Original Research Article

Comparative Analytical Study of Two Different Drug Regimens in Treatment of Covid 19 Positive Patients in Index Medical College Hospital and Research Center, Indore, India

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Received: 12-01-2021 / Revised: 13-03-2021 / Accepted:27-03-2021

Abstract

Background: SARS-CoV-2 is a novel virus that first emerged in Wuhan, China. Considering the novel nature of the coronavirus, there are not yet any proven treatment strategies. In this emergency, there is no specific pharmacologic treatment that specifically targets and kill the virus or control the infection and improve the clinical outcomes. Several drugs were repurposed for this illness based on in-vitro studies or minimal evidence to combat the rapid spread of the COVID-19 pandemic.**Aims and objectives:** To compare efficacy of two regimens', Regimen 1 (hydroxychloroquine and azithromycin) and Regimen 2 (hydroxychloroquine, azithromycin and ivermectin) in Covid-19 positive patients.
Materials and methods: An observation study on 100 Covid 19 positive patients having age between 20-60 years of either sex was conducted from April to May 2020. Patients below 20 years of and above 60 years of age and having chronic conditions like hypertension, diabetes and others were excluded. Group 1 received oral hydroxychloroquine 400 mg twice a day with azithromycin 500 mg once a day. Both medications were given by per oral route for a period of 7 days. Group 2 received hydroxychloroquine 400 mg twice a day with azithromycin 500 mg once a day and ivermectin 12 mg once a day. All medications were given by per oral route for a period of 7 days.**Results:** Mean age of patients in Group 1 and Group 2 was 37.62 ± 11.609 years and 38.20±11.73 years respectively (p=0.804). No significant difference was obtained between the SpO_2 concentration (p=0.778). When we did final the COVID-19 testing, it showed that majority of the patients were found negative in the group 2, whereas 94% were found to be positive in the group 1. This difference was statistically significant with the p value of <0.001. **Conclusion:** The treatment with HCQ, azithromycin, and ivermectin had a better success rate compared to HCQ and azithromycin. Based on the results, ivermectin could be the potential therapeutic agents for the COVID-19 disease. The study had various limitations; so further randomized controlled trial is required for the results to be implemented on the larger population.

Keywords: HCQ, azithromycin, ivermectin, COVID-19, SARS-CoV-2

Introduction

The Coronavirus Disease 2019 (COVID-19) -by causing a pandemic-imposed major global challenge because of its rapid transmission and high mortality worldwide [1,2].As SARS-CoV-2 is a novel virus, there are not yet proven treatment options. In this emergency, a specific pharmacological agent is required which can either kill or control the spread of virus and simultaneously improve the outcome.[3]. It usually takes duration of several years to develop a treatment protocol for a drug.Several drugs were repurposed based on in-vitro studies or minimal evidence to combat the rapid spread of the COVID-19 pandemic. Extensive efforts to determine the efficacy and safety of several pharmacological agents were investigated using randomized trials and observational studies[4]. Early treatment would be optimal before the disease becomes severe. Recently, studies have shown that dexamethasone is effective in reducing all-cause mortality and the need of ventilation. Remdesivir seems to reduce the duration of symptoms and the occurrence of severe adverse events in mild to moderate disease[5].Current considerations for treatment include Lopinavir/ritonavir, favipiravir, and remdesivir, which are all currently in wide use in the case of moderate to severe COVID19 patients. Recently, an antiparasitic drug, Ivermectin, which has been in use for greater than 30 years, having a wide range of bioactivity has been described as highly effective in an in-vitro study against SARS-CoV-2 [6,7]. Ivermectin possibly acts by preventing entry of viral proteins to the host cell nucleus[8].Various studies have shown antiviral effects of Ivermectin in-vitro against

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several RNA viruses, e.g., Influenza A virus, Zika virus, Chikungunya virus, Dengue virus, Yellow fever virus; DNA viruses e.g., BK polyomavirus and Equine herpesvirus type 1[9].HCQ-Azithromycin combination therapy has also been shown to be a possibly effective combination therapy in the treatment of SARS-CoV-2 [10]This study was done to compare the efficacy of two regimens containing hydroxychloroquine and azithromycin vs hydroxychloroquine, azithromycin and ivermectin.

