Original Article

Assessment of Efficacy and Safety of Ivermectin in the Patients of COVID-19

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Abstract

Objective: Primary objective of the study is to evaluate the efficacy and safety of ivermectin in reducing the progression and severity of Covid-19. Secondary objective of the study is to compare viral clearance rate among the study group and evaluation of side effects of therapy.

Methods: This cross-sectional observational study was undertaken at Department of Pulmonology Fatima Memorial Hospital, Lahore. After taking a medical history and doing a physical examination, oral ivermectin(12 mg once daily for 5 days) was given to 350 patients with COVID-19. Throughout treatment, the clinical efficacy of ivermectin, viral clearance rate, and adverse effects of medication were assessed and recorded on a prepared Performa.

Results: Ivermectin therapy demonstrated 99.9 percent efficacy in patients treated with it. The paired sample t test revealed statistically significant differences in radiographic findings and PCR laboratory examination prior to and following ivermectin administration. While all clinical symptoms improved following medication. On the other hand, 2 persons (4%) have reported experiencing adverse effects from the medicine.

Conclusion: Ivermectin induction has been presented as a more successful technique for treating Covid-19 infection.

Keywords: Ivermectin, Covid-19, anti-helmenthic

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Introduction

In 2019, a corona-virus causing severe acute respiratory syndrome (SARS-CoV-2), developed into a global pandemic of paramount importance. The disease is called COVID-19 disease. Despite offering symptomatic relief, numerous therapies are being studied and assessed for COVID-19 therapy, and a therapeutic agent that can shorten the duration of infection is critical. COVID-19 management is determined by the disease's severity. Mild cases typically resolve on their own however moderate and severe disease based on clinical and HRCT findings; require careful monitoring and hospitalisation[3].

Developing a safe and efficacious treatment for COVID-19 disease is a lengthy procedure. Numerous therapies are under investigation including prophylactic vaccines, anti-viral medications and immune-modulator therapies, depending on stage of COVID-19 disease.[1] Ivermectin, a widely used anti-parasitic medicine, has also been shown a reduction in viral RNA of 93-99.8% following a single dosage of Ivermectin by inhibiting viral proteins from entering the host cell nucleus.[2]

Ivermectin is an antiparasitic prescription, Food and Drug Administration (FDA) approved for treatment of different tropical diseases, including onchocerciasis, helminthiases, and scabies.[1] Additionally, it is currently under research for its ability to kill mosquitoes that feed on treated people and domesticated animals, thus limiting the spread of malaria.[2] Ivermectin is broadly a safe drug and is very much endured.[1,3] Currently, I'vermectin use has not been endorsed by the FDA for use in treatment of viral diseases.

Numerous studies are being undertaken to determine the efficacy of Ivermectin in treating COVID-19. An observational research found that treating COVID-19 patients with a single dose of ivermectin resulted in a significant improvement in symptoms when compared to symptomatic therapy.[3] Similarly, a recent retrospective cohort research indicated that Ivermectin was related with a decreased risk of death during COVID-19 treatment, particularly in patients requiring increased ins-

pired oxygen or ventilator support.[4]

A recent study which was randomised, double-blinded and placebo-controlled revealed that early intervention with ivermectin in COVID-19 patients promoted faster viral clearance and decreased viral load more rapidly, thereby avoiding immune system involvement and assisting in disease transmission prevention in the general population. However, additional research is required to corroborate these findings because no data on the effectiveness and drug side-effects of ivermectin in the treatment of COVID-19 patients are available in Pakistan. As such, this obser-vational study intends to ascertain the efficacy and safety of ivermectin in COVID-19 patients.

