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Review

Covid-19 and Antiviral Drugs Used In Its Treatment

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ABSTRACT:

The new coronavirus, the seventh family member of β coronaviruses, entered our lives as 2019-nCoV. The first outbreak was seen in December 2019 in Wuhan, China. It has been reported as a zoonotic disease. 2019-nCoV; causes fatal diseases affecting the lungs, heart, liver and the whole body. 2019-nCoV interacts with ACE-2 and infects epithelial cells, initiating endothelial activation, localized inflammation, tissue damage, and dysregulated cytokine release. Antiviral drugs that selectively bind to viral proteases block the proteolytic cleavage of protein precursors necessary to produce infectious, thereby preventing viral replication. Newly designed antiviral drugs act not on viral entry into host cells but instead by blocking one or more steps of virus replication within the cell. Appropriate analytical methods are required to monitor the precise amount, distribution, metabolism, adsorption and elimination of these drugs and their metabolites in biofluids and tissues. These methods are; The preparation of plasma samples includes protein precipitation (PP), solid phase extraction (SPE), liquid-liquid extraction (LLE), or a combination of two or more of these.

Keywords: Antiviral drugs, extraction, Sars-Cov-2

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1.INTRODUCTION

The coronavirus belonging to the Coronaviridae family can be divided into four main genera (α, β, γ and δ) [1]. The new coronavirus belongs to the β coronavirus genus, and 2019-nCoV has entered our lives. After the outbreaks of severe acute respiratory syndrome (SARS)-CoV in 2003 and Middle East respiratory syndrome (MERS)-CoV in 2012, the coronavirus, which was initially reported as 2019-nCoV, then renamed as SARS-; It causes respiratory tract infection, severe pneumonia, and progressive consequences, up to death [2]. Although these coronaviruses have been isolated from different human and animal hosts at different times and places, they all belong to the coronavirus type associated with severe acute respiratory syndrome [3]. The first outbreak appeared in Wuhan, China, in December 2019. It turned out that most of the patients who were first introduced to 2019-nCoV made frequent purchases from the Huanan South Seafood Market in Wuhan, where

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seafood, pheasants, chickens, bats and other animals were sold. Therefore, it has been assumed that the associated disease is a zoonotic disease [4]. According to the data of the World Health Organization, as of March 15, 2020, SARS-CoV-2 spread rapidly with 34 in China, and then 144 countries became infected with the virus [5]. Existing antiviral drugs have been meticulously studied and the most effective treatment method has been tried to be created in order to interfere with the virus spreading so rapidly.

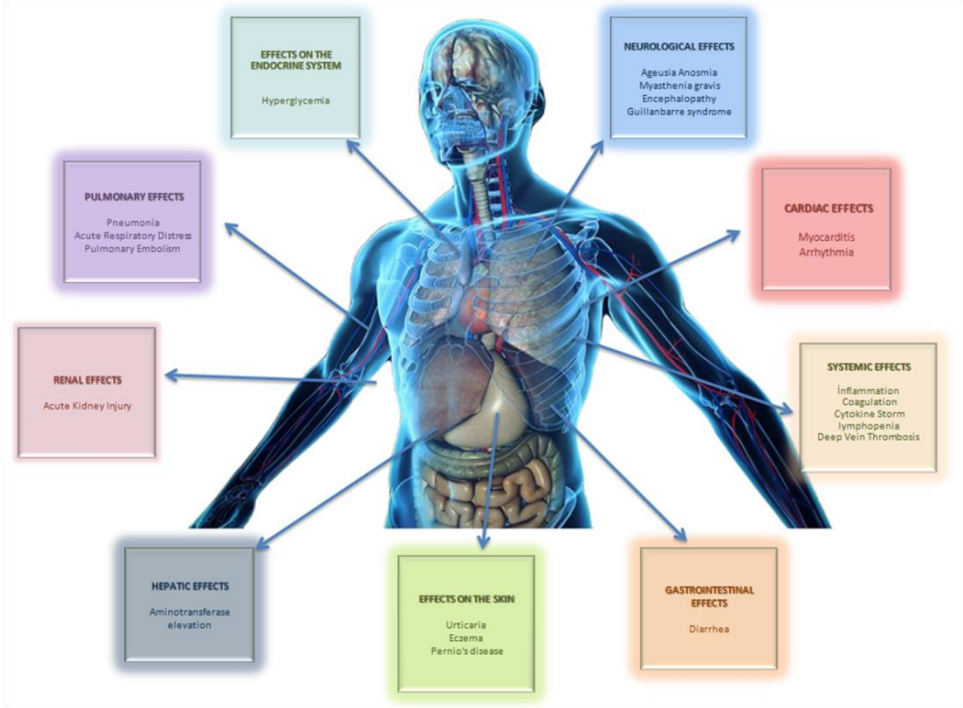

Figure 1. Sars-Cov-2 impacts on health [6]

1..1. Clinical Symptoms of Covid 19

Asymptomatic patients do not have any symptoms, only the test is positive. The patient with mild symptoms has flu-like symptoms. In moderate cases, pneumonia is usually seen, but hypoxemia is usually absent. In severe cases, there is pneumonia accompanied by hypoxemia [7].

