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Effect of Interferon in the Treatment of COVID-19: A Clinical Trial Study

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ABSTRACT

Background and Aim: COVID-19 is a pandemic disease that causes high rate of mortality and morbidity around the world. Except conducting many studies during this period, there is no definite treatment for COVID-19. Interferon is one of the controversial drugs for the treatment of COVID-19. In this study we aimed to evaluate the effect of interferon in the treatment of COVID-19.

Methods: In this double blind randomized clinical trial, 30 patients were treated with beta interferon in addition to the medical regimen of COVID-19 (hydroxychloroquine 200 mg twice a day and Kaletra 400 mg) as intervention group and 30 patients were treated only with hydroxychloroquine 200 mg twice a day and Kaletra 400 mg as control group. Demographic, historical, clinical and outcome of patients were compared between the two groups.

Results: There were no statistically significant differences between age, sex, smoking, past medical history, clinical manifestations, laboratory data and CT scan manifestations of patients between the two groups (P-values > 0.05). Interferon had a positive effect on prolonged QT in ECG. Patients who received interferon had shorter ICU admission time, lower mortality rate, and higher discharge rate (P-values < 0.05).

Conclusion: Interferon is an effective treatment in patients who are admitted to hospital due to COVID-19.

INTRODUCTION

In the last days of 2019, a group of atypical pneumonia cases were reported from the Chinese city of Wuhan. A month later, the World Health Organization (WHO) discovered the disease and named it coronavirus disease 2019 (COVID-19). In addition, the International Committee on the Classification of Viruses (ICTV) identified the responsible virus as "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2). As it spread throughout the world, it was finally recognized as a Public Health Emergency of International Concern (PHEIC) and it was not long before it was declared a pandemic (1, 2). Although the symptoms of Covid-19 can vary from mild flu- like symptoms to respiratory and multi- organ failure, most patients do not experience the severe form of the disease. However, due to its high level of contagion, COVID-19 has caused a high global death. SARS-CoV-2 has killed more than 500,000 people as of July 7, 2020. These numbers are probably underestimated. Despite extensive global efforts, there are still no proven therapeutic options to treat this disease (3-6).

Various drugs have been proposed to treat COVID-19. The US Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for Remdesivir (GS-5734) based on a preliminary analysis of data from a trial conducted by the National Institutes of Health (NIH). However, the available data are far from conclusive because a well- designed and accurate trial conducted by Wang et al showed a higher mortality rate in the Remdesivir group compared to the placebo group, although the difference was not statistically significant. They also failed to find any remarkable benefit for treatment with Remdesivir (7, 8).

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Given the conflicting evidence regarding even the most promising pharmacological treatments, more robust data are needed to discover a much- needed effective treatment (4).

SARS-CoV-2 is a betacoronavirus that shares most of its genes with two others previously known deadly viruses, Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV2). Furthermore, excessive and destructive inflammation is a common clinical feature of MERS, severe acute respiratory syndrome (SARS), and COVID-19 (9-11). Consequently, it has been suggested that, as in the case of SARS and MERS, regulators and modulators of the immune response, such as interferons (IFNs), may reduce SARS-CoV pathogenesis (12-14).

IFNs are natural antiviral and immunomodulatory factors that initially react to viral infections. During SARS and MERS, the expression and subsequently the function of type I IFNs is significantly suppressed, and the administration of exogenous type I IFNs has been shown to reduce the severity of symptoms of these diseases. Among all type I IFN products evaluated, various studies, including a systematic review, have shown that IFN-β is a much more potent coronavirus inhibitor than IFN-α. In addition, interferon beta-1b (IFNβ1b) and interferon beta-1a (IFNβ1a) were shown to have the strongest inhibitory effects on MERS-CoV and SARS-CoV2 (12, 13, 15-18). In this study, we decided to examine interferon as a treatment for Covid-19.

MATERIALS and METHODS

In this study, which was conducted as a double blind randomized clinical trial that was performed on patients who were admitted to Imam Hosein hospital (Tehran- Iran) in 2021, 60 patients were enrolled into the study. They enrolled into the study randomly with “Random allocation software”.

The inclusion criteria were a positive PCR test for COVID-19, admission to Imam Hossein Hospital, and peripheral blood oxygen saturation below 88% despite receiving oxygen for 3 days. The exclusion criteria were the occurrence of any complication caused by the drug and no consent for participating into the study.

