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Original Research

Use of anti-viral therapy in treatment of Covid 19

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ABSTRACT:

Aim: To find out the effective treatment as an antiviral agent for COVID-19, to determine the correlation between sociodemography with clinical outcomes and duration of treatment, and to determine the relationship between comorbidities with clinical outcomes and duration of treatment for COVID-19 patients. **Methods:** A prospective cohort study was conducted in this study. This study included only confirmed COVID-19 patients who were admitted to the hospital during April-May 2020. Convenience sampling was used to select 100 patients, but only 60 patients were suitable for inclusion. **Results:** The survival analysis for COVID-19 patients using the Kaplan Meier method showed that patients receiving Oseltamivir + Hydroxychloroquine had an average survival rate of about 83% after undergoing treatment of about ten days. Gender ($p = 0.550$) and age ($p = 0.280$) did not have a significant correlation with the duration of treatment for COVID-19 patients. **Conclusion:** The most effective antiviral agent in this study based on treatment duration was the combination of Oseltamivir + Hydroxychloroquine. The higher the patient's average treatment duration is, the lower the average survival rate for COVID-19 patients.

Keywords: COVID-19; Treatment; Antiviral Therapy, Oseltamivir, Hydroxychloroquine, favipiravir, chloroquine

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INTRODUCTION

In the late 2019, a novel type of coronavirus emerged from Wuhan, China, causing patients to show pneumonia-like symptoms.[1,2] Later on, the virus spread around the world, and the World Health Organization announced a COVID-19 pandemic in March 2020. By March 17, 2020, 190,000 COVID-19 cases and approximately 7500 deaths from the virus were identified.[3] This large number of infected patients in only three months since the first reported case of COVID-19 demonstrates that the disease is extremely contagious.

COVID-19 is caused by Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), which belongs to the family Coronaviridae. The family that has been responsible for two other viral outbreaks in recent years, the first ofwhichwas in 2003 caused by Severe Acute Respiratory Syndrome coronavirus (SARS-CoV).[4] The second outbreak occurred in 2012 and 2015 due to the spread of Middle East respiratory syndrome coronavirus (MERS-CoV), another virus from the same family.[5,6] These two epidemics infected many people at the time of their peak, but after the diseases regressed, limited reports of laboratory accidents or animal-to-human transmission were published. Until today, no treatments have been reported for COVID-19.[7]

Although some casereports or observational studies have reported a few antiviral drugs being effective in improving the outcome of COVID-19 patients [8], no definitive cure has been discovered so far. Recently, a Chinese research team proposed a treatment protocol for management of COVID-19 patients, which included moxifloxacin, levofloxacin (consider tolerance) and arbidol administration.[8] However, the underlying evidence for the mentioned treatment protocol is unclear, as there are no clinical trials performed on this matter. Several antiviral therapies have been considered to be potentially effective in treating COVID-19, including oseltamivir, ganciclovir, arbidol and lopinavir / ritonavir. Many clinical trials are currently underway to evaluate the

efficacy of different medications on the outcome of COVID-19 patients [9], but their results have not been published yet. On the other hand, the quality of thesestudies is rather unclear. Treatments used for SARS-CoV or MERS-CoV may be useful in the treatment of COVID-19, due to the fact that all of these viruses are from the same family, and they all cause respiratory diseases. Nevertheless, a consensus is yet to be reached on this matter.

The aim of the study is to find out the effective treatment as an antiviral agent for COVID-19, to determine the correlation between sociodemography with clinical outcomes and duration of treatment, and to determine the relationship between comorbidities with clinical outcomes and duration of treatment for COVID-19 patients.

METHODS

STUDY DESIGN AND SETTING

The research was carried out at a non-profit hospital in United States. The study used a prospective and retrospective cohort design, included 100 COVID-19 patients, but only 60 patients were suitable for inclusion criteria. All COVID-19 patients who got favipiravir and/or oseltamivir and / or chloroquine and / or hydroxychloroquine were included in the study. Patients having comorbid HIV/AIDS or cancer and pregnant patients were excluded from the study.

DATA COLLECTING AND HANDLING

The researcher would define the patients by the list of patients in the ward. Before taking the medical record data, the researcher would explain the research and its purpose to the patients with the staff's help. The informed consent was signed as an agreement of the study from the patients. The data were arranged according to socio-demography status and current medication and transferred to clinical research form (CRF). Data were analyzed descriptively by Chi-Square and Kaplan Meier test using SPSS 22 version software. Significance correlation was showed by P-value < 0.05.

