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Hydroxychloroquine Pre-Exposure Prophylaxis for COVID-19 in Healthcare Workers from India: A Meta-Analysis

Raphael B. Stricker*, Melissa C. Fesler

Union Square Medical Associates, San Francisco, CA, USA

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ABSTRACT

To date, the COVID-19 pandemic has resulted in more than 200 million cases of SARS-CoV-2 infection and more than four million deaths world-wide. 1 Although novel COVID-19 vaccines have become clinically available, the safety and efficacy of these vaccines remains open to question. 2 Alternate approaches to prevention of disease have received little attention, and one medication, hydroxychloroquine (HCQ), has been attacked and dismissed based on flawed studies and political controversy that obscured the value of this treatment as pre-exposure prophylaxis (PrEP) for SARS-CoV-2 infection.

To date, the COVID-19 pandemic has resulted in more than 200 million cases of SARS-CoV-2 infection and more than four million deaths world-wide [1]. Although novel COVID-19 vaccines have become clinically available, the safety and efficacy of these vaccines remains open to question [2]. Alternate approaches to prevention of disease have received little attention, and one medication, hydroxychloroquine (HCQ), has been attacked and dismissed based on flawed studies and political controversy that obscured the value of this treatment as pre-exposure prophylaxis (PrEP) for SARS-CoV-2 infection.

A British study of 120,075 healthcare workers (HCWs) found that these subjects had a 7–8 fold greater risk of developing severe COVID-19 compared to non-HCWs [3]. With this background, the Indian Council of Medical Research (ICMR) National Taskforce for COVID-19 formulated guidelines for weekly HCQ PrEP in high-risk HCWs [4]. We used internet search engines to identify 11 cohort studies of weekly HCQ PrEP in HCWs from India based on the ICMR protocol [5–15]. These case-control studies enrolled a total of 7616 high-risk HCWs who were tested for SARS-CoV-2 infection as an endpoint after varying lengths of time following weekly HCQ PrEP or no treatment.

We have performed a preliminary meta-analysis of these studies, as shown in Table 1. In the 11 studies that included HCWs who used any HCQ PrEP, the infection rate was significantly decreased (RR 0.56, $p = 0.0040$). In the five studies that included HCWs who took at least six doses of weekly HCQ PrEP, the infection rate was reduced even further (RR 0.25, $p < 0.0001$). The uniform ICMR treatment protocol used in these studies argues against bias related to variations in dosing of HCQ. There were minimal adverse events reported in the HCQ-treated subjects, consistent with other safety reports for HCQ use in COVID-19 trials [16,17].

Our meta-analysis suggests that weekly HCQ PrEP is safe and effective in preventing COVID-19 in a high-risk group of HCWs. Although severity of disease was not reported for infected subjects in most of the studies, prevention of infection implies a lower risk of severe illness in treated HCWs. It is important to recognize that these studies exclusively analyzed HCQ PrEP and excluded HCQ post-exposure prophylaxis (PEP) or treatment of SARS-CoV-2-infected individuals. Lumping of these groups in prior studies has resulted in flawed analysis and inaccurate conclusions about the safety and efficacy of HCQ PrEP [18]. Although the cohort studies have limitations in terms of retrospective design and subject homogeneity, they suggest that HCQ PrEP could serve as a stop-gap approach to COVID-19 prevention until universal vaccination is achieved. Further randomized trials of HCQ PrEP should be conducted to evaluate this promising method of prevention for COVID-19 and future pandemics.

* Corresponding author at: Union Square Medical Associates, 450 Sutter Street, Suite 1504, San Francisco, CA 94108, USA.
E-mail address: rstricker@usmamed.com (R.B. Stricker).

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Table 1
HCQ PrEP studies in healthcare workers from India.

Study	HCQ (n)	No HCQ (n)	RR (95% CI)	P-value[a]
1. Chatterjee et al., 2020	365	386		
HCQ any dose infection	172	193	0.90 (0.60-1.35)	0.62
HCQ ≥ 6 doses infection	12/68		0.04 (0.01-0.16)	<0.0001
2. Bhattacharya et al., 2020	54	52		
HCQ any dose infection	4	20	0.19 (0.07-0.53)	0.0013
HCQ ≥ 6 doses infection	NA			
3. Khurana et al., 2021	90	91		
HCQ any dose infection	54	40	1.36 (1.02-1.82)	0.033
HCQ ≥ 6 doses infection	6/22		0.62 (0.30-1.28)	0.19
4. Goenka et al., 2020	237	885		
HCQ any dose infection	19	115	0.62 (0.39-0.98)	0.041
HCQ ≥ 6 doses infection	1/77		0.10 (0.01-0.71)	0.021
5. Yadav et al., 2021	178	221		
HCQ any dose infection	17	27	0.78 (0.44-1.39)	0.40
HCQ ≥ 6 doses infection	6/125		0.39 (0.17-0.93)	0.033
6. Kadnur et al., 2020	248	86		
HCQ any dose infection	2	5	0.14 (0.03-0.70	0.017
HCQ ≥ 6 doses infection	NA			
7. Dev et al., 2021	260	499		
HCQ any dose infection	155	351	0.74 (0.61-0.90)	0.0024
HCQ > 6 doses infection	NA			
8. Mathai et al., 2020	491	113		
HCQ any dose infection	10	22	0.10 (0.05-0.21)	<0.0001
HCQ ≥ 6 doses infection	NA			
9. Datta et al., 2020	146	135		
HCQ any dose infection	16	19	0.78 (0.42-1.45)	0.43
HCQ ≥ 6 doses infection	NA			
10. Behera et al., 2021	186	186		
HCQ any dose infection	7	12	0.56 (0.19-1.63)	0.29
HCQ ≥ 6 doses infection	NA			
11. Badyal et al., 2021	1,234	1,473		
HCQ any dose infection	415	611	0.81 (0.73-0.90)	<0.0001
HCQ ≥ 6 doses infection	247/981		0.28 (0.21-0.37)	<0.0001
Total				
HCQ any dose	3,489	4,127		
Infection	871 (25%)	1,428 (35%)	0.56 (0.37-0.83)	0.0040
HCQ ≥ 6 doses	1,273			
Infection	272 (21%)		0.25 (0.13-0.50)	<0.0001

HCQ, hydroxychloroquine; PrEP, pre-exposure prophylaxis; NA, not available; RR, adjusted risk ratio; CI, confidence interval.
[a] Treated subjects versus untreated controls.

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Competing interests

None declared.

Ethical approval

Not required.

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