1.2. Treatment Mechanisms

Two different methods are used to use existing drugs in the treatment of Sars-Cov-2; The first is the prevention of virus entry into the host cells and the second is the prevention of various steps of virus replication within the cell [8].

1.3. Blocking Viral Entry

SARS-CoV-2 enters the host cell by binding to specific cell surface receptors such as human angiotensin converting enzyme (hACE). It releases its RNA in epithelial cells (ECs). Here it is secreted to replicate to neighboring cells for further infection and spread through the nasal passage to the alveolar region of the lung. It has been subjected to many antiviral tests in both in vitro studies and clinical studies. Most of the antivirals tested are protease inhibitors. Redesigned antivirals; Like ACE2 receptor blockers, it does not affect viral entry into host cells, but acts by blocking

the steps of virus replication within the cell. For example; endocytosis can be inhibited, endosome maturation and release of viral genome can be inhibited. In addition, virus replication, transcription and translation of viral proteins can be inhibited [7].

1.4. Antiviral drugs

Favipiravir; Favipiravir is an antiviral agent used for new strains of influenza that survive more severely from seasonal flu [9]. Favipiravir is a prodrug that can be converted to an active form by intracellular phosphoribosylation and is a selective and potent inhibitor of RNA-dependent RNA polymerase (RdRp) of RNA viruses [10].

Remdesivir; Remdesivir, a monophosphoramidate prodrug, is an adenine nucleotide analogue. Remdesivir has broad-spectrum antiviral activity, including filovirus and coronavirus [11]. It shows its effect by interfering with the viral RNA dependent RNA polymerase (RdRp) enzyme. Thus, it causes a delay in chain termination and stops RNA synthesis and viral replication [12].

Ribavirin; Ribavirin is a guanine analog, it acts by inhibiting viral RNA-dependent RNA polymerase. Its effectiveness against other viruses in the coronavirus family has prompted a re-study of Ribavirin for Sars-Cov-2. However; It has been found to have limited in vitro activity against SARS-CoV-2, requiring an additional drug and high concentrations for an effective treatment [13]. The reproductive toxicity and the hemolytic anemia is the mostserious side effects of Ribavirin [14].

Lopinavir-ritonavir; Lopinavir is a protease inhibitor and an antiviral agent effective against Human Immunodeficiency Virus (HIV) [15]. The lopinavir-ritonavir combination has been studied against the SARS-CoV-2 virus. Potent inhibition of cytochrome (CYP) P450 3A4 combined with protease inhibitors in combination with low-dose ritonavir significantly increased the plasma concentration and efficacy of administered lopinavir [16].

Umifenovir; Umifenovir is a broad spectrum antiviral agent. It has activity against Hepatitis C, Hepatitis B, Ebola Virus, Polio Virus, Lassa Virus.3 It inhibits membrane fusion of the viral envelope by targeting the interaction between viral S-proteins and ACE2 receptors [17].

Oseltamivir; Oseltamivir, a neuraminidase inhibitor; It is an antiviral agent with strong efficacy against influenza A and influenza B viruses [18]. Oseltamivir targets neuraminidase distributed on the surface of influenza virus to inactivate influenza virus [19].

1.5. Methods Used for Extraction of Antiviral Drugs

Existing antiviral drugs have been reworked for the treatment of Covid-19. Most of the therapeutic drug monitoring studies are human plasma; carried out in various biological matrices such as urine, saliva, breast milk, cerebrospinal fluid, sperm plasma, feces, poultry muscle and cell lysates. In the preparation of plasma samples; protein precipitation (PP), liquid-liquid extraction (LLE), solid phase extraction (SPE) methods are more preferred. Protein precipitation is most

preferred as it is more affordable. The organic solvent is added to the plasma, thereby changing the solubility of the proteins in water. This causes crashing. The precipitate is separated by centrifugation. It is preferred to use acetonitrile/methanol mixtures in different ratios as a precipitating agent in the precipitation of antiviral drugs. Also, in some cases, acetonitrile acidified with 0.01% HCl or water adjusted with 8% (v/v) trichloroacetic acid (TCA) or methanol alone has been used [20]. In addition to the above, the QuEChERS method was used to extract antiviral drugs from biofluids and biological tissues. The method involved a solvent extraction with acetonitrile followed by cleavage with magnesium sulfate and sodium chloride. The final step involved a dispersive solid phase extraction (d-SPE) cleanup before gas chromatography with electron capture detection (GC-ECD) analysis [21].

2. CONCLUSION

State of the art analytical techniques; diagnosis, quantitative amount, and therapeutic effects of antiviral drugs allow for a comprehensive understanding. In this way, more effective treatments will definitely emerge, despite the covid-19 epidemic that has been affecting our lives since 2019.

Conflict of Interest

Author has no personal financial or non-financial interests.

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