The patients were divided into two groups of 30 people and the first group received beta interferon in addition to the usual medical regimen of COVID-19 (hydroxychloroquine 200 mg twice a day and Kaletra 400 mg) and the second group (control) received only the usual medical regimen. Then the clinical results of the patients in the hospital and after 28 days were recorded and finally the clinical results of the treatment of the two groups were compared.

Patient information includes demographic information, smoking, symptoms of COVID-19, underlying disease, high BMI, state of consciousness, blood pressure, CT scan manifestations, oxygen saturation, Electrocardiogram (ECG), laboratory findings before and after treatment, ward and ICU admission status, clinical status of patients and outcomes (death or discharge) were recorded.

Statistical analysis

Frequency and percentage were used to describe the data. Fisher's exact test and Chi-square test were used for qualitative variables. All analyzes were performed by SPSS 25.0 statistical software. P-value less than 0.05 was considered statistically significant.

Ethical considerations

The ethical principles of the research were observed and no fees were imposed on the patients. This research received the code of ethics from the committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1399.699).

RESULTS

The aim of this study was to evaluate the effect of interferon in the treatment of COVID-19. Demographic and smoking information are seen in Table 1. Sixty patients were entered into the study and were randomly divided into two groups of 30 receiving treatment and the control group.

In terms of clinical manifestations, 21 (70.0%) patients in interferon group had severe disease and 22 (73.3%) patients in other group had severe disease. 7 (23.3%) patients in interferon group had moderate disease and 3 (10.0%) patients in other group had moderate disease. 2 (6.7%) patients in interferon group had critical disease and 5 (16.7%) patients in other group had critical disease. There was no statistically significant difference between the two groups based on disease severity (P-value = 0.234).

In Table 2, we assessed the clinical data of all patients. In the control group, the most common clinical symptoms were dyspnea with the number of 25 (83.3%) and in the group treated with Interferon, the most common clinical symptoms were also dyspnea equal to 24 (80%). There were no statistically significant differences between the two groups in terms of clinical data (all P-values > 0.05).

CT scan for all patients was performed. The findings of CT scan (including consolidation, ground glass opacity, nodules, effusion, pericardial effusion and cardiomegaly) had no differences between the two groups (all P-values > 0.05). Electrocardiogram (ECG) was performed for all patients and there were no significant differences between the two groups in sinus rhythm, QT interval, and other features of ECG between the two groups before and after the treatment (all P-values > 0.05). All data are seen in table 3.

In table 4 we represent O2 saturation before and after treatment in both groups. Based on our findings, interferon had a positive significant effect on oxygenation

(P-value < 0.001). We also assessed ward admission, ICU admission, outcome (death or discharge).

The laboratory data of all patients based on groups and before and after treatment are seen in table 5.

Table 1. Demographic and historical data of patients

		Interferon		P-value
		no	yes	
age	< 40	2 (6.7%)	5 (16.7%)	0.335
	40-50	4 (13.3%)	1 (3.3%)	
	51-60	7 (23.3%)	6 (20.0%)	
	61-70	9 (30.0%)	6 (20.0%)	
	> 70	8 (26.7%)	12 (40.0%)	
sex	male	15 (50.0%)	16 (53.3%)	> 0.999
	female	15 (50.0%)	14 (46.7%)	
smoking	no	28 (93.3%)	25 (83.3%)	0.424
	yes	2 (6.7%)	5 (16.7%)	
Diabetes		6 (20.0%)	10 (33.3%)	0.382
HTN		8 (26.7%)	10 (33.3%)	0.779
Heart failure		8 (26.7%)	11 (36.7%)	0.58
malignancy		1 (3.3%)	0 (0.0%)	> 0.999
Pulmonary disorder		4 (13.3%)	3 (10.0%)	> 0.999
Steroid therapy		8 (26.7%)	7 (23.3%)	> 0.999
BMI > 40		4 (13.3%)	3 (10.0%)	> 0.999
Other disorder		4 (13.3%)	6 (20.0%)	0.731
Opium use	yes	0 (0.0%)	2 (6.7%)	0.492
Allergy history		1 (3.3%)	0 (0.0%)	> 0.999