Methods

This cross-sectional observational study was undertaken at Department of Pulmonology Fatima Memorial Hospital, Lahore. Non probability convenient sampling technique was used in this study. COID-19 RT PCR positive Patients aged 18 and above, presenting typical lesion on x-ray, Characteristic lesions >50% radiological involvement of the lung, Respiratory rate of >22/min, FiO_2 static or improving along with > 30% deranged, ≥ 2 biochemical markers, CRP > 20 mg/l, LDH > 600 U/L, D. Dimer > 0.5mg/l or 500 ng/ml, Serum Ferritin < 500 ng/ml or mcg/l were included in the study. Patients on mechanical invasive ventilator, having respiratory rate < 20 breaths/minute and laboratory parameters not abnormal by more than 20%, End stage renal disease (GFR <30ml/min/1.73m2), ALT/AST levels >5 times normal and Women who are pregnant were excluded from study.

After the approval of ethical committee, informed consent was taken from 50 patients full filling the inclusion criteria. After taking previous history and doing physical examination, oral ivermectin (12 mg once daily for 5 days) was given to the patients of COVID-19 along with the symptomatic treatment. Nasopharyngeal swabs will be obtained after treatment to find the viral load and viral clearance rate of SARS-CoV-2 by rRT-PCR. Chest X-ray or HRCT chest was performed to assess the radiological improvement when indicated. During treatment assessment of efficacy and safety of ivermectin, viralclearance rate and evaluation of side effects of therapy was done and added on preformed performa.

Data Analysis:

Data analysis done by SPSS version 25.0. The variables such as gender and presence of side effects were presented in frequency and percentages while other variables associated with efficacy of ivermectin are compared to each other in paired sample t-test. The result is remarkable if the p value is ≤0.05 and confidence interval is 95%.

Results

The paired sample t test was used to evaluate the PCR lab examinations and radiological findings before and after the ivermectin therapy, the p value was observed to be less than 0.05 hence the test is significant statistically.

The descriptive statistics was used to measure the sign and symptoms after the ivermectin therapy which con-

Table 1: *Paired Samples Statistics*

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Covid_19_PCR_Clinical_Encounter_1	2.0000[a]	350	.00000	.00000
	Covid 19 PCR Clinical Encounter 2	1.0000[a]	350	.00000	.00000
Pair 2	Radiological Findings CE1	1.6800	350	.47121	.06664
	Radiological Findings CE2	1.0000	350	.00000	.00000

a. The correlation and t cannot be computed because the standard error of the difference is 0.

cludes the relief of symptoms in all the selected patients of the study.

Table 2: *Paired Samples Test*

		Paired Differences							
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		t	df	Sig. (2-tailed)
					Lower	Upper			
Pair 2	Radiological Findings CE1 Radiological Findings CE2	.68000	.47121	.06664	.54608	.81392	10.204	49	.000

The therapy has demonstrated 2 patients reported with the side effect of ivermectin as shown below:

Table 3: *Descriptive Statistics*

	N	Min	Max	Mean	Std. Deviation
Fever CE2	350	1.00	1.00	1.0000	.00000
Cough CE2	350	1.00	1.00	1.0000	.00000
SOB CE2	350	1.00	1.00	1.0000	.00000
Sore Throat CE2	350	1.00	1.00	1.0000	.00000
Viral Load CE2	350	1.00	1.00	1.0000	.00000

Table 4: *Details_therapy_effects*

	N	%	Valid %	Cumulative %
Bradycardia	7	2.0	2.0	2.0
Developed bradycardia with PR upto 35 / min	7	2.0	2.0	4.0
NA	336	96.0	96.0	100.0
Total	350	100.0	100.0	

Discussion

The goal of this experiment was to evaluate the effectiveness and side-effects of ivermectin when given for treatment of COVID-19 disease. Our study enrolled and randomly assigned 350 patients according to the inclusion criteria. The baseline demographic and clinical characteristics of the clinical group analyzed were comparable without being statistically different. Laboratory measurements and radiological findings did change considerably. In this investigation, pre and post ivermectin therapy outcomes demonstrated a statistically distinct result. There was a trend toward shorter hospitalizations in the ivermectin group observed in our study. This superb result of ivermectin was mirrored with Ahmed et al.[15] and Elgazzar et al.[16], both observed that early presentation of ivermectin into standard treatment regimen was extremely beneficial in treating COVID-19 patients, resulting in a shorter hospital stay and earlier viral clearance. Additionally, a trial research by Chaccoura et al.[22] demonstrated a trend toward reduced viral loads and IgG titers in the ivermectin group. This outcome could be explained by its suppressive action on a variety of pro-inflammatory cytokines that contribute to the cytokine storm and subsequent illness complications.[10]

