Effect of ACEIs (Angiotensin-Converting Enzyme Inhibitors) and ARBs (Angiotensin II Receptor Blockers) on as Coronavirus Disease 2019 (Covid-19)

Halit Demir
halitdemi@gmail.com

Ayhan Guler
ayhanguler93@gmail.com

Nihat Ata

Follow this and additional works at: https://academicworks.livredelyon.com/health_sci

Part of the Medicine and Health Sciences Commons

Recommended Citation
Demir, Halit; Guler, Ayhan; and Ata, Nihat, "Effect of ACEIs (Angiotensin-Converting Enzyme Inhibitors) and ARBs (Angiotensin II Receptor Blockers) on as Coronavirus Disease 2019 (Covid-19)" (2020). Health Sciences. 49.
https://academicworks.livredelyon.com/health_sci/49

This Book is brought to you for free and open access by Livre de Lyon, an international publisher specializing in academic books and journals. Browse more titles on Academic Works of Livre de Lyon, hosted on Digital Commons, an Elsevier platform. For more information, please contact livredelyon@gmail.com.
Coronavirus Disease (COVID-19)

Editors
Prof. Dr. Belgin SIRIKEN & Asst. Prof. Dr. Ayhan GULER

ISBN: 978-2-38236-040-8
Coronavirus Disease

(COVID-19)

Editors
Prof. Dr. Belgin SIRIKEN & Asst. Prof. Dr. Ayhan GULER

LIVRE DE LYON

Lyon 2020
PREFACE

In the historical process, there have been pandemic periods that affect the whole world from time to time. According to the definition of WHO (World Health Organization), a pandemic is considered to have started only when the following 3 conditions are met:

- The emergence of a disease that the population has not been exposed to before
- The causative agent of the disease infecting people and causing a dangerous disease
- Spread of the disease factor easily and continuously among people

A disease or medical condition cannot only be considered a pandemic because it is widespread and kills large numbers of people, but must also be contagious. For example, although cancer is a disease that causes many deaths in humans, it is not considered a pandemic because it is not contagious. There have been major epidemics in world history. Antoninus (Galen) Plague (165-180 AD), Justinian plague epidemic (AD 541-542) Black Plague (1346 - 1350), Fifth Cholera Pandemic (1879 - 1881), Modern Plague (third plague pandemic) (1894-1903), Sixth Cholera Pandemic (1899-1923).


It is also obvious that these pandemics, which affect the history and development of humanity, will cause bigger problems in the future with the increasing human population and the depletion of world resources. As scientists, this study aims to provide information to the public about the definition, development and spread of the virus that causes the current
Covid-19 pandemic and to present it as a book section to share with researchers.

We would like to thank the publishing house and our colleagues who contributed to the publication of this publication.

Best regards

Prof. Dr. Belgin SIRIKEN
Asst. Prof. Dr. Ayhan GULER
CONTENTS

Preface..................................................................................................................I
Referees....................................................................................................................V

Chapter I
A Review: General Outlook of Coronavirus and SARS-CoV-2.............1

Chapter II
Covid-19: Update Pathogenesis and Clinical Effects.......................19

Chapter III
Epidemiology of Covid-19.................................................................29

Chapter IV
Effect of ACEIs (Angiotensin-Converting Enzyme Inhibitors) and ARBs (Angiotensin II Receptor Blockers) on Coronavirus Disease 2019 (Covid-19)..................................................41

Chapter V
Covid-19 and Food Safety............................................................49

Chapter VI
“Covid-19” in the Framework of a Dystopian Element.................59
Referees
Prof. Dr. Birgül IŞIK, Dicle University, Turkey
Prof. Dr. Hasan YELER, Cumhuriyet University, Turkey
Assoc. Prof. Dr. Rana ISIK, American Hospital, Turkey
Chapter IV

EFFECT OF ACEIs (ANGIOTENSIN-CONVERTING ENZYME INHIBITORS) AND ARBs (ANGIOTENSIN II RECEPTOR BLOCKERS) ON AS CORONAVIRUS DISEASE 2019 (COVID-19)

Halit Demir¹ & Ayhan Güler² & Nihat Aka³

¹Van Yüzüncü Yıl University, Faculty of Science, Department of Chemistry, Biochemistry Department, 65100, Van-Turkey.

²Education Faculty of Physical Education and Sports Department, University of Hakkari, Turkey.

³Van Yüzüncü Yıl University, Health Services Vocational School, Van-Turkey

1. Introduction

Unknown cause of pneumonia was emerged in Wuhan, China in December 2019 (Sayın et al., 2020). In these patients, the pneumonia agent was found to be 'severe acute respiratory syndrome coronavirus 2 (previously known as SARS-CoV-2; 2019-nCoV) (Alimoglu and Erol, 2020). This disease was identified by the World Health Organization (WHO) in February 2020 as Coronavirus Disease-2019 (Corona Virus Disase 2019; COVID-19) (Givi et al., 2020). On March 10, 2020, it was announced that the first SARS-CoV-2 positive case was seen in our country (https://covid19.saglik.gov.tr). Infection occurs through airway and contact. Although the virus has been noted in urine and feces, fecal-oral transmission is still controversial. The virus affects everyone regardless of race, gender, age, and country, but it does more harm in the elderly, smokers, patients with hypertension and those with chronic disease. (Jin et al., 2020; COVİD-19 (SARS – CoV2) Enfeksiyon
Rehberi, 2020). The average half of patients have comorbid diseases such as hypertension, diabetes and cardiovascular disease (https://www.facs.org/about-acs/covid-19).