***Based on fisher exact test**

Table 2. Clinical data of all patients based on the two groups

		Interferon		P-value
		no	yes	
fever		13 (43.3%)	14 (46.7%)	> 0.999
Malaise		15 (50.0%)	17 (56.7%)	0.796
Headache		3 (10.0%)	2 (6.7%)	> 0.999
Sore throat		1 (3.3%)	0 (0.0%)	> 0.999
Cough		18 (60.0%)	21 (70.0%)	0.589
Chest pain		4 (13.3%)	2 (6.7%)	0.671
Dyspnea		25 (83.3%)	24 (80.0%)	> 0.999
Nausea		6 (20.0%)	8 (26.7%)	0.761
Diarrhea		4 (13.3%)	2 (6.7%)	0.671
Vomiting		3 (10.0%)	2 (6.7%)	> 0.999
Loss of consciousness		3 (10.0%)	3 (10.0%)	> 0.999
faint		1 (3.3%)	0 (0.0%)	> 0.999
Dysgeusia		2 (6.7%)	0 (0.0%)	0.492
Body pain		5 (16.7%)	6 (20.0%)	> 0.999
consciousness	awake	28 (93.3%)	27 (90.0%)	> 0.999
	Lethargic	2 (6.7%)	3 (10.0%)	
Blood pressure	Hypotension	1 (3.3%)	1 (3.3%)	> 0.999
	normal	27 (90.0%)	27 (90.0%)	
	Hypertension	2 (6.7%)	2 (6.7%)	

P-value based on fisher exact test

Table 3. CT scan and ECG (before and after treatment) results

		interferon		P-value
		no	yes	
CT GOO	no	3 (10.0%)	2 (6.7%)	> 0.999
	yes	27 (90.0%)	28 (93.3%)	
CT nodule	no	29 (96.7%)	25 (83.3%)	0.195
	yes	1 (3.3%)	5 (16.7%)	
CT consolidation	no	21 (70.0%)	18 (60.0%)	0.589
	yes	9 (30.0%)	12 (40.0%)	
CT plug effusion	no	23 (76.7%)	23 (76.7%)	> 0.999
	yes	7 (23.3%)	7 (23.3%)	
CT cardiomegaly	no	28 (93.3%)	29 (96.7%)	> 0.999
	yes	2 (6.7%)	1 (3.3%)	
CT pericardial effusion	no	30 (100.0%)	29 (96.7%)	> 0.999
	yes	0 (0.0%)	1 (3.3%)	
ECG				
Prolonged QT1	no	24 (80.0%)	23 (76.7%)	> 0.999
	yes	6 (20.0%)	7 (23.3%)	
Prolonged QT2	no	25 (83.3%)	29 (96.7%)	0.195
	yes	5 (16.7%)	1 (3.3%)	
P-within		0.753	0.028	
sinus1	no	1 (3.3%)	1 (3.3%)	> 0.999
	yes	29 (96.7%)	29 (96.7%)	
sinus2	no	0 (0.0%)	0 (0.0%)	-----
	yes	30 (100.0%)	30 (100.0%)	
P-within		0.5	0.5	

Table 4. Admission, outcome and oxygen situation in the two groups

		interferon		P-value
		no	yes	
Ward admission	0	0 (0.0%)	0 (0.0%)	0.843
	1-5	6 (20.0%)	8 (26.7%)	
	6-10	6 (20.0%)	8 (26.7%)	
	11-15	7 (23.3%)	5 (16.7%)	
	15-20	5 (16.7%)	3 (10.0%)	
	> 20	6 (20.0%)	6 (20.0%)	
ICU admission	0	2 (6.7%)	14 (46.7%)	< 0.001
	1-5	1 (3.3%)	6 (20.0%)	
	6-10	9 (30.0%)	2 (6.7%)	
	11-15	6 (20.0%)	0 (0.0%)	
	15-20	3 (10.0%)	0 (0.0%)	
	> 20	9 (30.0%)	8 (26.7%)	
outcome	tarkhis	18 (60.0%)	27 (90%)	0.015
	marg	12 (40.0%)	3 (10%)	
O2sat1	< 80	8 (26.7%)	8 (26.7%)	0.338
	80-85	6 (20.0%)	2 (6.7%)	
	85-90	5 (16.7%)	11 (36.7%)	
	90-95	8 (26.7%)	6 (20.0%)	
	95 <	3 (10.0%)	3 (10.0%)	
O2sat2	< 80	0 (0.0%)	0 (0.0%)	<0.001
	80-85	2 (6.7%)	0 (0.0%)	
	85-90	6 (20.0%)	0 (0.0%)	
	90-95	10 (33.3%)	0 (0.0%)	
	95 <	12 (40.0%)	30 (100.0%)	
P-within		0.003	< 0.001	

