Epidemiology and Infection

Title: Efficacy and Safety of Hydroxychloroquine/chloroquine against SARS-CoV-2 Infection: A Systematic Review

Author list: Jogender Kumar[1], Siddharth Jain[1], Arushi Yadav[2], Jitendra Meena[1]*

[1]Post Graduate Institute of Medical Education and Research, Chandigarh; India

[2]Government Medical College and Hospital, Chandigarh; India

Supplementary Material

Table S1: Search Strategy

PubMed	(((((("hydroxychloroquine"[MeSH Terms]) OR ("hydroxychloroquine"[Title/Abstract])) OR (chloroquine[Title/Abstract])) OR (chloroquine[MeSH Terms])) AND (((((((("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept]) OR (coronavirus[MeSH Terms])) OR ("severe acute respiratory syndrome coronavirus 2"[Title/Abstract])) OR ("2019 ncov"[Title/Abstract])) OR ("covid 19"[Title/Abstract])) OR ("sars cov 2"[Title/Abstract])) OR ("coronavirus"[Title/Abstract]))))	
Embase	('severe acute respiratory syndrome coronavirus 2':ab,ti OR 'coronavirus disease 2019':ab,ti OR 'sars cov 2':ab,ti) AND (hydroxychloroquine:ab,ti OR chloroquine:ab,ti)	
Web of Science	TS=(hydroxychloroquine OR Chloroquine) AND TS=(SARS-CoV-2 OR Coronavirus OR Coronavirus 2019 OR COVID-19)	
Cochrane Library	ID	Search
	#1	COVID-19
	#2	Coronavirus
	#3	SARS-CoV-2
	#4	severe acute respiratory syndrome coronavirus 2
	#5	#1 or #2 or #3 or #4
	#6	MeSH descriptor: [SARS virus] explode all trees
	#7	#5 or #6
	#8	hydroxychloroquine
	#9	chloroquine
	#10	#8 or #9
	#11	MeSH descriptor: [Hydroxychloroquine] explode all trees
	#12	#10 or #11
	#13	#7 AND #12

Supplementary Table S2: Risk of Bias assessment for Cohort studies

	Selection				Comparability		Outcome			
Study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Adjust for the most important risk factors	Adjust for other risk factors	Assessment of outcome	Follow up length	Loss to follow up rate	Quality
Huang et al. 2020	*	*	*	*	-	-	*	*	*	Fair
Grimaldi et al. 2020	*	*	*	*	-	-	*	*	*	Fair
Karolyiet al. 2020	-	*	*	*	-	-	*	*	*	Poor

Supplementary Table3: Subgroup analysis: As per disease severity

Outcome	**Type of Study**	**Mild to moderate disease**		**All categories (including Severe Disease)**	
		No. of studies (Participants)	**RR/RD (95% CI)**	**No. of studies (Participants)**	**RR/RD (95% CI)**
All-cause mortality	RCT	5 (2337)	1.20 (0.47 - 3.06)	4 (6834)	1.1 (1.00 - 1.21)
	Prospective Cohort	1 (373)	-	2 (414)	0.84 (0.27 - 2.62)
Need for mechanical ventilation (post randomization)	RCT	1 (332)	1.09 (0.50 - 2.35)	3 (5970)	1.12 (0.95 - 1.33)
Need for ICU admission (post randomization/enrolment)	RCT	-	-	2 (224)	0.85 (0.40 - 1.79)
	Prospective Cohort	1 (373)	-	1 (109)	38.57 (2.16 - 689.10)
Clinical Recovery	RCT	-	-	2 (4910)	1.19 (0.72 - 1.95)

Radiological recovery	RCT			1 (62)	1.47 (1.02 - 2.11)
Virological Recovery by day 28 of illness (PCR becomes negative)	RCT	1 (150)	0.95 (0.78 - 1.15)	1 (30)	1.00 (0.88 - 1.13)
	Prospective Cohort	1 (373)	1.21 (1.11 - 1.31)		
Progression to severe disease	RCT	1 (150)	3.00 (0.12 - 72.49)		
Serious adverse events	RCT	6 (4645)	0.83 (0.40 - 1.72)	2 (2186)	1.30 (0.95 - 1.78)
Time to clinical recovery	RCT	1 (150)	1.00 (0.02 - 1.98)	1 (194)	-0.09 (-0.78 - 0.60)
Time to virological recovery	RCT	1 (150)	1.00 (0.03 - 1.97)	1 (194)	-0.63 (-1.40 - 0.14)
	Prospective Cohort	1 (373)	-6.00 (-6.69, - 5.31)	1 (109)	-2.50 (-5.88 - 0.88)
Duration of hospital stay	RCT	1 (332)	0.10 (-1.37 - 1.57)	1 (194)	-0.23 (-0.92 - 0.46)
	Prospective Cohort	1 (373)	-1.00 (-2.15 - 0.15)	1 (109)	-1.00 (-3.19 - 1.19)