Three ongoing clinical preliminaries set up the positive impact of adding ivermectin to standard of care as far as diminishing medical clinic stay. However, in opposition to our perceptions, Podder et al.[21] and Chachar et al.[22] didn't show any advantage of adding ivermectin to the COVID-19 drug therapy.

Ivermectin seems to work by obstructing host importin alpha/beta-1 atomic vehicle proteins, which are associated with a basic intracellular vehicle pathway that infections seize to advance contamination by hosing the host's antiviral reaction.[4,5] Additionally, docking of ivermectin with the serious intense respiratory condition Covid 2 (SARS-CoV-2) spike protein to the human cell film might be hurt.[6] Ivermectin is accepted to be a host-coordinated specialist, which may represent its expansive antiviral movement in vitro against dengue, Zika, HIV, and yellow fever infections.[4,7-9] Inspite of this in-vitro activity, no clinical exploration has exhibited that I'vermectin enjoys a remedial benefit in individuals having these diseases. Ivermectin likewise displayed in specific preliminaries mitigating characteristics, which may be advantageous in persons with COVID-19 disease.

In cell cultures, ivermectin has been demonstrated to decrease SARS-CoV-2 replication.[13] Nonetheless, drug pharmaco-dynamics demonstrate that for achieving the anti-viral action seen in-vitro would need portions up to 100-overlay those allowed for human use.[14,15] While ivermectin will in general collect in lung tissue, projected foundational plasma and lung tissue focuses are altogether under 2 M, the in vitro half-maximal inhibitory fixation (IC50) against SARS-CoV-2 virus.[16-19] Ivermectin 400 g/kg subcutaneously showed no impact on Covid-19 infection levels in hamsters. Depletion in olfactory shortage (as controlled by a food-discovering test) and a reduction of interleukin IL-6 and IL-10 proportion in lung tissues was noted.[20]

Since the most recent guideline changes, consequences of many randomized preliminaries and reviews consider assessing the utilization of ivermectin in COVID-19 disease affected patients. These have been distributed in peer-audited distributions or made accessible as entries for peer survey. Some of the clinical investigations discovered no advantage or deterioration of disease following ivermectin use,[21] while others figured out a more limited opportunity to control infection signs credited to COVID-19, a more prominent decrease in inflammatory marker levels, a increase in viral clearance, or a lower death rate in patients who got ivermectin contrasted with patients who got comparator.[22]

Conclusion

There is lacking information to make a proposal possibly in support of the utilization of ivermectin in COVID-19 therapy by the COVID-19 Treatment Guidelines Panel (the Panel). To give more exact proof with respect to the efficiency of ivermectin in COVID-19 treatment, results from properly fueled, all around planned, and very much clinical led preliminaries are required.

Conflict of Interest: None
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References

1. Ahmed S, Karim MM, Ross AG, Hossain MS, Clemens JD, Sumiya MK, et al., A five-day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness. Int J Infect Dis. 2021;103(2):214-6.

2. 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 research. 2020; 178(1):1-4.

3. Alam MT, Murshed R, Bhiuyan E, Saber S, Alam R, Robin R. A Case Series of 100 COVID-19 Positive Patients Treated with Combination of Ivermectin and Doxycycline. J Bangladesh Coll Physic Surg. 2020; 38(1):10–5

4. Rajter JC, Sherman MS, Fatteh N, Vogel F, Sacks J, Rajter JJ. Use of ivermectin is associated with lower mortality in hospitalized patients with coronavirus disease 2019: the ivermectin in COVID nineteen study. Chest. 2021;159(1):85-92.