***Based on fisher exact test**

Table 5. Laboratory findings in the two groups

		Interferon		P-value
		no	yes	
WBC1	leukopeni	5 (16.7%)	7 (23.3%)	0.803
	normal	20 (66.7%)	18 (60.0%)	
	leukocytosis	5 (16.7%)	5 (16.7%)	
WBC2	leukopeni	3 (10.0%)	0 (0.0%)	0.065
	normal	25 (83.3%)	30 (100.0%)	
	leukocytosis	2 (6.7%)	0 (0.0%)	
LYMPH1	lymphopenia	29 (96.7%)	28 (93.3%)	> 0.999
	normal	1 (3.3%)	2 (6.7%)	
	lymphocytosis	0 (0.0%)	0 (0.0%)	
LYMPH2	lymphopenia	29 (96.7%)	25 (83.3%)	0.195
	normal	1 (3.3%)	5 (16.7%)	
	lymphocytosis	0 (0.0%)	0 (0.0%)	
neutrophil1	neutropeni	0 (0.0%)	0 (0.0%)	> 0.999
	normal	4 (13.3%)	5 (16.7%)	
	neutrophily	26 (86.7%)	25 (83.3%)	
neutrophil2	neutropeni	0 (0.0%)	0 (0.0%)	0.333
	normal	4 (13.3%)	8 (26.7%)	
	neutrophily	26 (86.7%)	22 (73.3%)	
BUN1	normal	20 (66.7%)	17 (56.7%)	0.596
	high	10 (33.3%)	13 (43.3%)	
BUN2	normal	12 (41.4%)	20 (66.7%)	0.069
	high	17 (58.6%)	10 (33.3%)	
Cr1	normal	26 (86.7%)	26 (86.7%)	> 0.999
	high	4 (13.3%)	4 (13.3%)	
Cr2	normal	25 (83.3%)	18 (60.0%)	0.084
	high	5 (16.7%)	12 (40.0%)	
AST1	low	2 (6.7%)	5 (16.7%)	0.459
	normal	10 (33.3%)	10 (33.3%)	
	high	18 (60.0%)	15 (50.0%)	
AST2	low	1 (3.3%)	0 (0.0%)	0.513
	normal	28 (93.3%)	28 (93.3%)	
	high	1 (3.3%)	2 (6.7%)	
ALT1	low	3 (10.0%)	3 (10.0%)	0.846
	normal	8 (26.7%)	10 (33.3%)	
	high	19 (63.3%)	17 (56.7%)	
ALT2	low	2 (6.7%)	2 (6.7%)	0.959
	normal	19 (63.3%)	20 (66.7%)	
	high	9 (30.0%)	8 (26.7%)	
ALP1	low	8 (26.7%)	8 (26.7%)	> 0.999
	normal	22 (73.3%)	22 (73.3%)	
	high	0 (0.0%)	0 (0.0%)	
ALP2	low	18 (60.0%)	19 (63.3%)	> 0.999
	normal	12 (40.0%)	11 (36.7%)	
	high	0 (0.0%)	0 (0.0%)	
CPK1	normal	12 (40.0%)	13 (43.3%)	> 0.999
	high	18 (60.0%)	17 (56.7%)	
CPK2	normal	27 (90.0%)	25 (83.3%)	0.706
	high	3 (10.0%)	5 (16.7%)	
ESR1	normal	0 (0.0%)	0 (0.0%)	-----
	high	30 (100.0%)	30 (100.0%)	
ESR2	normal	8 (26.7%)	9 (30.0%)	> 0.999
	high	22 (73.3%)	21 (70.0%)	
CRP1	normal	0 (0.0%)	1 (3.3%)	> 0.999
	high	30 (100.0%)	29 (96.7%)	
CRP2	normal	10 (33.3%)	9 (30.0%)	> 0.999
	high	20 (66.7%)	21 (70.0%)	
PCT1	normal	26 (86.7%)	27 (90.0%)	> 0.999
	high	4 (13.3%)	3 (10.0%)	
PCT2	normal	30 (100.0%)	30 (100.0%)	-----
	high	0 (0.0%)	0 (0.0%)	
D.dimer1	normal	5 (16.7%)	4 (13.3%)	> 0.999
	high	25 (83.3%)	26 (86.7%)	
D.dimer2	normal	11 (36.7%)	7 (23.3%)	0.399
	high	19 (63.3%)	23 (76.7%)	