RESULTS

Table 1: Correlation between socio-demography and duration of treatment

Indicators	Duration of treatment		Total	P value
	≥14 days	≤14 days		
Gender				
Male	25	15	40	0.550
Female	12	8	20	
Age				
19-38 years	6	4	10	0.280
39–58 years	14	6	20	
59–78 years	15	5	20	
79–85 years	5	5	10	

Based on Table 1, based on gender, most of the patients were male, 40 people (66.66%). However, there is no clear trend in which COVID-19 is more likely to be diagnosed[8]. A confirmed diagnosis indicates that there have been laboratory tests done. In other words, there is approximately the same number of cases among men and women worldwide. There is no proof from this national survey data that men are more likely than women to contract it.

DISCUSSION

The median age of COVID-19 patients was 56 years, ranging from 18–87 years, and most patients were male.[8] Whereas in Guan et al., the patients' median age was 47 years, and 41.9% of patients were women.[9]

No particular treatment for coronavirus infection has been prescribed until now, except for careful supportive care.[10] Regulation of the source of infection, personal protective proceduresto minimize the risk of transmission, and early identification, isolation, and supportive treatment for infected patients are the solution to this disease. There are not adequate antibacterial agents.

Also, there are no antiviral agents useful for the treatment of SARS and MERS.[11]All patients in the study received antibacterial agents, 90% received antiviral therapy, and 45% received methylprednisolone. Depending on the seriousness of the condition, the doses of oseltamivir and methylprednisolone differ. However, there were no significant findings observed.[12]

For a long time ago, Chloroquine (CQ) and its hydroxyl analog, Hydroxychloroquine (HCQ), have been using as antimalarial agents. Besides that, many studies have explored these drugs for the possibility of medication activity for other infectious diseases.[13]Chloroquine's mechanism for viruses is Chloroquine causes coating inhibition and/or changes in post-translational modification of newly synthesized proteins in viruses, especially inhibition of glycosylation.[14] Chloroquine interfering with terminal glycosylation of the cellular receptor, angiotensin-converting-enzyme-2 (ACE2), effectively prevented the spread of SARS-CoV in cell culture, which lead to Chloroquine or Hydroxychloroquine may have indirect antiviral effects.[15] Components of SARS-CoV receptors and

orthomyxoviruses, sialic acid, might be inhibited by Chloroquine or Hydroxychloroquine.[16]

Based on China's study, Chloroquine's effects in vitro using Vero E6 cells infected with SARS-CoV-2 at a multiplicity of infection (MOI) 0.05. This study showed that chloroquine, with an Effective Concentration (EC) of 90 of 6.90 μM, effectively reduces viral replication, which can easily be accomplished with standard doses due to its strong penetration into tissues, including the lungs. By increasing endosomal pH and interfering with SARS-CoV cellular receptors' glycosylation, chloroquine is known to block viral infection. The authors also speculate that the drug's documented immunomodulatory effect could improve the antiviral effect in vivo.[17]

Favipiravir, formerly known as T-705, is a purine nucleotide prodrug, favipiravir ribofuranosyl- 50-triphosphate. The RNA polymerase is inhibited by the active agent of favipiravir,stopping viral replication. Most of the preclinical evidence for favipiravir is derived from the activity of influenza and Ebola; however, the agent has also demonstrated broad activity against other RNA viruses.

A significant correlation was found among the overall comparisons between survival analysis and treatment duration of COVID-19 patients. In a study conducted by Thai et al., it was shown that the mean duration of hospital stay was 21 days. The multivariable Cox regression model shows that age, residence, and contamination sources are significantly associated with extended stays in hospitals.[19]

Meanwhile, in a study conducted by Wang et al., the mean duration of hospital stay was 19 days. Adjusted multivariate analysis showed that longer length of stay in hospital was associated with a factor of age 45 and more, those who were admitted to a provincial hospital, and those who were seriously ill. There was no gender difference.[20]

CONCLUSION

The number of COVID-19 patients who died in this study was 27.8%.The most widely used antiviral agent for patients with confirmed COVID-19 was the combination of Oseltamivir + Chloroquine. The antiviral agent therapy rated the most effective based on the duration of treatment was the combination of Oseltamivir + Hydroxychloroquine, which had the highest survival rate at around 83% after undergoing treatment for about ten days ($p = 0.027$). However, large sample size and multicenter study would help find the most effective antiviral agent for COVID-19.

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