Materials and methods

We conducted an observation study on 100 Covid 19 positive patients having age between 20-60 years of either sex at Index Medical College Hospital and Research Centre, Indore, India from April 2020 to May 2020 after dividing them in to Group 1 (n=50 Covid 19 positive patients treated in Index hospital in month of April 2020) and Group 2 (n=50 Covid 19 positive patients treated in index hospital in month of May 2020) Patients below 20 and above 60 years of age and having chronic conditions like hypertension diabetes and others were excluded.

Group 1 received hydroxychloroquine 400 mg twice a day with azithromycin 500 mg once a day for a period of 7 days. Group 2 received hydroxychloroquine 400 mg twice a day with azithromycin 500 mg once a day and ivermectin 12 mg once a day for 7 days. Treatment was instituted by per oral route in both cases.A written informed consent was obtained from each patient before starting the study. The patient's clinical history was recorded prospectively in a case record form. Basic investigation like ECG, X-ray and CBC was also performed. Outcome was evaluated by RT PCR report and average time taken for the conversion of positive patients to negative was compared by applying appropriate test. Since the patients presenting to our facility already had a single positive Rt-PCR test done by the Government facilities, so only a single Rt PCR test was done in the facility. Both groups were monitored clinically and basis of investigations.Data analysis was performed using IBM SPSS ver. 20 software. Frequency distribution and cross tabulation was performed to prepare tables. Quantitative data was expressed as mean and standard deviation whereas categorical data was expressed as number and percentage. Paired t- test was performed to compare the mean. Significance level was assessed at 5%.

Results

Mean age of patients in Group 1 and Group 2 was 37.62±11.609 years and 38.20±11.73 years respectively (p=0.804). No significant difference was obtained between the Spo2 concentration (p=0.778). There was no mortality or clinical deterioration was noted in the groups during the tenure. No adverse reactions to the drugs were reported in any of the groups.

Table 1: Showing gender distribution between groups

Sex	Groups		Total	P value
	Group 1	Group 2		
Female	17 (34)	15 (30)	32	0.668
Male	33 (66)	35 (70)	68	

Table 2: Comparing clinical status between groups

Clinical status	Groups		P value
	Group 1	Group 2	
Asymptomatic	4 (8)	35 (70)	<0.001
Breathlessness	1 (2)	0 (0)	
Cold/cough	18 (36)	12 (24)	
Fever	23 (46)	0 (0)	
SOB	10 (20)	0 (0)	
Running nose	1 (2)	0 (0)	
Sore throat	7 (14)	3 (6)	

In Group 1 mean time difference from the date of initiation of treatment and second test was significantly longer (7.24±2.75 days) as compared to 5.22±1.21 days in Group 2 (p=0.021). Similarly mean difference of time between the two tests was significantly shorter in Group 2 (7.34±1.28 days) as compared to Group 1 (10.38±3.3 days) (p<0.001). There was no mortality and adverse drug reaction in either group.

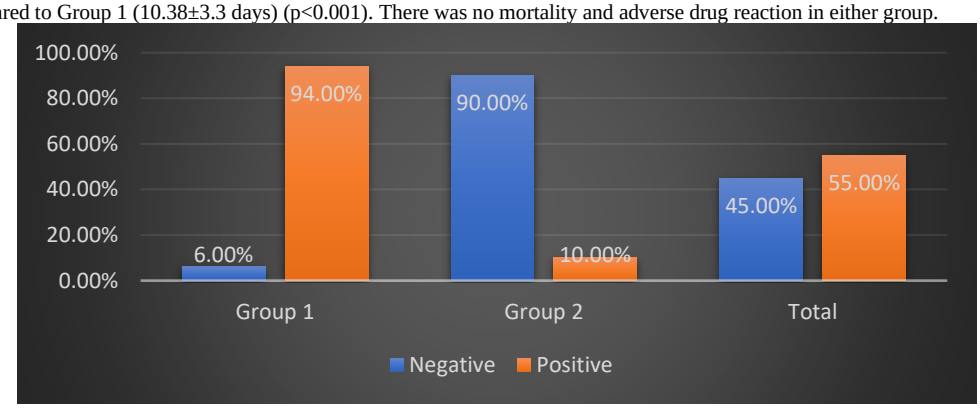

Fig 1:Comparing results of final Covid 19 testing between groups

Figure 1 shows that in Group 2 after treatment majority of the patients were found negative for Covid 19 (90%) as compared to Group 1 where 94% of the patients were found positive (p<0.001).

