID-19. About half (51%) of the doctors recommend HCQ prophylaxis to their colleagues, but 19% disagree, while the remaining were not sure about it. However, the majority of the participants (90%) agree to the fact that they need more scientific data regarding the use of HCQ as prophylaxis for COVID-19.

Over half of the participants (52%) informed that they recommended HCQ prophylaxis. The source of recommendation was from hospital administration (47.5%) followed by colleagues (20%) or self-administration (20%). About 62% of the participants started HCQ prophylaxis, and their primary reason was their job as HCWs (25%), gaining benefit against COVID-19 (23%), being involved in the care of COVID-19 patients (16%), or having had contact with a COVID-19 positive case (6%).

The majority (75%) of the participants taking HCQ prophylaxis had gone through the information about HCQ before initiating the prophylaxis, but no screening tests were done in half of them. About 28% of participants also took additional medications like azithromycin, ivermectin, antacids, vitamin, and minerals. Most participants who started HCQ prophylaxis (75%) were taking regular therapy as per standard guidelines.

The Adverse Drug Reactions (ADRs) were observed in about 21% of cases, and the most common ADRs reported were headache, diarrhea, nausea, skin rashes, and myalgia (Table 3). Among the 20% of participants who discontinued HCQ prophylaxis, ADRs were responsible only in 3% of the cases, and major reasons for discontinuation cited were either completion of 7 weeks of therapy or uncertainty regarding the efficacy of HCQ.

Discussion

In the present study, the knowledge, attitude, and practices of doctors on the use of HCQ as prophylaxis for COVID-19 were assessed. Doctors are at high risk of occupational exposure to COVID-19 as they are directly involved in patient care. To reduce the chances of contracting COVID-19, the National Task Force constituted by ICMR recommended using HCQ prophylaxis for asymptomatic HCWs and other high-risk populations. The paucity of published data on the use of HCQ as a prophylactic measure for COVID-19 infection among HCWs, motivated the conception of the current study to assess the knowledge, attitudes, and practices on the use of HCQ as prophylaxis for COVID-19 among doctors.

The recommendation made by the regulatory bodies for using HCQ prophylaxis against COVID-19 has drawn mixed reactions from scientists across the world. A few of them questioned the use of HCQ in the treatment or prevention of COVID-19 without concrete evidence from clinical trials, while others thought that HCQ provides reasonable protection against COVID-19. The rapid spread of disease and limited treatment options available has forced the use of this repurposed drug even though there was limited evidence. Besides, some independent studies published in reputed journals reported no benefit of HCQ in preventing or treating COVID-19 [7, 11]. Later, the drug regulators like the US FDA re-

Table 1. Results of questions related to awareness of HCQ prophylaxis among doctors

Questions	Subgroup	No. (%)
How do you come to know about HCQ prophylaxis? (Multiple answers)	Social media	52 (35.6)
	Friends	43 (29.3)
	Journal	53 (36.1)
	Regulatory agencies	64 (43.8)
Which agency has recommended the HCQ prophylaxis for SARS-CoV-2	ICMR	116 (78.9)
	FDA	4 (2.7)
	Both	24 (16.3)
	None	3 (2)
What are the indications for giving HCQ prophylaxis?	Critically sick patients	3 (2)
	Contacts of COVID-19 patient	41 (27.9)
	Health care workers	87 (57.8)
	As decided by the treating physician	15 (10.2)
What is the efficacy of HCQ prophylaxis for preventing SARS-CoV-2 infection?	It provides complete protection	1 (0.7)
	It provides some protection	56 (38.1)
	Its role is under study	87 (59.2)
	It does not have any role	3 (2)
How many doses of HCQ have to be taken for prophylaxis?	400 mg twice on day 1 and then 400 mg/ week	126 (87.7)
	400 mg once on day 1 and then 400 mg/ week	10 (8.8)
	200 mg twice on day 1 and then 200 mg/ week	11 (7.5)
	200 mg once on day 1 and then 400 mg/ week	0 (0)
What is the maximum duration of HCQ prophylaxis recommended?	4 weeks	12 (8.2)
	5 weeks	2 (1.4)
	6 weeks	18 (12.2)
	7 weeks	115 (78.2)
What are the contraindications for HCQ prophylaxis? (Multiple answers)	Retinopathy	94 (63.8)
	Children under 15 years	90 (61.2)
	Hypersensitivity to aminoquinolines	44 (29.9)
	Liver failure	127 (86.4)
What are the common side effects of HCQ? (Multiple answers)	Anorexia	80 (54.4)
	Itching	44 (29.9)
	Headache	92 (62.6)
When would you perform the screening tests for HCQ toxicity?	Before starting the prophylaxis	101 (68.7)
	After starting prophylaxis	6 (4.1)
	After experiencing adverse effects	20 (13.6)
	Not needed	20 (13.6)
When you go through the information about HCQ prophylaxis in COVID-19 infection?	Before starting the HCQ prophylaxis	81 (55.1)
	After starting the HCQ prophylaxis	8 (5.4)
	Never need any such information	2 (1.4)
	Never took HCQ prophylaxis	56 (38.1)

Table 2. Results of question related to attitude of doctors towards HCQ prophylaxis

Question	n	5 (%)	4 (%)	3 (%)	2 (%)	1 (%)	Mean	Median
Do you think that HCQ prophylaxis is important?	147	2.5	15.6	41.8	38.5	2.5	3.22	3
Do you think that it decreases the likelihood of contracting COVID-19 infection?	147	0.8	32	43.4	15.6	8.2	3.03	3
Do you think that you need more information about HCQ prophylaxis?	147	40.8	49.7	4.8	2	2.7	4.23	4
Will you recommend your colleagues to take HCQ prophylaxis?	147	4.8	46.3	29.9	14.3	4.8	3.31	4

5: Strongly agree; 4: Agree; 3: Not sure/don't know; 2: Disagree; and 1: Strongly disagree.