DISCUSSION

In this study, which was conducted as a clinical trial with the aim of assessment of the effect of interferon in the treatment of COVID-19, 60 patients were included in the study and were randomly divided into two groups of 30 receiving treatment and a control group. There was no difference in terms of age, sex, and smoking between the two groups, and the two groups were the same before starting the treatment. The most common symptom in both groups was dyspnea, which was mentioned by more than 80% of patients. Prevalence of symptoms, level of consciousness, and blood pressure status were the same between the two groups. It was seen that the oxygen level was significantly different before and after receiving interferon. In fact, before the treatment, two groups had similar O2 saturation levels, but in the interferon group, after the treatment, the two groups were significantly different, and interferon increased the oxygen saturation level. Regarding hospitalization, it was found that there was no difference between the two groups before and after treatment, but regarding ICU hospitalization and mortality, the interferon group had a shorter hospitalization and less mortality.

In Alavi et al.'s study, it was found that in the population treated with IFNβ1a, there was a significant difference in time to clinical improvement (TTCI) compared to the control group; while IFNβ1b did not show a significant difference compared to the control. Mortality in both intervention groups was lower than the control group that it was 20% in the IFNβ1a group and 30% in the IFNβ1b group compared to 45% in the control group. There was no significant difference between the three arms in terms of side effects (19). In the present study, it was found that interferon had a good effect on patients' outcome. This drug improved oxygen saturation, reduced days of hospitalization in ICU and reduced mortality. In our study, it was seen that the mortality rate in the interferon treatment group was 10%, while the mortality rate in the control group was 40%. One of the differences between the current study and Alavi et al.'s study is that in Alavi et al.'s study, patients were studied in three treatment arms of 20 patients, and two drugs, IFNB1A and IFNB1B, were also compared. The fact that the mortality rate in the interferon groups in Alavi et al.'s study is higher than in our study may be due to the difference in the sample size and the older study of Alavi et al., because the treatment of COVID-19 has continuously changed during the last two years.

In the study of Rahmani et al., the efficacy and safety of interferon (β-1b) IFN was evaluated in the treatment of patients with severe COVID-19 and it was observed that the clinical improvement time in the IFN group was significantly shorter than the control group ((9 (6–10) vs. 11 (9-15) days, p = 0.002, HR = 2.30; 95% CI 1.33–3.39)). On day 14, the percentage of discharged patients in the IFN and control groups was 78.79% and 54.55%, respectively (OR = 3.09; 95% CI: 1.05-9.11, p = 0.03). The rate of admission to the intensive care unit in the control group was significantly higher than in the IFN group (66.66% vs. 42.42%, p = 0.04). There was no significant difference in the length of hospitalization and hospitalization in the intensive care unit between the groups. all-cause mortality in 28-day in the IFN and control groups was 6.6% and 18.18%, respectively (p = 0.12) (20). In the current study, it was seen that the discharge rate in the interferon group was 90%, but this rate was 60% in the control group (27 people versus 18 people). The ICU admission was significantly higher in the control group. In the control group, only 6.7% of the patients were not admitted to the ICU, while in the treatment group, 46.7% of the patients were not admitted to the ICU. The mortality rate was 10% in the interferon group and 40% in the control group. Although it was seen in two studies that interferon had a good effect in the treatment of covid-19 patients, the numerical value of the obtained results was different. This difference may be due to the difference in the severity of the disease of Covid-19 in the patients of the two studies. The patients of our study were in three critical, severe, and moderate groups, but the disease of all the patients of Rahmani et al.'s study was severe.

