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Case Report

Treatment of Covid 19 Infection with Oselatamivir as First Line Antiviral Therapy for Non-Hospitalized Patients

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Abstract

Covid-19 treatments are evolving, trying to catch up to the evolution of the virus itself as new variants continue to surface. In this article, four cases of two vaccinated and two unvaccinated individuals with mild to moderate Covid-19 are presented that have been treated with Oseltamivir, an influenza neuraminidase enzyme inhibitor. The use of Oseltamivir was the main antiviral drug in a combination regimen containing an antibiotic and a steroid. Oseltamivir has achieved symptom improvement in as little as 48 hours after commencement of treatment, with full resolution and subsequent conversion of a positive Covid-19 PCR to negative within 7-10 days, indicating a possible use of Oseltamivir as an alternative to Ritonavir boosted Nirmatrelvir (Paxlovid).

Keywords: Covid-19; Oseltamivir; Covid-19 vaccines.

Introduction

Ever since March of 2020 when the WHO declared the novel coronavirus originating from Wuhan a 'pandemic', the medical and scientific research spheres have been in a constant race against time to understand the rapidly spreading virus. Not only has the virus been spreading faster than anything in recent years, it has also been leading to a million deaths in the U.S., all while evolving in the process.

All these factors have kept scientists trying to understand the etiology of the disease but also synchronize the development of treatment options. As their knowledge on virus structure and functions have evolved from pulmonary intravascular coagulation to cytokine storms and severe acute respiratory

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distress syndromes [1], so has the virus itself. Today there are variants of coronavirus from Alpha to Omicron, with the WHO labeling Delta and Omicron to be their current variants of concern (VOC) [2].

In the pursuit for developing a definitive treatment for Covid-19, numerous therapies have been considered. Drugs such as Hydroxychloroquine, Ivermectin, Dexamethasone, Oseltamivir, Favipiravir, Remdesivir, Ritonavir and Nirmatrelvir have been studied under clinical trials [3], along with convalescent plasma and oxygen delivery mechanisms like BiPAP, CPAP and invasive ventilation. As our understanding grows, so does our critical analysis of the current treatment protocols and consequently, latest guidelines are revised on a regular basis to keep up. The current WHO guideline favors the use of Nirmatrelvir/Ritonavir combination (Paxlovid) as first line antiviral therapy for non-hospitalized adult patients not needing supplemental oxygen while also recommending against using convalescent plasma and Ivermectin, both of which were popular treatment options in the first year of the pandemic [4].

Oseltamivir is also being studied as a viable alternative to Paxlovid monotherapy, especially in combination with a steroid, an antibiotic and Zinc. Four cases of non-hospitalized women with Covid-19 are presented in this review which have been given Oseltamivir as the main anti-viral agent to see its efficacy in treating the symptoms of the disease. Two of the patients were vaccinated and two unvaccinated.

Case Report

Case 1

47-year-old female presented with low grade fever, mild non-productive cough and generalized mild-moderate body aches for the past 2 days. History and examination revealed mild shortness of breath and no indicators of upper respiratory tract infection or any environmental or occupational factors significant for her presentation. Vital signs included mild tachycardia and normal blood pressure and oxygen saturation. She had already been vaccinated with Johnson and Johnson's Covid-19 vaccine. A PCR test for Covid-19 was ordered which came back positive.

Patient was started on oral Oseltamivir Phosphate 75mg twice daily for 5 days, along with inhaled Budesonide 400 microgram (Pulmicort) 2 inhalations twice daily, oral Azithromycin 500mg for 3 days, and Zinc supplementation of 220mg twice daily. Since the patient's saturation remained normal throughout the assessment and exertional shortness of breath was only mild, supplemental oxygen and hospitalization were not indicated. Follow up visit was scheduled after 5 days.

On follow up, the patient reported significant improvement in symptoms in the first 48 hours of commencement of treatment. After 5 days of antiviral medication, repeat Covid-19 PCR was ordered, the result was negative.

Case 2

44-year-old female presented with a 1-day history of fever, body aches, productive cough, and changes in taste. History and

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examination were positive for exertional dyspnea. Prior medical history revealed she had already received the Pfizer BioN-Tech vaccine in late 2021. Upon her 2nd dose of Pfizer, past medical history revealed the patient had experienced vaccine induced myocarditis/pericarditis symptoms, which fortunately remained self-limiting. Vaccine induced myocarditis and pericarditis is a growing concern among Covid-positive cases as well as vaccine specific pathology leading to myocarditis/pericarditis symptoms [5]. Patient examination revealed all vital signs were within normal limits. Although oxygen saturation was hovering between 92% and 95%, which was consistent with her shortness of breath.