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stricted HCQ for research purposes only, and WHO halted the use of HCQ even for the clinical trial citing adverse risk-benefit profile. The series of conflicting scientific evidence for HCQ prophylaxis lead to a dilemma among HCW, especially doctors who are trained to practice evidence-based medicine. To understand how physicians make an informed choice for themselves in this exceptional situation, we decided to assess the knowledge, attitudes, and practices on using HCQ as prophylaxis to prevent COVID-19 infection.

In the present study, we found that about two-thirds of the doctors were aware of the recommendations from ICMR and took HCQ prophylaxis with the understanding that the role of HCQ in COVID-19 is still a subject for further research. About one-third of the participants believed that HCQ decreases the likelihood of contracting COVID-19 infection and could be an additional preventive measure for HCWs. However, most participants felt the need for more concrete scientific evidence to strengthen these recommendations.

About 62% of the participants initiated HCQ prophylaxis and had taken at least one dose of HCQ. This finding was similar to the one reported by Bhattacharyya et al., who reported that the HCQ prophylaxis was accepted by 76% of the HCWs. Since our study included primarily doctors who were aware of the limited evidence of the effectiveness of HCQ prophylaxis against COVID-19, perhaps relatively lesser acceptance was observed [12].

About 70% of the participants knew the correct dose, duration, and contraindications associated with HCQ, but a screening test (ECG) was done only in half of the participants initiating HCQ prophylaxis. Despite the emphasis lay by the revised ICMR guidelines regarding ECG monitoring before or anytime during the course of prophylaxis, this advisory was not ultimately followed. The reason could be the fact that HCQ is a widely prescribed drug and overall is associated with mild ADRs. Only 30 participants in the study reported ADR from HCQ, which was mild in severity and was not the primary reason for discontinuing HCQ prophylaxis.

Most participants (75%) who initiated HCQ prophylaxis had good adherence to the therapy. This finding was in agreement with the study by Bhattacharyya et al., who also reported good adherence among 85% of HCWs starting HCQ prophylaxis. In the present study, the primary reason for discontinuing HCQ prophylaxis

Table 3. Results of questions related to practices for HCQ prophylaxis among doctors (n: 147)

Question	Subgroup	No. (%)
Have you been formally advised to take HCQ prophylaxis?	Yes	77 (52)
	No	70 (48)
Have you taken HCQ prophylaxis?	Yes	91 (62)
	No	56 (38)
Has any baseline screening test (ECG or blood test) been done before starting HCQ?	Yes	75 (51)
	No	72 (49)
Did you take any other medication as prophylaxis along with HCQ?	Yes	41 (28)
	No	106 (72)
Did you experience any adverse effects?	Yes	31 (21)
	No	116 (79)
Did you discontinue the HCQ prophylaxis?	Yes	30 (20.4)
	No	117 (79.9)

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was quoted as lack of clarity regarding the use of HCQ beyond eight weeks. The revised ICMR guidelines recommend using HCQ prophylaxis beyond eight weeks but with strict monitoring of clinical and ECG parameters. Another reason for discontinuing the HCQ was conflicting scientific evidence regarding the efficacy of HCQ prophylaxis in COVID-19. But we have to keep in mind that overall knowledge of the disease is limited, and it will take some time to develop the evidence. Interestingly, during recent years, trends in drug development have shifted towards lifestyle diseases while the drug research in infective diseases has taken a back seat. The medicines like chloroquine, azithromycin, and ivermectin that have been repurposed for prophylaxis against COVID-19 have also been approved against a wide variety of other infective diseases in India [13].

We observed ADRs in 21% of the participants, and the most common were headache, gastrointestinal side effects, and skin allergy. However, ADRs were responsible for the discontinuation of therapy in less than 3% of cases. Similar findings were also observed by Bhattacharyya et al., who reported ADR in 18% of participants with common ones were gastrointestinal side effects followed by skin allergic reactions and headache. Bhattacharyya et al. also observed that less than 2% of HCWs required discontinuing prophylaxis due to these adverse effects [12].

Conclusion

Overall, we can conclude from the present study that most of the participating doctors were aware of the recommendations of regulatory agencies regarding HCQ prophylaxis in COVID-19 but felt for more concrete scientific evidence. Most participants taking HCQ prophylaxis had good adherence to therapy and felt that it could provide additional protection for HCWs from COVID-19. However, they did not screen or monitor themselves with ECG and choose to terminate prophylaxis beyond eight weeks, perhaps due to the need for more rigorous monitoring for clinical and ECG parameters. This study also helps us to understand how doctors who are trained to practice evidence-based medicine make an informed choice for themselves in this exceptional situation. The case where the recommendation to use HCQ is based on insufficient clinical data and conflicting scientific evidence for its efficacy in COVID-19. The findings from this study also serve as feedback for regulatory agencies to address the concerns raised by the doctors and devise a more effective implementation strategy when such a recommendation is made in the future.

This is a pilot study conducted on only 145 doctors working in one hospital. A multi-centric study with a larger sample size will be needed to understand attitudes and practices followed by doctors working in different hospitals involved in the care of COVID-19 patients.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Institutional Ethics Committee of ABVIMS & Dr RML Hospital wide letter no 394.43/2020.IEC/ABVIMS/RMLH.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

Writing – original draft: Proteesh Rana; Investigation, conceptualization: Manik Ghadlinge; Data collection and data analysis: Pratap Singh; Methodology: R. D. Chandane; Preparation of questionnaire, content validation of the questionnaire: Arjun Khanna.

Conflict of interest

The authors declared no conflict of interest.

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