Some studies have shown that decreased expression of IFN-γ by circulating CD4+ T cells is associated with higher levels of pro-inflammatory cytokines such as IL-6 and TNF-α, which are higher in severe cases than in moderate cases (21). On the other hand, increased serum IFN-γ production has been observed in individuals after admission to the intensive care unit (ICU), compared to healthy individuals (22). However, up-regulation of IFN-γ was observed within 3-10 days after symptom onset in upper respiratory tract cells from symptomatic cases, suggesting its involvement in the antiviral response from early stages of the disease (23). In fact, it seems that treatment with interferon in more severe patients causes a better response.

In the study by Davoudi Monfared et al., a total of 42 patients in the IFN group and 39 patients in the control group were compared. Clinical response time was not significantly different between IFN and control group (9.7 ± 5.8 vs. 8.3 ± 4.9 days, respectively, P = 0.95). On day 14, 66.7% versus 43.6% of patients in the IFN group and the control group were discharged, respectively. 28-day overall mortality was significantly lower in the IFN than in the control group (19% vs. 43.6%, respectively, P = 0.015). They concluded that early administration significantly reduced mortality (24). In our study, it was seen that 90% of patients in the interferon group were discharged, while this rate was 60% in the control group. Also, mortality was lower in the interferon

group. In our study, the clinical response time was not evaluated, but our study also emphasized the good performance of interferon for the treatment of hospitalized patients following COVID-19.

In the study by Hung et al., who evaluated the efficacy and safety of combined interferon beta-1b, lopinavir-ritonavir, and ribavirin for the treatment of patients with COVID-19, the mean number of days from the onset of symptoms to initiation of treatment was 5 days (IQR 3-7). The combined group had a shorter mean time from initiation of treatment to negative nasopharyngeal swab ($p = 0.0010$). Adverse events included self-limited nausea and diarrhea with no difference between the two groups. No patient died during the study. The conclusion was that initial triple antiviral therapy was safe and superior to lopinavir-ritonavir alone in reducing symptoms and shortening the duration of viral shedding and hospitalization in patients with mild to moderate covid-19 (24). In the current study, it was observed that interferon treatment is very effective on the clinical results of patients. The point that represents the difference between the two studies, but emphasizes the good performance of interferon in the treatment of COVID-19, is that despite the fact that the effect of interferon was evaluated very positively in two studies, but the patients of our study had moderate to severe COVID-19, but the patients in Hong et al.'s study had mild to moderate disease. Based on the findings of these two studies, it can be said that interferon is a good drug for the treatment of patients with COVID-19, and this issue is not related to the severity of the disease, but more studies are needed to prove this issue.

In the study of Seifi et al., which was conducted with the aim of investigating the effects of treatment with INF-β 1-a (interferon beta-1a) and IFN-β 1-b (interferon beta-1b) on hospitalized patients with COVID-19, the treatment results of 100 patients with COVID-19 who were treated with IFN-β 1-a and IFN-β 1-b during the hospitalization period were evaluated. The mean discharge time of IFN-β 1a recipients was almost equal to IFN-β 1-b recipients, respectively 9 (5-10) days and 7 (5-11) days, and the mortality rate among IFN-β 1- recipients was 10% and among the recipients of IFN-β 1-b was 14%, which was not statistically significant ($p = 0.190$). The rate of hospitalization in the ICU for IFN-β 1-a and IFN-β 1-b recipients was 26% and 36%, respectively. In addition, no significant difference was observed between these two intervention groups in terms of length of stay in ICU (1 (0-2) versus 1 (0-4.25 ($P = 0.357$)). Between the two studied groups there was no significant difference in terms of the frequency of mechanical ventilation and the duration of hospitalization. It was concluded that there was no significant difference between the two groups in terms of reducing the time of disease, clinical improvements and other outcomes (25). This study is comparable to the study by Alavi et al. (19) and as seen in that study, there was no significant difference between the two forms of interferon for treatment.

CONCLUSION

It is concluded that interferon improves the results of hospitalized patients with moderate to critical disease and adding it to the treatment protocol leads to better results. These better outcomes include improved oxygen levels, reduced intensive care unit admission rates, reduced mortality, and increased discharge rate. Interferon as a suitable treatment based on our study and other studies, should be added to the treatment protocol of Covid-19 disease. It is necessary to investigate the effect of this treatment in mild to moderate patients in the future.

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CONFLICT OF INTEREST

All authors declare no conflicts of interest.

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