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Original Research Article

Effect of hydroxychloroquine in viral clearance in nCOV-19 infected patient admitted in tertiary care centre, Ranchi, Jharkhand, India

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ABSTRACT

Background: In view of recent publications of conflicting evidence on the safety and efficacy of hydroxychloroquine as prophylaxis and as a treatment for COVID-19 patients, we need to assess the effect of hydroxychloroquine in COVID-19 patients of authors own local population.
Methods: In this retrospective chart review study, categorization of confirmed COVID-19 cases nasopharyngeal swab of RT-PCR was done into a group of patients who received hydroxychloroquine standard dose and another control group who did not receive hydroxychloroquine. The main comparing parameter was to see virus clearance days across both groups.
Results: A total of 112 patients were included for the study, and grouped of 72 patient who received HCQS and remaining 40 patients as control. The virus clearance time in days was found to be 9.01±3.08 for HCQS group and for control group it was 8.64±2.34 days (Man Whitney U test value = 2.13, p=0.756).
Conclusions: There is no significant difference found in attaining virus negative status with use of HCQS administration in this study.

Keywords: COVID -19, Hydroxychloroquines, Virus clearance

INTRODUCTION

A new variant of virus named novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in the Hubei Province of China. It rapidly spread, resulting in a global pandemic. The disease is designated COVID-19, which stands for coronavirus disease.[1] The virus that causes COVID-19 is designated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); previously, it was referred to as 2019-nCoV.

The absence of an effective treatment against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has led clinicians to redirect drugs that are known to be effective for other medical conditions to the treatment of COVID-19. Key among these repurposed therapeutic agents are the antimalarial drug chloroquine and its analogue hydroxychloroquine, which is used for the treatment of autoimmune diseases, such as systemic lupus erythematosus and rheumatoid arthritis.[2,3] Initial studies found both chloroquine (CQ) and its derivative hydroxychloroquine (HCQ) inhibits SARS-CoV-2 effectively in vitro. This led clinicians to believe that both drugs may have good potential in the treatment of COVID-19. However, the use of this class of drugs for COVID-19 is based on a small number of anecdotal

experiences that have shown variable responses in uncontrolled observational analyses, and small, open-label, randomized trials that have largely been inconclusive.[4,5] The combination of hydroxychloroquine with a second-generation macrolide, such as azithromycin (or clarithromycin), has also been advocated, despite limited evidence for its effectiveness.[6] As compared to chloroquine, hydroxychloroquine (HCQS) has better tolerability and safety profile. In addition to mild side effects of hydroxychloroquine (HCQS) i.e., nausea, vomiting, stomach pain or cramps, loss of appetite, weight loss, diarrhea, dizziness, headache, ringing in your ears, mood changes, nervousness, irritability, skin rash, it can cause QT prolongation and can increase the risk of cardio toxicity (arrhythmia). So, screening ECG is required before starting hydroxychloroquine (HCQS) and not recommended for trial in person below age of 15 years.

In view of this, authors planned this retrospective chart review study to see the effect of HCQS treatment to confirmed COVID-19 cases, in terms of virologic clearance in days as confirmed by naso-pharyngeal swab negativity of RT-PCR documented SARS-CoV- with a control group.

METHODS

This study is a retrospective chart review, to see the effect of hydroxychloroquine (HCQS) in virological clearance of RT-PCR documented SARS-CoV-2 positive patients. This study is chart review of dedicated COVID Health Centre (DCHC), Rajendra Institute of Medical Sciences (RIMS), Ranchi between 31st March 2020 to 30th May 2020.

The information of all hospitalized patients with confirmed COVID-19 were included in this study if they fulfilled the primary criteria of being RT-PCR documented SARS-CoV-2 positive in nasopharyngeal and throat sample at admission regardless of their clinical status. There was record of all patients detailed history, that was taken and clinical examination was done at the time of admission. The treating physician screened for their suitability for administering HCQS and decided about HCQS administrating or not. The main contra indication to HCQS was patients with significant cardiac, renal co-morbidity, higher age, ECG abnormality, pregnancy, lactation and patients unwilling to take HCQS. Authors made this group in this study as control group.

