DOI: https://doi.org/10.53350/pjmhs21155999

ORIGINAL ARTICLE

Ivermectin may not be a Miraculous Drug to Improve PF Ratio and Virus Clearance in COVID-19 patient

ABID MUSHTAQ[1], SABA ZARTASH[1], MUHAMMAD JAVED[2], MUHAMMAD ASIM RANA[3], MOHAMMAD AHAD QAYYUM[4], TAHIRA BIBI[5], MUHAMMAD MUNEEB ULLAH SAIF[6], MUHAMMAD MANSOOR HAFEEZ[7]
[1]Senior Registrar, Department of Pulmonology & Critical Care
[2]Associate Professor of Medicine, , Services Institute of Medical Sciences, Lahore
[3]Consultant Physician, Head Department of Internal and Critical Care Medicine,
[4]Consultant Nephrologist/Medical Director, Head Department of Nephrology,
[5]Resident ICU, [6]ICU Senior Nurse, Bahria International Hospital, Lahore
[7]Assistant Professor, Institute of Molecular Biology and Biotechnology, University of Lahore, Lahore
Correspondence to: Dr. Muhammad Asim Rana E-mail: drasimrana@yahoo.com Cell 0343-5807006

ABSTRACT

Aim: To evaluate the effectiveness of Ivermectin in COVID 19 infection in terms of virus clearance and symptomatic improvement.
Study design: Prospective Quasi experimental study
Place and duration of study: Study was carried out in COVID treatment units of Services Institute of Medical Sciences and Bahria International Hospital COVID treatment centre from April 15, 2020 to November 30, 2020
Methodology: One hundred COVID19 confirmed patients for this study and divided into 2 groups. Both groups were given standard treatment including Oxygen, therapeutic anticoagulation and hydroxychloroquine therapies. Group-1 was given Ivermectin for 6 days and group 2 didn't receive Ivermectin.
Results: The significance value represented as p value (p=.825) was greater than the table value at 0.05 in all aspects, which shows that Ivermectin has no effect in improving PF ratio in COVID19 patients. Out of 50 only 4 patients who received Ivermectin got COVID19 PCR negative after 6 days but on the other hand 3 patients who did not receive Ivermectin also got their PCR negative after 6 days of treatment.
Conclusion: Ivermectin does not seem to be effective in improvement of PF ratio and virus clearance in COVID19 patients.
Keywords: SARS-CoV-2, COVID-19, PF ratio, Ivermectin, Virus clearance, Anti-viral treatment, Viral clearance

INTRODUCTION

In December, 2019, a new kind of viral of pneumonia was declared by China that was later diagnosed as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] Afterwards it was called Covid-19 (coronavirus disease 2019) by World Health Organization. The disease commonly presents with cough, fever, and shortness of breath (SOB). The incubation period is 5-9 days after contact with an infected person.[2] Since then a large number of people have been infected with a huge number of fatalities reported.[3] Due to the global spread of Covid-19, it has been declared as a pandemic on March 11, 2020[4]. On 27th of February 2020, Pakistan reported its first two confirmed cases of COVID-19, both of patients had just came back to Pakistan from Iran.[5]

In the beginning of a new epidemic the treatment options were limited.[6] Currently no vaccine or definitive treatment against virus has been identified and approved to treat critically ill patients. The main stay for COVID19 symptomatic cases remains supportive care, including Oxygen supplementation, mechanical ventilation, anticoagulation, fluids and management of complications like superadded infections. Combination treatment of anti-viral drugs and low-dose systematic corticosteroids have been encouraged to treat COVID-19 patients[7].

Received on 12-12-2020
Accepted on 14-04-2021

Ivermectin, an anti-parasitic medicine, which has been described to be very effective in-vitro against SARS-CoV-2 has come up the surface of evidence-based medicine as an antiviral drug[8]. Ivermectin is a multipurpose drug with exceptional characteristics, which made it an attention-grabber for basic and applied research (in particular for drug repurposing): it appears as an antibacterial[9] antiviral, and also has anticancer activities[10], besides being potentially beneficial for the treatment of some chronic pathologies as a result of its action on a wide range of cellular targets[11].

Ivermectin has been confirmed to inhibit COVID 19 virus in vitro by Caly et al[8] who by using cell lines observed that Ivermectin was successful in eliminating 99.98% of the viral RNA within 48 hours in the 'in vitro' samples. Considerable reduction in viral RNA in both supernatant as well as in cell linked viral RNA was observed[8]. Considering that Ivermectin could prove to be a powerful antiviral, it has been proposed that it may be useful as a potential treatment for the new coronavirus associated syndrome, a repurposed use of an old drug with a new point of view.[10]

In our present study we focused to assess the effectiveness of Ivermectin in improvement the ratio of partial pressure of Oxygen to fraction of inspired Oxygen (PaO_2/FiO_2) also written as PF ratio and virus clearance in COVID19 patient.

