Hydroxychloroquine in the prophylaxis of COVID 19: A survey of safety on the healthcare workers in India

INTRODUCTION

Attempts of repurposing of chloroquine (CQ) and its less toxic congener hydroxychloroquine (HCQ) were being done in the COVID-19 scenario, which raised debates. Research findings revealed that CQ acted both at “entry” and at “post-entry stages” of novel coronavirus in the Vero E6 cells.[1] The reports of initial clinical trial from France also revealed reduction of the viral load with HCQ.[2] Due to its action on the virus at stages before and after entry to the cells, the drugs could be candidates for both prophylaxis and treatment of COVID-19. The Indian Council of Medical Research (ICMR) suggested HCQ as a prophylaxis for COVID-19 disease for the healthcare workers (HCWs) along with other standard precautions since March 2020 on experimental basis.[3] Although safe use of CQ and HCQ was reported in malaria, rheumatoid arthritis, and many other conditions for years, controversies mounted with the negative results from the clinical trials and sporadic reports of serious adverse events later in the COVID-19 scenario.[4-6] Safety issues relating to HCQ prophylaxis therefore need evaluation in the Indian context as many of the HCWs had been using the drug since the recommendation by the ICMR.

MATERIALS AND METHODS

HCQ tablets were distributed among the HCWs of a tertiary care medical college hospital from Eastern India, who opted for using it for COVID prophylaxis. All users were instructed to report in case of any adverse event. Later, an online survey was conducted among the doctors and nurses for administrative purpose during the last week of May till 1st week of June 2020. Other than age, department of work, and contact number to cross verify, three questions were asked: (i) “if you have taken prophylaxis for COVID-19, what was the drug (HCQ or CQ)?,” (ii) “what was the dose,” and (iii) “did you experience any form of side effects after using the drug? If yes, please type the symptom/problems experienced.”

RESULTS

A total of 70 participants (68 doctors, 2 nurses) including 51 (73%) males and 19 (27%) females responded to the survey, with an average age 38.18 ± 11.46 (mean ± standard deviation) and with a range between 24 to 65 years. All used HCQ prophylaxis in the ICMR-recommended dose (800 mg loading single day, followed by weekly 400 mg). Prophylaxis was continued till 7 weeks by 34 (48.6%), till 9 weeks by another 34 (48.6%), and discontinued by 2 (2.9%) respondents.

“No side effect” was reported by 70% (n = 49) of the participants. At least one nonserious side effect was reported by 30% (n = 21) - gastrointestinal 14% (n = 10) and central nervous system 9% (n = 7). Transient headache, nausea, dyspepsia, diarrhea, and/or loose stool were the most reported side effects (n = 3), followed by dizziness and palpitation (n = 2). The two patients reporting palpitation were investigated further. The first one, a 27-year-old female had a transient chest discomfort only after the first dose. The second participant, a 58-year-old long-standing hypertensive and type 2 diabetic male reported episodes of palpitation and occasional missed beats 3 days after consuming HCQ dose of the 4th week till 3–4 days after the dose of the 5th week. Although he discontinued taking HCQ after the 5th week, his electrocardiography (ECG) and Holter monitoring reports were within normal limits. Due to the presence of background diseases, possibility of tachycardia from hypoglycemia from multiple antidiabetic agents, and vague temporal association, we had assigned the causality as “possible” in the WHO-UMC causality assessment scale which indicates a weaker causal association.

DISCUSSION

This retrospective collection of data from the HCWs found that HCQ is tolerated well as prophylaxis for COVID-19 in the ICMR-recommended dose at least till 9 weeks. Like most of the previous studies, transient nausea, dyspepsia, and headache remained the most commonly reported side effects in the present survey. Study from France on “early COVID” patients found HCQ “safe” among the
participants as well as the clinical trial on “postexposure prophylaxis” of COVID-19 from the United States and parts of Canada. In contrast, a clinical trial from China reported two serious adverse events. However, they had used a 4.5 times higher loading and higher maintenance dose compared to the ICMR-recommended prophylaxis.

The lower dose of HCQ, compared to other studies, probably the relatively healthy and non-COVID-infected population, could have contributed to limited side effects from HCQ here. It could be assumed that, due to young age of most of the participants, they are less likely to take in regular medications for comorbidities and hence possibilities of limited drug interaction from concurrent medications with HCQs.

However, as a limitation, these data were retrospective in nature, not recruited established COVID patients, and relied on participant-reported side effects. Further, the possibilities of asymptomatic QT prolongation could not be ruled out without ECG monitoring. In spite of the above limitations, it should be noted that most of the respondents of the survey were medical doctors who are expected to detect their own symptoms more reliably than general people. In conclusion, HCQ appears well tolerated in HCWs in the ICMR-recommended dose for COVID-19 prophylaxis. However, larger prospective study with more in-depth cardiac monitoring is recommended to validate our findings.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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