The all HCQS group cases were given HCQS at a dose of 400 mg P. O. on day one and 200 mg next 4 days. There was fixed duration re assessment of RT-PCR testing for corona by naso-pharyngeal swab. This primary endpoint of virological clearance at day-7 was repeated after 2 days if it had been negative to reconfirm the patient status. All test was done by RT-PCR with samples from nasopharynx and throat.

Statistical analyses

Data was entered in Microsoft excel (2016) and further the collected data of all patients was statistically analyzed, using statistical package for Social Sciences (SPSS, Inc., Chicago, Illinois) version 10.0.

Data analysis included means and standard deviations for each group, and clinical subgroup of the sample. Chi square test was used for categorical variables to determine if differences existed between the groups. The Non parametric Mann whitney U test was used for comparison of continuous variable and statistically significant levels are reported for p values less than or equal to 0.05. Highly significant levels are p values less than 0.001.

RESULTS

A total of 112 patients were included for the study, Table 1 summarizes the sample characteristics of the whole sample. The mean age of the sample was 31.36±14.84 years and mean days for attaining virus free status with treatment it was found to be 8.88±2.84 days. Similarly, across the variables there was 60.7% males and 39.3% females and 91.1% of sample population was below 55 years of age. There were 04 patients of CMP, 09 patients of diabetes, 06 patients of hypertension and 01 each patient of hypothyroidism and CKD. There was only 02 (1.8%) death in this study sample population during admission (Table 1).

Among the total sample size of 112 patients the treating team decided to treat 72 patients with HCQS and remaining 40 patients were treated without HCQS. We attempted to categorize sample as per their risk factors involved, summation of risk factors and recovery in terms of virus clearance days.

Authors considered age of 55 and above as a risk factor, then female gender with pregnancy and during puerperium, presence of chronic medical illness like diabetes, hypertension, cardiomyopathy, chronic kidney disease and thyroid disease. The study groups were observed across for frequency distribution and Pearson chi square test was done to compare (Table 2). Authors found significantly higher treatment allocation by HCQS to patients below 55 years of age (chi square=14.09, df=1, p=0.000); there was significant male predominance for receiving HCQS (chi square=8.65, df=1, p=0.003). However, the presence or absence of combined physical illness was similar across group (chi square = 0.504, df=1, p=0.478). But when we included the patients of combined physical illness with pregnant and puerperium female patients, There was significant less patients received HCQS, (chi square=18.61, df=1, p=0.000); additionally on inclusion of patients 55 years and above to this high risk group, there was significantly low allocation of HCQS to high-risk group. Authors further divided the study sample among patients recovering in

terms of becoming virus free on testing within 7 days of treatment and another group recovering after 7 days. There were 41 patients recovered within 7 days out of which 27 received HCQS and 14 did not, for slow recoveries 45 received HCQS and 26 did not (chi square=0.69, df=1, p=0.793) (Table 2).

Table 1: Socio demographic characteristics and distribution of the sample (N=112).

Variable		Total sample (n=112)
Mean age±SD in years		31.36±14.84
Mean days for attaining virus free status ±SD		8.88±2.84
		N (%)
Gender	Male	68 (60.7%)
	Female	44 (39.3%)
Old population above 55 years (R1)	Below 55 years	102 (91.1%)
	Above 55 years	10 (8.9%)
Mortality	Discharged/admitted	110 (98.2%)
	Death	02 (1.8%)
Recovery	Within 7 days	41 (36.6%)
	After 7 days	71 (63.4%)
CMP	Present	04 (3.6%)
	Absent	108 (96.4%)
Diabetes	Present	09 (8%)
	Absent	103 (92%)
CKD	Present	01 (0.9%)
	Absent	111 (99.1%)
HTN	Present	06 (5.4 %)
	Absent	106 (94.6%)
Hypo thyroidism	Present	01 (0.9 %)
	Absent	111 (99.1%)
Other significant issues R2	Pregnancy	12 (10.7%)
	Puerperium	06 (5.4%)
Treatment	HCQS given	72 (64.3%)
	HCQS not given	40 (35.7%)
All physical illness included R3	Present	11 (9.8%)
	Absent	101 (90.2%)
Risk group R1 +R2 + R3	Present	34 (30.4%)
	Absent	78 (69.6%)

Table 2: Group comparison.