MATERIALS AND METHODS

This prospective quasi experimental study was jointly carried out at COVID Treatment Units of Services Institute of Medical Sciences and Bahria International Hospital Lahore from April 15, 2020 to November 30, 2020. A total of 100 participants were divided into 2 groups each consisting of 50 participants. Both groups were given same therapeutic anticoagulation, steroids and Oxygen therapies. Group one was given Ivermectin12 mg daily for 6 days and group two didn't receive Ivermectin. Laboratory including CBC, CRP, LDH, D-Dimers, serum ferritin and arterial blood gas were sent on daily bases to follow the course of disease but we took lab values for this study at first day of admission to hospital and after 6 days of administration of drugs, and to calculate PF ratio we took PaO_2 value from morning daily ABGs report. Assessment of virus clearance was done by RT-PCR of nasopharyngeal swab which was carried out after 6 days of administration of Ivermectin.

For Data analysis we described demographic data into descriptive form, laboratory values were analyzed in form of mean, and effectiveness of Ivermectin in improvement of PF ratio was analyzed with help of paired T- test.

RESULTS

Initial PF ratio of group one was 225.94 after administration of Ivermectin PF ratio of group one was 223.94 after 5 days, this change was minor. Similarly, the initial PF ratio of group 2nd that was not given Ivermectin changed from 271.16 to 269.38 after 5 day according to results change in PF ratio in both groups was almost same (Table 2).

Table 3 elaborated the results of CRP changes after Ivermectin administration in group one and changes in group 2nd without Ivermectin. According to the table initial CRP in 1st group was 112.88 and decreased up to 103.96 after administration of Ivermectin, on the other hand initial CRP 128.47 in group 2nd and decreased upto 120.11 without Ivermectin after 5 days. This improvement in CRP was almost same in both groups.

Table 4 elaborated the results of Ferritin changes in response to Ivermectin, initial Ferritin in 1st group was 619.40 and decreased up to 613.14 after administration of Ivermectin, beside this initial Ferritin 548.14 in group 2nd and decreased upto 535.96 without Ivermectin after ten days. This improvement in Ferritin was almost same in both groups.

The calculated significance value for (p=.825) was greater than the table value at 0.05 in all sections, which shows that Ivermectin has no effect in improving PF ratio in COVID19 patients. But as compare to group which did not receive Ivermectin their p value (p=.917) which is greater than group one p value (p=.825) which mean Ivermectin helped in improving pf ratio but that improvement is not considerable (Table 5).

At first day all of the patients were COVID PCR positive, after administration of Ivermectin for 6 days, 4 patients got negative PCR but similarly in second group which did not receive Ivermectin also got 3 negative PCR, which shows there is no such effectiveness of Ivermectin in virus clearance in COVID19 patients (Table 6).

Table 1: Frequency of genders

Gender	Group I		Group II	
	No.	%	No.	%
Male	28	56.0	34	68.0
Female	22	44.0	16	32.0
Mean age	54.74 years		52.54 years	

Table 2: Mean PF ratios

PF ratio	Mean	No.
Initial PF Ratio in Group-1	225.94	50
Last PF Ratio in Group-1	223.94	50
Initial PF Ratio in Group-2	271.16	50
Last PF Ratio in Group-2	269.38	50

Table 3: Mean CRP

CRP	Mean	No.
Initial CRP in Group-1	112.88	50
Last CRP in Group-1	103.96	50
Initial CRP in Group-2	128.47	50
Last CRP in Group-2	120.11	50

Table 4: Mean ferritin

Ferritin	Mean	No.
Initial Ferritin in Group-1	619.40	50
Last Ferritin in Group-1	613.14	50
Initial Ferritin in Group-2	548.14	50
Last Ferritin in Group-2	535.96	50

Table 5: Paired Samples Test

	Paired difference					t	df	Sig. (2-taled)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Initial PF Ratio - Last PF Ratio (Pair 1)	2.000	63.639	9.000	-16.086	20.086	.222	49	.825
Initial PF Ratio - Last PF Ratio (Pair 2)	1.780	120.513	17.043	-32.469	36.029	.104	49	.917

Table 6: Comparison of Ivermectin

	COVID19 PCR at 1st day	COVID19 PCR After 6 days of treatment
Group 1 (Ivermectin group)	50 Positive	46 Positive and 4 Negative
Group 2 (Didn't receive Ivermectin)	50 Positive	47 Positive and 3 Negative