X-rays of the chest were inconclusive and blood tests showed mild increase in WBC counts. Covid-19 PCR was ordered, which resulted to be positive. Decision was ultimately made to treat the patient in a community setting without hospitalization. The patient was advised rest and self-isolation at home. Similar to case 1, Oseltamivir, Azithromycin, Pulmicort, and Zinc.

On a follow-up via phone call 3 days after starting treatment the patient reported resolution of her fever and body aches, with improvements on her shortness of breath. A second follow-up was scheduled for 7 days after commencing treatment, in which all of the patient's symptoms had resolved and subsequent Covid-19 PCRs also turned out negative.

Case 3

29-year-old female with no prior Covid-19 vaccinations presented with low grade fever, productive cough, reduced sense of smell and taste, moderate body aches and shortness of breath for the past 2 days. Vital signs showed tachycardia, and a normal oxygen saturation. Oseltamivir Phosphate, Pulmicort, Azithromycin, and Zinc were commenced, all for a total of 5 days alongside advised self-isolation and bed rest at home.

Follow-up after completion of the 5-day course, this patient reported rapid and significant improvement in symptoms within 2 days of starting treatment. Subsequent PCRs were also obtained on each follow up and she tested negative on the second PCR i.e., 10 days after commencement of treatment.

Case 4

40-year-old female with no prior Covid-19 vaccination history presented with a 36-hour-old cough, headache, loss of smell and taste, moderate body aches as well as mental confusion. Covid rapid test was done which was positive.

Patient was advised to self-isolate and start regimen of Oseltamivir with Azithromycin and Pulmicort in addition to zinc supplementation. Subsequent follow-ups showed a rapid improvement in symptoms but a relatively slower recovery from the body aches and mental confusion. PCR on the 10th day post-treatment came out negative with complete resolution of symptoms.

Discussion

As seen with the four cases mentioned above, were female with symptoms indicative of mild to moderate Covid-19, but without the clinical need for hospitalization. In all 4 cases, oral

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Oseltamivir (an antiviral), oral Azithromycin (antibacterial) and inhaled Budesonide (corticosteroid) with additional Zinc supplementation. In all four cases, symptom improvement was reported as early as 48 hours after commencement of treatment regimen. All four cases responded well to treatment without lingering symptoms.

Oseltamivir is a selective inhibitor of influenza A and influenza B viral neuraminidase enzymes. After absorption and metabolism into the active component GS4071, it is distributed majorly to the upper and lower respiratory tract circulations. Oseltamivir has established efficacy against influenza if administered early on in the course of the disease [6], as it effectively prevents viral entry into the host cell by inhibiting the neuraminidase enzyme that cleaves cell surface proteins to make an entry portal into the host cell [7].

Oseltamivir is gaining interest among the scientific community for its effect on symptom improvement in Covid-19 patients. A 2021 study by Sotaru Chiba in which 16 medical personnel with suspected Covid-19 were treated with Oseltamivir as well as antibacterial therapy, and up to 63% of patients (10/16) had fever resolution after 24h. Furthermore, it was seen that those who received Oseltamivir earlier (within 24h of symptom onset) had a greater fever resolution than those who received it later (after 24h of symptom onset [8].

On the other hand, the Ritonavir booster Nirmatrelvir (Paxlovid) has also the risk of drug interactions leading to its contraindicated use alongside CYP450 inducers like Rifampin and St. John's Wort [8]. Furthermore, combination with antibacterial therapy, particularly Erythromycin, also increases risk of adverse drug interactions, and Paxlovid is best avoided in patients with cardiac arrhythmias using Amiodarone or Flecainide, those on anticoagulants like Warfarin for Atrial Fibrillation and those utilizing statin therapy for conditions like post-MI and Hypercholesterolemia [9].

Given the rise of metabolic and lifestyle diseases around the globe such as heart disease, diabetes and obesity, Oseltamivir can be considered as a viable alternative to Paxlovid for those already on medication. As for symptom resolution for mild to moderate Covid-19 not fulfilling clinical criteria for hospitalization, Oseltamivir in combination with corticosteroids and an antibacterial agent like Azithromycin can be a good alternative to Paxlovid monotherapy as it would not only cover the antiviral spectrum of Covid-19, but also provide protection against virus mediated inflammation as well as bacterial superinfection that may otherwise increase severity of original Covid-19 infection to that of clinically significant Pneumonia which would increase chances of hospitalization. Another advantage of Oseltamivir is its equal efficacy in vaccinated and unvaccinated individuals [10].

Conclusion

With the evolution of Covid-19 variants and the projected appearance of a Delta and Omicron hybrid, dubbed the 'Deltacron' variant, vaccination, and social protection by way of wearing face masks and maintaining

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distance offers the best hope in preventing serious Covid-19 cases in the future. However, for those already infected and have mild to moderate disease, Oseltamivir may be considered as an alternative to Paxlovid monotherapy for certain situations. More research will be required to quantitatively compare efficacy of both antiviral formulations against each other.

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