Variables	Sub variables	Study groups		Pearson chi squar	DF	p value
		HCQS group-72	Control group - 40			
Age	Above 55 (R1)	1	9	14.09	1	0.000*
	Below 55	71	31			
Gender	Male	51	17	8.65	1	0.003*
	Female	21	23			
Combined physical illness	Absence	66	35	.504	1	0.478
	Presence (R2)	6	5			
CPI + preg+perp	Complicated (R3)	8	19	18.61	1	0.000*
	Uncomplicated	64	21			
Risk cat +age	High risk (R4)	8	26	35.32	1	0.000*
	Low risk	64	14			
Recovery type	Early = 7 days	27 (37.5%)	14 (35%)	.069	1	0.792
	Delayed	45 (62.5%)	26 (65%)			
Category on mean (8.88)	Below 9 days	44 (61.1%)	29 (72.5%)	1.470	1	0.225
	Above 9 days	28 (38.9%)	11 (27.5%)			

Table 3: Mean scores, SD, and Mann - Whitney U test across HCQS and control groups.

		Mean±SD	Mean rank	U	W	Z	p value
Age	HCQS	31.62±9.47	60.24	1.17	1.99	-1.63	0.101
	Control	30.88±21.52	49.76				
Virus clearance time	HCQS	9.01±3.08	56.67	1.35	2.13	-0.31	0.756
	Control	8.64±2.34	54.76				

The mean age of the HCQS group was 31.62 years (±9.47 years) and for control group it was 30.88±21.52 (Man Whitney U test value=1.17, p=0.101). The main analysis was virus clearance time in days, which was 9.01±3.08 for HCQS group and for control group it was 8.64±2.34 days (Man Whitney U test value=2.13, p=0.756) (Table 3).

DISCUSSION

In this retrospective chart review study, authors aimed to see the effect of HCQS treatment to confirmed COVID-19 cases, in terms of virus clearance in days as confirmed by nasopharyngeal swab negativity of RT-PCR documented SARS-CoV-2. Authors categorized the whole patients who were admitted with confirmed RT-PCR test for corona virus based on whether they received HCQS or not. Authors tried to see that which group attained virus negative status earliest, the result showed that at the end of 7th day 37.5% of HCQS group turned negative, in comparison to 35% in control group. However, it is statistically non-significant (p=0.792), then further authors analysed mean duration of negativity attainment and it was 9.01±3.08 and 8.64±2.34 days respectively for HCQS and control groups (p=0.756). This result shows us that there is no significant difference in attaining virus negative status with use of HCQS administration. This study findings are in accordance to the few recent studies and as well as meta-analysis of 3 studies showing no benefit of HCQS on viral clearance.[5,7]

However, there are various reasons possible for this result, firstly the comparative groups were significantly different in terms of age, gender, comorbid medical conditions and as a cumulative higher risk (Table 2). The main reason being that HCQS is known for its possible side effects, due to which treating physicians do not use among higher aged and co morbid medical conditions. This significant bias among HCQS and control makes them non comparable. However, HCQS group shows non-significant slightly longer virus clearance time then control. This is in concordance to certain studies certain studies showing results that hydroxychloroquine actually prolongs the virus clearance time.[8-10] However, this study by Mallat et al had very small sample (n=34) confirmed cases of COVID 19 only and all lack of good design, poor sampling and lack of randomization. However, there are studies with contradictory findings over action and role of hydroxychloroquine in covid-19 disease, but the role of co prescribed medications, individual susceptibility and various unknown factors contributing to the found results.

The main limitation of the study is inability to know the exact day one of acquiring coronavirus infection. Many of such cases found positive on different day of their infection acquisition and admitted with different phase of their illness progression. It would be further difficult among asymptomatic cases, which was the majority of ours sample. No one patient comes on first day of their infection, neither there is provision for daily testing during pandemic due to limited resources. The daily and frequent testing are clinically unnecessary and wastage of resources, but fixed duration testing does not accurately measure virus clearance time. With these limitations we also cannot make comparable groups as ideal desirable design to allocate or not HCQS to patients of COVID-19. However, authors can conclude that this retrospective chart review result shows us that there is no significant difference in attaining virus negative status with use of HCQS administration.

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