

## SAFETY OF HYDROXYCHLOROQUINE FOR COVID-19 PROPHYLAXIS AMONG HEALTHCARE WORKERS: AN OBSERVATIONAL STUDY

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Received: 21 July 2020, Revised and Accepted: 20 August 2020

### ABSTRACT

**Objective:** Indian Council of Medical Research recommended hydroxychloroquine (HCQ) for prophylaxis of COVID-19 for healthcare workers and the Food and Drug Administration approved its use in the treatment and prophylaxis of COVID-19 disease. Even though HCQ is adequately tolerated in usual circumstances, still questions about the harmful effects of the drug remain a cause for concern in adults treated with HCQ. The objective of this study was to evaluate the major and minor adverse effects of prophylactic HCQ for COVID-19 among healthcare workers.

**Methods:** Our analysis was intended to analyze HCQ's adverse drug reaction profile for COVID-19 prophylaxis in prophylactic doses in health-care staff. This was a cross-sectional study carried out among healthcare workers taking HCQ prophylaxis for COVID-19. The study was carried out over 08 weeks period from April to May 2020. The data were obtained regarding age, sex, comorbidities, and possible adverse effects. A pretested and validated online questionnaire was provided to the participants to assess the harmful effects that they experienced when taking HCQ. Furthermore, pre and post 8 weeks prophylaxis, individuals underwent general and systemic examination, along with ECG and blood sugar level monitoring.

**Results:** The research group comprised 70 previously healthy and health-care staff. In 70 patients, 27 minor adverse effects were reported (18.9%). Headache was the most frequently reported symptoms followed by nausea and vomiting, itching, and skin rashes. There was no statistically relevant variation in harmful effects due to age or number of doses administered. However, none of the adverse effects was serious or debilitating.

**Conclusion:** With adequate pre-prophylaxis evaluation, health education, and regular monitoring, HCQ prophylaxis is safe and devoid of any serious adverse effects in previously healthy individuals.

**Keywords:** Adverse drug reaction, COVID-19, Healthcare workers, Hydroxychloroquine, Prophylaxis.

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### INTRODUCTION

Monitoring and documenting adverse drug reactions (ADRs) encourage safe use of drugs by ensuring that benefits outweigh the risks that drug use may pose [1]. The liability for major morbidity and mortality rests with ADR. Originally commonly used as an anti-malarial medication, hydroxychloroquine (HCQ) has long been employed as an important treatment choice for persistent rheumatic disorders, such as rheumatoid arthritis and systemic lupus erythematosus [2]. HCQ has recently been promoted by the Indian Council Medical Research for COVID-19 prophylaxis [3-5]. Only recently, the Food and Drug Administration (FDA) has permitted for emergency use in the care of serious COVID-19 illness in hospitalized patients [6]. Table 1 showing some of the ongoing clinical trials of HCQ.

ICMR has suggested HCQ chemoprophylaxis (400 mg BD and then 400 mg once a week later) for asymptomatic health care staff treating patients with suspected or verified COVID-19 as well as for asymptomatic household contacts with reported cases [9]. HCQ was found to influence the function of the immune system by mediating an anti-inflammatory reaction, which may minimize harm related to the excessive inflammatory response [10]. Given recent reports of some serious adverse effects, including deaths of HCW with the use of HCQ, apprehensions, and anxiety, exist in the minds of HCW regarding the possibility of significant adverse effects and the control of adverse effects [11,12]. Therefore, it would be beneficial to record and evaluate the adverse effects experienced by health-care staffs who are currently taking COVID-19 HCQ chemoprophylaxis as recommended by the ICMR. In consideration of this, our research was intended to examine the ADR profile of HCQ in health-care staff in recommended prophylactic doses for COVID-19.

**Table 1: Some of the ongoing clinical trials of hydroxychloroquine for chemoprophylaxis in healthcare workers against COVID-19**

Trial registration no.	Country	Number of centers and study design	Study population	Nature of study volunteers	Interventional group(s)	Comparison group(s)	Primary outcomes
NCT04303507 [7]	Europe and Asia	Multi-center randomized	40000	Contact or healthcare	Hydroxy chloroquine	Placebo	Number of symptomatic COVID-19 infections
NCT04308668 [8]	USA	parallel-group trial	1500	worker exposed to a patient with COVID-19			Incidence and severity of COVID-19
NCT04318015 [8]	Mexico	Parallel group RCT	400	adult household			Symptomatic COVID-19
NCT04318444 [8]	USA	Community-based randomized clinical trial	1600	contacts of COVID-19 patients			Number of participants with symptomatic, labconfirmed COVID-19

## METHODS

This was an observational and prospective study undertaken at tertiary care non-designated COVID hospital where we refer the COVID-19-positive cases to COVID-designated hospital. The period of the study was 2 months beginning from April 2020 through May 2020. A total of 70 healthcare workers of either gender who were willing for HCQ as chemoprophylaxis for COVID-19 and who were actively served in the operation theater (OT) were selected as the study subjects. Such healthcare workers included anesthesiologists, OT technicians, OT nursing staffs, and ward sahayikas. A detailed education capsule on the drug and its adverse effect profile was conducted for all participants before the start of the study. All the study subjects were checked for the presence of any comorbidity (diabetes and hypertension) and/or previous history of any drug allergies and only recruited in the study after the confirmation about no suffering from any previous comorbidity. None of the study subjects was suffering from any comorbidity or had any prior history of any drug allergy.

