Journal of Communicable Diseases
Volume 54, Issue 1 - 2022, Pg. No. 84-89
Peer Reviewed & Open Access Journal

Research Article

Effectiveness of Anti-TB Medicines in Treating Patients Experiencing COVID-19 Symptoms

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DOI: https://doi.org/10.24321/0019.5138.202254

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How to cite this article:
Al-Musawi JFH. Effectiveness of Anti-TB Medicines in Treating Patients Experiencing COVID-19 Symptoms. J Commun Dis. 2022;54(1):84-89.

Date of Submission: 2022-02-17
Date of Acceptance: 2022-02-28

A B S T R A C T

Introduction: COVID-19, the life-threatening disease caused by the pathogenic SARS-CoV-2 virus, has limited treatment or measures for curing the infected persons. However, many antibiotics have been tried with varied results.

Objective: To assess the effectiveness of anti-tubercular medicines in treating patients who are experiencing COVID-19 symptoms.

Methods: The present research work included nearly 2885 patients experiencing COVID-19 symptoms, who were categorised into two groups. The first group comprised nearly 1399 patients who were injected with 1 gm/day of streptomycin dose for a period of 10 days and 600 mg/day dosage of rifampicin was administered for a period of 10 days depending on the clinical symptoms. The second group (1486 patients) received 1 gm ceftriaxonein 100 ml saline solution for a continuous period of 12 hours continued for 10 days and 500 mg oral azithromycin continued for treatment for 5 days.

Results: The use of ceftriaxone 1 gm twice daily for 10 days and azithromycin 500 mg twice daily for 5 days improved 1486 (51.51%) patients, and streptomycin 1 gm twice daily for 10 days made nearly 1399 (48.49%) patients respond well, considering the significant level for improving the total number of patients confirmed with COVID-19. Additionally, the researchers have proved that patients treated with both streptomycin and rifampicin had higher percentages of recovery from COVID-19 signs and symptoms, with 304 patients (21.72%) aged between 46 years and 55 years old and 305 patients (21.80%) aged between 56 years and 65 years. Individuals treated with both ceftriaxone and azithromycin showed good improvement [374 (25.16%) and 339 (22.81%) patients aged 36-55 years]. The present study also confirmed that the treatment using a combined form of rifampicin and streptomycin was more successful in 78% of males and 61% of females. Also, considering the treatment using both azithromycin and ceftriaxone, there was no change of improvement among the patients.

Conclusions: The combined form of rifampicin and streptomycin is seen to have a significant effect with a good immune response for treating COVID-19 patients.

Keywords: COVID-19, Anti-tuberculosis, Rifampicin, Streptomycin, Azithromycin, Ceftriaxone, Anti-TB

Introduction

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a contagious disease caused by Coronavirus 2 (later named COVID-19) that is transmitted through coughing and sneezing. Its first case was in Wuhan, China, in December of 2019. Since then, it has spread over the world, causing a pandemic. Some of the most common clinical symptoms experienced by patients of COVID-19 are fever, exhaustion, trouble in breathing, and an inability to taste and smell. The symptoms begin to appear after nearly 1-14 days of viral exposure. Eighty-one percent of those who were admitted had mild or moderate symptoms (up to mild pneumonia), whereas 14% had severe symptoms, such as dyspnoea and hypoxia, or more than 50% lung involvement on imaging (respiratory failure, shock, or multi-organ dysfunction).[1] COVID-19 has been categorised into four groups.[2,3,4]

COVID-19 affects individuals differently. The majority of infected individuals experience mild to moderate illness and recover without hospitalisation.[5] Sore throat, diarrhoea or constipation, a rash on the skin or discolouration of the toes and fingers are the most typical symptoms.[6] Serious symptoms are breathing problems or respiratory infections, pain in chest, blurred vision, and difficulty speaking. Normally, it requires nearly 5-6 days from the time of infection for symptoms to manifest, but it can take up to 14 days.[7,8] COVID-19, the life-threatening disease caused by the pathogenic SARS-CoV-2 virus, has limited treatment or measures for curing the infected persons.[9,10] Thus, COVID-19 management relies heavily on supportive care, which includes symptomatic alleviation, fluid therapy, and oxygen support as well as prone positioning if necessary.[8,9,10] When combined with ceftriaxone, azithromycin is the first antibacterial agent used to treat COVID-19.[5,7]

