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Mini Review

The Role of Interferon Beta Administration in COVID-19 Treatment

Salam Sardiah[1]* and Lewa' Alzaleq[2]

[1]*Department of Clinical Pharmacy, Jordan University of Science and Technology, Jordan*

[2]*Department of Mathematics and Statistics, Washington State University, USA*

***Corresponding author:** Salam Sardiah, Clinical Pharmacy Department, The Jordan University of Science and Technology, Irbid, Jordan.

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Abstract

Coronavirus disease 2019 (COVID-19) is still a major challenging pandemic in our century and has become a public health concern. Although many safe COVID-19 vaccines are introduced to the public, new variants of the virus still exist, which make the infection more severe and associated with faster spread. Until now, there is a lack of effective therapeutic options for treatment, so many efforts have been raised to find promising effective agents. Interferons (IFNs) are a group of cytokines produced in response to infections with antiviral and immune-modulating actions. Previous studies revealed IFNs efficacy in Severe Acute Respiratory Syndrome-Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV). It's recommended that early administration of IFN-β (within 7 days from the onset of symptoms) might improve survival rate and clinical response and decrease mortality among COVID-19 patients.

Keywords: Interferon β, COVID-19, Coronavirus, SARS-CoV-2

Introduction

COVID-19 is the first global pandemic in the century, which is associated with a novel coronavirus called Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2). The clinical presentation of the illness can progress from asymptomatic infection to severe pneumonia with acute respiratory distress syndrome and finally death. It commonly manifests with fever, dry cough, myalgia, shortness of breath, and sore throat [1]. Patients are treated by symptomatic and supportive treatment including hydration, antipyretics, analgesics, proper nutrition, and antitussives [2].

Covid-19 treatment protocols include many treatment options according to cases severity, such as Lopinavir, ritonavir, hydroxychloroquine, remdesivir (which has approved valid results regarding safety and efficacy), corticosteroids, and immunoglobulins [3]. Except for the remdesivir, the efficacy of other drugs is still not significant. The rising number of cases and the widening geographical transmission of the disease raise concerns about finding other effective therapeutic options. Cytokine storm and tackling dysregulated immune response have been occasionally reported in COVID-19, immunomodulatory agents are effective treatment choices. Interferons (IFNs) are a family of cytokines that have antiviral, anti-proliferative, and immunomodulatory effects [4], so they have been suggested as a promising therapeutic option for COVID-19. Therefore, we conducted this review to summarize the outcomes of adding IFN-β to COVID-19 treatment protocols.

Discussion

Interferons are a group of signaling proteins produced as a body-defensive response to virus, bacteria, and tumor cells attacks. They are divided into three major types: type I IFN (mainly α and β), type II IFN (γ), and type III IFN (λ). IFN-β1a or IFN-β1b are the most potent IFN-I subtype in the inhibition of SARS-CoV [5] and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) [6].

Interferon-Stimulated Genes (ISGs) activation is responsible for the antiviral actions of IFNs. Those genes have a novel role in signaling and immunomodulation by the slowdown of cell metabolism and

secretion of cytokines to activate adaptive immunity [7]. IFN-β has anti-inflammatory effects due to its protective activity in lungs through upregulating Cluster Differentiation 73 (CD73) in lung endothelial cells and decreasing the vascular leakage [8].

Several studies have shown that IFN-β could be a promising therapeutic choice, alone or in combination with other antiviral drugs, in the treatment of SARS, since it inhibits SARS-CoV replication and shows prophylactic protection and potential antiviral effects after infection [9]. Early administration of IFN-β1a significantly increases the discharge rate on day 14 and decreases 28-day mortality with improved survival rate [10]. A randomized clinical trial that evaluated the efficacy and safety of IFN β1b in the treatment of patients with severe COVID-19 showed that the administration of IFN-β1b reduced the time to reach a clinical improvement and significantly decreased the ICU admission rate and the need for invasive mechanical ventilation insertion [11]. The role of combining IFN-β with conventional COVID-19 therapy has been proved by many clinical trials. A Prospective non-controlled trial evaluated the effectiveness of this combination. The results showed a decrease in Virological clearance results within 10-days and a significant recovery in the imaging studies after 14-days in patients who received IFN-β1a along with hydroxychloroquine and lopinavir/ritonavir without mortality or significant adverse drug reactions [12]. In another multicenter phase 2 clinical trial, 86 patients were randomly assigned to take an early triple combination of IFN-β1b, lopinavir-ritonavir and ribavirin for 14 days. In comparison with the administration of lopinavir-ritonavir alone, the IFN-combination group had a shorter time from the start of the treatment to negative nasopharyngeal swab and a rapid complete alleviation of symptoms, which means a lower duration of hospital stay [13].

Most studies have used the dose of 44 micrograms/ml (12 million IU/ml) of IFN-β subcutaneously three times a week for two consecutive weeks or until discharge. Regarding safety outcomes, none of the randomized clinical trials reported any significant adverse effects of IFN-β among the intervention groups.

Conclusions

In summary, given the rapid widespread of COVID-19 infection and the lack of approved effective treatment options and since interferons stand out for having a solid biological rationale due to their direct antiviral and immune-modulating effects. We recommend that early administration of IFN-β (within the first 7 days from the onset of symptoms) may improve survival rate and clinical response and decrease mortality among patients. Additionally, the combination of IFN-β with two or more standard COVID-19 drugs may enhance IFNs antiviral response and thus lead to more beneficial impacts. More clinical trials are needed to test IFN-β efficacy in COVID-19 patients.

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Competing Interests

The authors declare no competing interests.

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