The participants were given an online pretested and validated study questionnaire, named chloroquine prophylaxis for novel corona pandemic through the Google™ platform and distributed to all the study subjects through another online social networking platform called WhatsApp™. Due to the nature of COVID-19 and restrictions on personal interview and examination, only an online symptom questionnaire for adverse effects was administered. The study questionnaire was composed of five sections, namely, neuropsychiatric symptoms, skin disorders, neurological side effects, gastrointestinal side effects, and cardiac side effects experienced by the study subjects during chloroquine prophylaxis for COVID-19. The responses were collected for each of the five sections. In addition, a pre-prophylaxis and 8 weeks post-prophylaxis estimation of random blood sugar and evaluation of electrocardiogram among the study subjects were carried out. The drug HCQ (400 mg) was administered among all the study subjects on the 1<sup>st</sup> day and then again 400 mg for 7 weeks on a weekly basis.

Informed consent was obtained from the participants for participating in the study. Since the prophylaxis was recommended by ICMR, Ethical committee clearance was not sought.

## RESULTS

The study group included 70 healthcare workers, with age ranging from 21 to 54 years. There was male superiority (92.85%), with most participants being under the age of 30, as shown in Table 2.

In 70 study participants, 27 adverse effects were reported (18.9%). Headache was the most commonly recorded symptoms accompanied by nausea and vomiting, itching, and skin rashes. There was no statistically relevant variation due to age, gender, and a number of doses taken, as shown in Table 3. Majority of the side effects of HCQ such as headache, nausea, vomiting, and rashes were noted after the second or third dose. It lasted only for a few hours and treated with symptomatically, or some of the subjects did not require any remedies. All these HCW who had minor adverse effects did not have any interference with daily routine work in the operation theatre. These unwanted effects did not occur in all the doses of the prophylaxis dose of HCQ. There were no adverse effects on eye or vision which required stoppage of drug or interventions.

## DISCUSSION

HCQ was proposed by ICMR for COVID-19 chemoprophylaxis for health care staff dealing with COVID-19 cases and high-risk COVID-19 cases contacts [13]. Permission has been given by the FDA for the use of HCQ in severe COVID-19 cases. There are contradictory reports on the effectiveness of HCQ in COVID-19 therapy, and relatively few evidence on the safety and efficacy of COVID-19 chemoprophylaxis are available in the published literature [14-16].

**Table 2: Profile of demographic status in the study subjects**

Serial Number	No.	Percentage
Gender		
Male	65	92.85
Female	05	7.15
Age (in years)		
≤30	31	44.28
31-45	25	35.71
≥46	14	0.20

**Table 3: Adverse drug reactions**

Symptoms suffered	Number of individuals with symptoms	Percentage
Diarrhea	2	1.4
Sweating	2	1.4
Hair loss	0	0
Mood changes	1	0.7
Neuropsychiatric symptoms		
Sleeplessness	1	0.7
Head ache	6	4.2
Dizziness and blurred vision	1	0.7
Other symptoms		
Nausea and vomiting	2	1.4
Itching	2	1.4
Skin rash	2	1.4
Loss of appetite	1	0.7
Cramps	1	0.7
Generalized weakness	1	0.7
Random blood sugar		
Hypoglycemia (<70 mg/dl)	0	0
Hyperglycemia (>200 mg/dl)	0	0
EKG changes		
Bradycardia	2	1.4
T wave inversions in single lead	2	1.4
QTc prolongation	1	0.7
Total individuals screened	70	100
Individuals with symptoms	27	18.9

Abdominal pain, nausea, and headache are the most frequently reported side symptoms, accompanied by followed by rash, pruritus, diarrhea, omitting, and blurred vision [17]. Headache and gastrointestinal ADRs such as nausea, abdominal pain/cramps, vomiting, and diarrhea were the most frequent ADRs to HCQ in our research, the incidences of which were comparable to reported literature [18,19]. Surprisingly, in our research, dizziness has been recorded more frequently than published literature [20-22]. Many of the ADRs may not be a clear adverse drug reaction since the burden of operating during lockdown and fear of having COVID-19 disease may have also led to these symptoms. Working with Personal Protective Equipments (PPE) might also compound the features of ADRs to prophylactic HCQ.

Our analysis drawbacks include the limited sample size for the harmful effects. This research on healthcare workers can be applied to a wider community, while healthcare workers can be assumed to be more conscious of it and more likely to disclose harmful consequences accurately. Extensive research is required to ensure the safety of the use of HCQ as COVID-19 prophylaxis among health-care staff and high-risk contacts in community hotspots.

## CONCLUSION

HCQ can be used safely in young patients or individuals without any comorbidities for chemoprophylaxis during COVID pandemic. Sadly, the risk factors for extreme COVID-19 illness (age older than 65 years and comorbidities) are also risk factors for significant adverse HCQ impact. A similar score must be developed for all serious HCQ ADRs to minimize the risk of drug toxicity.

**CONFLICTS OF INTEREST**

The authors declare no conflicts of interest.

**AUTHORS' CONTRIBUTIONS**

Dr. Krishna Prasad and Dr Sangeeta Khanna have prepared the conception, data collection, data analysis, interpretation, and drafting of the article and also, along with Dr Nitul Bewal and Dr Amit helped in writing the manuscript, supervised, revised, and edited the final version of the manuscript.

**AUTHORS FUNDING**

Nil

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