Preventing and treating acute bacterial exacerbations of Chronic Obstructive Pulmonary Disease (COPD) caused by *Haemophilusinfluenzae*, *Mycobacterium* catarrhalis, or *Streptococcus* pneumoniae is the primary goal of azithromycin usage.[9] An individual's risk of cardiovascular problems and other harmful effects must be evaluated against the benefits of long-term prevention.[8,10]

Ceftriaxone was patented in 1978 and received FDA approval in 1982 for medical application. It is included in the World Health Organization's Essential Medicines List.[11] In the month of September 2012, a novel type strain of coronavirus was identified, initially dubbed Novel Coronavirus 2012 but later dubbed the Middle East respiratory syndrome coronavirus (MERS-CoV).[12,13] By 30 October 2013, Saudi Arabia had reported 124 cases and 52 deaths.[14]

Patients and Method

Al-Hussein Teaching Hospital in Thi-Qar city managed a total of 2885 patients (investigated and treated). All the patients investigated complained of flu, fever, and headache; while others complained of severe cough, dyspnoea, and generalised body pain. In contrast, several people reported feeling nauseous, as well as losing their ability to taste and smell. For PCR and CXR, all patients with a simple cough and low-grade fever had upper respiratory specimens obtained, which were confirmed by their medical histories and clinical examinations. These included nasopharyngeal (NP) and oropharyngeal (OP) swabs. CT scans were performed on patients who complained of dyspnoea, particularly those who were elderly or who experiencedthe hyperglycaemic condition of diabetes mellitus (Figures 1 and 2). Other than the presence of C-reactive protein, all the patients who were investigated and managed ranged in age from 15 to 75 years.

Dosage and Duration of Treatment

Patients who received streptomycin at a dose of 1 gm/day for 10 days alone in intra-muscular mode were included in the first group, whereas those who received rifampicin at a dose of 600 mg/day for nearly 8-13 days, depending on the severity of their symptoms, were included in the second group. One gram of ceftriaxone was dissolved in 100 ml of saline solution in micro-drops with 100 cc capacity volume each for 14 hours for nearly 10 days. This along with 500 mg of azithromycin orally once daily for five days was given to 1486 patients in the second group. Table 1 shows the distribution of individuals who benefited from the medicines in their COVID-19-related clinical symptoms.

Dyspnoea (shortness of breath) was treated with oxygen and intravenous fluids, as well as hydrocortisone in doses of 50 mg (considered as low dose), 100 mg (considered as medium dose), and 500 mg (considered as high dose).[19] Heparin and the ophylline can be provided to many of these patients to prevent the development of deep vein thrombosis (DVT) in a dose of one ampule per 500 ml of normal saline. Paracetamol at a dose of 1 gm every 12 hours is among the other supporting drugs along with 100 mg of aspirin daily, 75 mg of clopidogrel daily, 100 mg of vitamin C daily, 2000 IU of vitamin D daily, and 50-100 mg of zinc daily, orally.[15,16]

Table 2 illustrates the age wise distribution of patients whose COVID-19 symptoms had improved. Table 3 shows the gender wise distribution of patients whose COVID-19 had improved.

Results

In this study, we discovered that 1399 patients (48.49%) improved after receiving streptomycin and rifampicin (streptomycin 1 gm/day and rifampicin 600 mg/day, for 10 days), while 1486 patients (51.51%) improved after receiving ceftriaxone and azithromycin (ceftriaxone 1 gm every 12 hours via IV infusion in 100 cc fluids for nearly 14 days and

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202254

500 mg of azithromycin daily continuously for 5 days in oral mode). This might reflect that 204 (14.58%) patients treated with both streptomycin and rifampicin improved from fever, cough, weakness, headache, dyspnoea, and muscle pains, compared to 208 (13.99%) patients treated with both ceftriaxone and azithromycin.

Similarly, 240 (17.15%) of those treated with both streptomycin and rifampicin improved from fever, headache, and flu, while 255 (17.16%) of those treated with both ceftriaxone and azithromycin improved.

Rifampicin and streptomycin helped only 105 (7.50%) of those who reported fever and headache, while azithromycin and ceftriaxone improved 107 (7.20%).

Nearly, 215 patients treated with rifampicin and streptomycin, who faced a lack of smell and taste improved, while 206 patients treated with both azithromycin and ceftriaxone improved as well, according to the present study. 222 (15.86%) patients regained their lack of smellonly due to the use of streptomycin and rifampicin, while 234 (5.74%) patients regained itonly due to the use of both azithromycin and ceftriaxone.