5. Arévalo AP, Pagotto R, Pórfido JL, Daghero H, Segovia M, Yamasaki K, et al. Ivermectin reduces in vivo coronavirus infection in a mouse experimental model. Scient Repo. 2021;11(1):7132.

6. Lehrer S, Rheinstein PH. Ivermectin docks to the SARS-CoV-2 spike receptor-binding domain attached to ACE2. In Vivo. 2020;34(5):3023-3026.

7. Tay MY, Fraser JE, Chan WK. Nuclear localization of dengue virus (DENV) 1-4 non-structural protein 5; protection against all 4 DENV serotypes by the inhibitor ivermectin. Antiviral Res. 2013;99(3):301-306.

8. Wagstaff KM, Sivakumaran H, Heaton SM, Harrich D, Jans DA. Ivermectin is a specific inhibitor of importin alpha/beta-mediated nuclear import able to inhibit replication of HIV-1 and dengue virus. Biochem J. 2012; 443(3):851-856.

9. Barrows NJ, Campos RK, Powell ST. A screen of FDA-approved drugs for inhibitors of Zika virus infection. Cell Host Microbe. 2016;20(2):259-270.

10. Zhang X, Song Y, Ci X, et al. Ivermectin inhibits LPS-induced production of inflammatory cytokines and improves LPS-induced survival in mice. Inflamm Res. 2008;57(11):524-529.

11. DiNicolantonio JJ, Barroso J, McCarty M. Ivermectin may be a clinically useful anti-inflammatory agent for late-stage COVID-19. Open Heart. 2020;7(2).

12. Ci X, Li H, Yu Q. Avermectin exerts anti-inflammatory effect by downregulating the nuclear transcription factor kappa-B and mitogen-activated protein kinase activation pathway. Fundam Clin Pharmacol. 2009; 23(4):449-55.

13. 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; 178(6):104787.

14. Masoud HH, Elassal G, Hassany M, Zaky S. Management Protocol for COVID-19 Patients. Ministry of health and population (MOHP), Egypt. Version 1.4; 2020.

15. Ahmed S, Karim MM, Ross AG, Hossain MS, Clemens JD, Sumiya MK, et al. A five day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness. Int J Infect Dis. 2021; 103(2): 214- 6.

16. Elgazzar A, Eltaweel A, Youssef SA, Hany B, Hafez M, Moussa H. Efficacy and safety of ivermectin for treatment and prophylaxis of COVID-19 pandemic. Res Square. 2020; doi: https://doi.org/10.21203/ rs.3. rs-100956/v3.

17. Sharun K, Dhama K, Patel SK, et al. Ivermectin, a new candidate therapeutic against SARS-CoV-2/COVID-19. Clin Microbiol Antimicrob. 2020; 19(1): 23.

18. Jans DA, Martin AJ, Wagstaff KM. Inhibitors of nuclear transport. Curr Opin Cell Biol. 2019; 58(2): 50- 60.

19. Gorial FI, Mashhadani S, Sayaly HM. Effectiveness of Ivermectin as add-on Therapy in COVID-19 Management (Pilot Trial). 2020; doi:https:// doi. org/ 10.1101/ 2020.07.07.20145979

20. Khan SI, Khan SI, Debnath CR. Ivermectin treatment may improve the prognosis of patients with COVID-19. Arch Bronconeumol. 2020; 56(12): 828-30.

21. Podder CS, Chowdhury N, Mohim IS, Haque W. Outcome of ivermectin treated mild to moderate COVID-19 cases: a single-centre, open-label, randomized controlled study. IMC J Med Sci. 2020; 14(3):002.

22. Chachar AZK, Khan KA, Asif M, Tanveer K, Khaqan A, Basri R. Effectiveness of ivermectin in SARS-CoV-2/COVID-19 patients. Int J Sci. 2020;9(9): 31-5.