Discussion

The drugs hydroxychloroquine, azithromycin and ivermectin are widely used in the developing world for the treatment of infections. Due to their affordability and ready availability, makes them very attractive alternative treatment of COVID-19 disease. Our study aimed to investigate the efficacy of HCQ and azithromycin vs HCQ, azithromycin and ivermectin. It was hoped that adding ivermectin to HCQ and azithromycin regimen would decrease viral load, duration of illness and stop transmission. Mean age in both the groups were

nearly the same. No significant difference was obtained between the Spo2 concentrations with the p value of 0.778. Total number of males was 68 out of 100 in the study suggested male predominance; however, this difference was statistically insignificantt with a *P* value of 0.668. However, the number of male and female in group 1 and group 2 was nearly the same. Majority of the patients in the group 1 were having fever as a clinical symptom followed by cold/cough, whereas in the group 2, majority of the patients were asymptomatic followed by cold/cough. This difference in the symptoms was statistically significant with the p value of <0.001. This may be a confounding factor in the results interpretation. When we did final COVID-19 testing, it showed that 45 patients out of 50 were found negative in the group 2. Out of 50 patients, majority were found positive (95%) in group 1 at the end of the study after 7 days. This difference was statistically significant with the p value of <0.001. These results could be due to different time interval for the second testing in both groups. A pilot study conducted in Iraq compared 71 patients receiving HCQ and azithromycin with 16 patients receiving a single oral dose of ivermectin on top. They found no difference on mortality (2/71 vs 0/16),but less hospitalization time in days (13.2±0.9 vs 7.6±2.8, p<0.001)[11].Results were promising in the group 2 suggesting that ivermectin could be potential therapeutic agent for the treatment of COVID-19, however larger randomized controlled trials are needed to extrapolate the results on the larger population.

Conclusion

Researchers have suggested various drug combination therapies to combat COVID-19 disease. According to this study, the treatment with HCQ, azithromycin, and ivermectin had a better success rate compared to HCQ and azithromycin. Based on the results, ivermectin could be the potential therapeutic agents for the COVID-19 disease. The study had various limitations; so further randomized controlled trial is required for the results to implement on the larger population.

References

1. Baby K, Maity S, Mehta CH, Suresh A, Nayak UY, Nayak Y. Targeting SARS-CoV-2 Main Protease: A Computational Drug Repurposing Study. Arch Med Res. 2020:1
2. Richman DD. Antiviral Drug Discovery to Address the COVID-19 Pandemic. mBio. 2020;11(5):e02134-20.
3. Yu H, Li C, Wang X, Duan J, Yang N, Xie L, et al. Techniques and strategies for the potential protein-targets discovery and active pharmaceutical molecules screening in Pandemic. Journal of Proteome Research. 2020:8
4. Sohag AAM, Hannan MA, Rahman S, Hossain M, Hasan M, Khan MK, et al. Revisiting potential druggable targets against SARS-CoV-2 and repurposing therapeutics under preclinical study and clinical trials: A comprehensive review. Drug Dev Res. 2020:10
5. Juul S, Nielsen EE, Feinberg J, Siddiqui F, Jørgensen CK, Barot E, et al. Interventions for treatment of COVID-19: A living systematic review with meta-analyses and trial sequential analyses (The LIVING Project). PLOS Medicine. 2020;17(9): e1003293.
6. Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. Antiviral Res. 2020:787
7. Õmura S. Ivermectin: 25 years and still going strong. Int J Antimicrob Agents. 2008;31:91–98.
8. Heidary F., Gharebaghi R. Ivermectin: a systematic review from antiviral effects to COVID-19 complementary regimen. J Antibiot (Tokyo) 2020;73:593–602.
9. Gautret P, Lagier J-C, Parola P, et al. Hydroxychloroquine and Azithromycin as a treatment of COVID- 19: results of an open-label non-randomized clinical trial. Int J Antimicrob Agents. 2020:9
10. Gautret P, Lagier J-C, Parola P, Hoang VT, Meddeb L, Sevestre J. Clinical and microbiological effect of a combination of Hydroxychloroquine and Azithromycin in 80 COVID-19 patients with at least a six- day follow up: an observational study. Mediterr-Infect.2020:101663
11. Gorial FI, Mashhadani S, Sayaly HM, Dakhil BD, Al Mashhadani MM, Aljabory AM, et al. Effectiveness of Ivermectin as add-on Therapy in COVID-19 Management (Pilot Trial). medRxiv. 2020:2020.07.07.20145979.

Conflict of Interest: Nil
Source of support:Nil