Rifampicin and streptomycin helped 117 (36%) patients who had lost their sense of taste, while azithromycin and ceftriaxone helped 189 patients (12.71%) who had lost their sense of taste.

Rifampicin and streptomycin were found to alleviate nausea and vomiting, headaches, fever, and flu symptoms in 81% of patients compared to 69% of patients treated with the combined dosage of azithromycin and ceftriaxone.

119 (8.50%) patients recovered from fever using rifampicin and streptomycin and 119 (8.50%) patients recovered from fever with ceftriaxone and azithromycin. 63 (4.50%) patients improved following treatment with both streptomycin and rifampicin for sleeplessness, depression, and suicidal thoughts if PCR test findings were positive; 67 (4.50%) patients improved following treatment with both azithromycin and ceftriaxone. Ipramine 10 mg twice a day for low-dose people is another option (Table 1).

Patients aged 46-65 years were more likely to improve from COVID-19 symptoms and signs when they had both rifampicin and streptomycin, with 304 (21.72%) patients aged between 46 and 55 years and 305 (21.80%) patients aged between 56 and 65 years having favourable results,while the age range of patients who were treated with both ceftriaxone and azithromycin and showed favourable results was 36-55 years [374 (25.16%) patients aged 36-45 years and 339 (22.81%) patients aged 46-55 years had significantly improved] (Table 2).

A slightly more number of males(788, 56.32%) were recovered as compared to females (611,43.76%) when both streptomycin and rifampicin were used (Table 3).

Table 1.Distribution of Signs and Clinical Symptoms in Improved Patients experiencing COVID-19 Symptoms administered with Groups of Antibiotics namely, Combined Dose of Azithromycin and Ceftriaxone or Combined Dose of Rifampicin and Streptomycin

Type of Drug used in Treatment	Dyspnoea Cough, Fever, Weakness, Muscles pain, Headache n (%)	Head-ache, Fever n (%)	Head-ache and Fever Only n (%)	Lack of Smell and Taste n (%)	Lack of Smell Alone n (%)	Lack of Taste Alone n (%)	Headache, Fever, Nausea and Flu n (%)	Only Fever n (%)	Insomnia, Depression, Suicide Attempts (PCR)+ n (%)	Total n (%)
Streptomycin + rifampicin	204 (14.58)	240 (17.15)	105 (7.50)	215 (15.36)	222 (15.86)	117 (8.36)	114 (8.14)	119 (8.50)	63 (4.50)	1399 (48.49)
Ceftriaxone + azithromycin	208 (13.99)	255 (17.16)	107 (7.20)	206 (13.86)	234 (15.74)	189 (12.71)	101 (6.79)	119 (8.00)	67 (4.50	1486 (51.50)
Total	412 (14.28)	495 (17.15)	212 (7.34)	421 (14.60)	456 (15.80)	306 (10.60)	215 (7.45)	238 (8.24)	130 (4.50)	2885 (100)

Table 2.Agewise Distribution of Improved COVID-19 Patients

Age (in years)	15-25 n (%)	26-35 n (%)	36-45 n (%)	46-55 n (%)	56-65 n (%)	66-75 n (%)	Total n (%)
Rifampicin and streptomycin	130 (9.29)	258 (18.44)	237 (16.94)	304 (21.72)	305 (21.80)	165 (11.79)	1399 (45.78)

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202254

Azithromycin and ceftriaxone	138 (9.28)	226 (15.20)	374 (25.16)	339 (22.81)	285 (19.17)	124 (8.34)	1486 (54.21)
Total	268 (9.29)	484 (16.77)	611 (21.17)	643 (22.28)	590 (20.45)	289 (1001)	2885 (100)

Table 3.Genderwise Distribution of Improved COVID-19 Patients

Type of Drug used	Male n (%)	Female n (%)	Total n (%)
Streptomycin + rifampicin	788 (56.32)	611 (43.67)	1399 (42.94)
Ceftriaxone + azithromycin	751 (50.53)	735 (49.46)	1486 (57.05)
Streptomycin + rifampicin	788 (56.32)	611 (43.67)	1399 (42.94)
Ceftriaxone + azithromycin	751 (50.53)	735 (49.46)	1486 (57.05)
Total	1539 (53.34)	1346 (46.65)	2885 (100)

Figure 1.CT Scan of COVID-19 Patients

Figure 2.CXR of COVID-19 Patients

Additionally, the combined effect of azithromycin and ceftriaxonemay be equivalent in 751 (50.53%) males and 735 (49.46%) females.