DISCUSSION

According to present study results out 50 only 4 patients who received Ivermectin got COVID19 PCR negative after 6 days but on the other hand 3 patients who did not receive Ivermectin also got PCR negative after 6 days. Initial PF ratio of group one was 225.94 after administration of Ivermectin PF ratio of group one was 223.94 after 5 days, this change was minor. Similarly, the initial PF ratio of

group 2nd that was not given Ivermectin changed from 271.16 to 269.38 after 5 day according to results change in PF ratio in both groups was almost same. The calculated significance value for (p=.825) was greater than the table value at 0.05 in all sections, which shows that Ivermectin has no effect in improving PF ratio in COVID19 patients

In contrast with present study, Rahman et al[12] conducted a study on the topic comparison of viral clearance between Ivermectin with doxycycline, hydroxychloroquine and azithromycin in COVID-19 patients and concluded that Ivermectin and Doxycycline combination is useful drug therapy in patients infected from COVID-19. As in present study we didn't use Doxycycline in combination with Ivermectin, so further robust studies are needed to find out the scope of this treatment.

In parallel of present study, a research report written on Ivermectin effectiveness in COVID-19 patients concluded that the present PK & PD data (pharmacokinetic and pharmacodynamic data) for Ivermectin has shown that in the doses which are routinely used for the treatment of parasitic diseases the SARS-CoV-2 inhibitory concentrations are almost not achievable. At present any dose of Ivermectin for the treatment of severe COVID 19 is logically not justified. So, considering this medicine as a broad-spectrum antiviral agent against COVID 19 is improper because it has proved to be unsuccessful beyond the *in vitro*. In lieu of unreliable data from controlled studies and the aforementioned pharmacokinetic considerations, the application of Ivermectin in COVID-19 patients is not to be encouraged[13].

No adverse effects however, were seen in group that received Ivermectin. There is data related to effectiveness of Ivermectin on viral clearance in human being affected from COVID-19 is lacking. We administered quite small dosage of Ivermectin keeping in view individual protection and especially the exact dose of Ivermectin which may be beneficial for viral clearance of COVID-19 on human being still needs to be determined.

CONCLUSION

There is no effectiveness of Ivermectin in improvement of PF ratio and virus clearance of COVID19 patients. But we need more studies for generalization of results. Furthermore, effectiveness of Ivermectin with combination of other drugs like doxycycline, hydroxychloroquine and azithromycin etc. should check by doing RCTs.

REFERENCES

1. Organization WH. Pneumonia of unknown cause - China. January 5, 2020. World Health Organization Novel Coronavirus - China 2020;12.

2. Covid C, Team R. Severe outcomes among patients with coronavirus disease 2019 (COVID-19)—United States, February 12–March 16, 2020. Morb Mortal Wkly Rep 2020;69(12):343-6.

3. Covid C, COVID C, COVID C, Chow N, Fleming-Dutra K, Gierke R, et al. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019 - United States, February 12–March 28, 2020. Morbidity and Mortality Weekly Report 2020;69(13):382.

4. Organization WH. Rolling updates on coronavirus disease (COVID-19).[cited 2020 April 14] Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen. Accessed; 2020.

5. Organization WH. Coronavirus disease 2019 (COVID-19): situation report, 72. 2020.

6. Weniger H. Organization WH Review of side effects and toxicity of chloroquine. 1979. 2020.

7. Liu Y, Li J, Feng Y. Critical care response to a hospital outbreak of the 2019-nCoV infection in Shenzhen, China. BioMed Central; 2020.

8. 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 2020:104787.

9. Lim LE, Vilchèze C, Ng C, Jacobs WR, Ramón-García S, Thompson CJ. Anthelmintic avermectins kill Mycobacterium tuberculosis, including multidrug-resistant clinical strains. Antimicrobial Agents Chemotherap 2013; 57(2):1040-6.

10. Juarez M, Schcolnik-Cabrera A, Dueñas-Gonzalez A. The multitargeted drug Ivermectin: from an antiparasitic agent to a repositioned cancer drug. Am J Cancer Res 2018;8(2):317.

11. Rizzo E. Ivermectin, antiviral properties and COVID-19: a possible new mechanism of action. Naunyn-schmiedeberg's Arch Pharmacol 2020:1.

12. Rahman MA, Iqbal SA, Islam MA, Niaz MK, Hussain T, Siddiquee TH. Comparison of Viral Clearance between Ivermectin with Doxycycline and Hydroxychloroquine with Azithromycin in COVID-19 Patients. J Bangladesh College Phys Surg 2020:5-9.

13. Momekov G, Momekova D. Ivermectin as a potential COVID-19 treatment from the pharmacokinetic point of view: antiviral levels are not likely attainable with known dosing regimens. Biotechnol Biotechnol Equipment. 2020;34(1):469-74