Discussion

Infection with the coronavirus strain linked to SARS-CoV-2 causes COVID-19.[23] COVID-19 patients and those who fear they may have the disease should also consider self-isolation at home. Instructions on how to isolate oneself have been published by health officials.[24] As a result, the vast majority of instances of COVID-19 are minor.

Some medical centres have attempted remdesivir,[17] while others have used paracetamol or nonsteroidal anti-inflammatory drugs (NSAIDs) to treat symptoms including fever, pains, and coughs. Other supportive treatments include proper fluid intake, rest, and nasal breathing.[18,19] Azithromycin and ceftriaxone were found to be effective together in several studies.[20]

Among the 2885 patients treated with glucocorticoids, vitamin C, vitamin D3, zinc supplementation, antiplatelet or anticoagulant medication, we found that streptomycin

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202254

and rifampicin were critical in the improvement of some COVID-19 patients, with 1399 (48.49%) patients improving from COVID-19 symptoms when compared to 1486 (51.50%) patients treated with the combined dosage of azithromycin and ceftriaxone.[21]

As Erha F and Binsel S state, "trying anti-tuberculosis drugs may improve the inflammatory reactions secondary to COVID-19 and reduce the harmful effects on the body of COVID-19 like those people who were vaccinated by BCG Vaccine in countries until they had this programme of BCG Vaccinations, they had little percentages of infection with COVID-19".[22]

304 patients (21.72%) of age groups between 46 and 55 years and 305 patients (21.80%) of age groups between 56 and 65 years treated with rifampicin and streptomycin had statistically significant effects when compared to those treated with the combined dosage of both azithromycin and ceftriaxone, the latter of which also had a statistically significant effect on treating COVID-19 patients, but their clinical effects were identified in the age groups of individuals ranging between 36 and 55 years. Efficacious tuberculosis prevention and treatment methods have been scaled up and are now being utilised around the world, according to a new WHO report.[23] The patients who need emergency treatment should continue receiving it throughout the pandemic, even if they contract COVID-19, in order to minimise transmission and development of medication resistance.

Patients with tuberculosis have a 50% chance of dying if they are left untreated, which may be much higher if they are elderly or have any comorbidity. Additional support for tuberculosis prevention and treatment should be provided in conjunction with COVID-19. COVID-19's response must not influence TB services if anti-TB medications are supported by other ages, such as anticoagulant or antiplatelet, as long as they are available. There is presently no approved prescription for COVID-19, thus there are no drug-drug interactions to be aware of while clinical studies are continuing.[24] According to Fateen Ata and colleagues, rifampicin-induced pneumonitis is an extremely unusual event and has only been documented in the literature in a few cases. As a result, the diagnosis of this disorder is difficult, especially in the COVID-19 age.

A study presented a case of a patient injected with rifampicin and experiencing pneumonitis with clinical symptoms, biological imaging, and histological features compatible with the respiratory based syndrome called acute respiratory distress syndrome (ARDS), which prompted SARS-CoV-2 testing to rule out the diagnostic approach of patients infected with COVID-19 induced pneumonia. Males and females treated with both rifampicin and streptomycin showed a slight difference in improvement, with 788 (56.32%) male patients who improved from COVID-19 compared to 611 (43.67%) female patients, while the effect of azithromycin and ceftriaxone was similar, with 751 (50.53%) male patients and 735 (49.46%) female patients who improved from COVID-19.

The study also shows that rifampicin and streptomycin helped 1399 (42.94%) of our 2885 research participants recover, and azithromycin and ceftriaxone helped 1486 (57.05%) of our study participants recover, among all the study participants.

COVID-19 researchers had earlier found that TB patients taking anti-bacterial medicines don't need any other medications, but those patients may need oxygen or steroids injected into them. This study supports their findings.

Conclusion

We conclude that the use of a combination of streptomycin and rifampicin has a significant effect on the treatment of signs and symptoms of COVID-19, as compared to the supportive treatment (oxygen, anticoagulants, zinc, and vitamins); steroid contraindicated for those patients with TB.

Source of Funding: Thi-Qar Medical College, (University of Thi-Qar).

Conflicts of Interest: None

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ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.202254