2. Clinic and Research

The incubation period is between 2 and 14 days. The clinical picture has three stages (Mason, 2020). Stage I: Asymptomatic period (first 1-2 days). The inhaled virus sticks to the nasal cavity epithelial cells and begins to multiply. Binding is done with ACE 2 (angiotensin converting enzyme 2) receptors. The spread in this process is not so great. However, these patients are probably the most dangerous group because they are not contagious without testing. In this process, it is the most suitable diagnostic method to show the virus in the nasal swab by PCR method. Stage II. Upper airway period: The virus begins to move down in the next few days. The patient begins with fever, fatigue and constant cough. In laboratory tests, leukocytosis, neutrophilia, lymphopenia, CRP elevation are remarkable. In this process, CXCL 10 can be considered a good marker. This marker will have an important place in the assessment of COVID-19 patients over time. 80% of COVID-19 cases are in stage I and II. It is recommended to follow these cases at home (COVİD-19 (SARS – CoV2) Enfeksiyon Rehberi, 2020). Stage III. Lung involvement period: 20% of cases experience this period. The virus immediately descended to the alveoli and damages type II pneumocytes. As a result of the occupation of the virus by binding to the ACE 2 receptor, an environment consisting of alveolar damage, fibrin-rich hyaline membrane and a small number of multinuclear cells is formed. The patient has intense mucus secretion that is excreted by coughing. Rapid viral proliferation and virus damage progress as a result of ACE 2 down regulation, antibody dependent development and extensive infiltration and cytokine storm as the virus binds. How cytokine storm is triggered is still an important topic of debate. This event became clear in primary HLH. Due to their genetic mutations (HLH 2-5, RAB 27, XIAP, LYST, etc.), NK and CD8 T cells are activated and cause cytokine
storm, killing power decreasing or decreasing. Activated macrophages phagocyte cells and cytopenias begin. Macrophage activation syndrome (MAS) has similar mechanisms in cases such as HLH, rheumatological diseases, infections, malignancies, and some metabolic diseases, but genetic predisposition of some hypersitokinemia has been demonstrated (in some cases, heterozygous performance mutations have been shown). The incident is thought to be caused by very severe (immunosuppressive use, heavy viral load, cancerous tissues). The situation in COVID-19 patients is slightly different from the nucleus (neutrophil exellellet traps) caused by the initial leukocyte counts, but they weave virus residues like cocoon, but their increase (viral load) causes hyperactivation of T cells(Barnes et al.,2020).

3.Use of COVID-19 and angiotensin converting enzyme inhibitors and receptor blockers

The coronavirus disease outbreak 2019 (COVID-19) is caused by a new coronavirus infection, officially called the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) (Coronaviridae Working Group of the International Committee for Taxonomy of Viruses).

Among the COVID-19 patients admitted to a hospital, the resulting data suggest that hypertension may be associated with an increased risk of COVID-19-related mortality(Guan et al.,2019;Zhou et al.,2020).

ACEIs (angiotensin converting enzyme inhibitors) and ARBs (angiotensin II receptor blockers) are part of the reninangiotensin-aldosterone system (RAS) inhibitory agents and are considered one of the first-line drugs for the treatment of the majority of patients with hypertension. (Flack and Adekola,2020 ;Kovell et al.,2015).

However, continued use of ACEI / ARB is controversial in the COVID-19 environment. The reason for this discussion is that the use of ACEIs and ARBs can increase the expression of the ACE2 receptor in animal-based studies(Igase et al.,2008;Ferrario et al.,2005). It is a necessary
entry point for the known cellular receptor and SARS-COV-2 infection (Wu et al., 2020).

Conversely, ACE2 expression after SARS infection has been shown to be downregulated, causing RAS over-activation and severe pneumonia progression (Kuba et al., 2005).

There is an interesting method of reasoning about the increased expression of ACE2 and virus entry into the cell through this receptor. Generally, it is believed that increased ACE2 expression should result in direct delivery of virus particles to the cell. According to popular speculation, ACEi causes a decrease in angiotensin II, leaving ACE2 receptors available for coronavirus access. However, the same ACEi leads to an increase in angiotensin I and it is well known to be a substrate for ACE2. As a result of angiotensin I – ACE2 interaction, angiotensin 1-9 is produced. Little is known about the functional aspects of this product. Although initially thought to be just an intermediate step in converting angiotensin I to angiotensin II, recent evidence has shown significant cardiovascular bioactivity (Flores et al., 2020). In addition, a number of active agents such as apelin-13, dynorphin A 1-13, des-Arg9-bradykinin, neurotensin 1-13 and kinetensin were metabolized by ACE2 (Vickers et al., 2002).

In this multicenter retrospective study, the in-hospital use of ACEI / ARB has found to be associated with the risk of COVID-19 all-cause mortality compared to the use of ACEI / ARB or the use of a different class of antihypertensive agents among hypertensive patients. Although unmeasured mixing is thought to have contributed to the observed protective relationship, these data suggest that the in-hospital use of ACEI / ARB is not associated with increased mortality in COVID-19. These findings provide clinical evidence to support have been recently published guidance statements from several international communities to continue ACEI / ARB in patients with COVID-19 (Available at: https://www.hfsa.org/, 2020; Available at: 
https://ishworld.com/news/a/A-statement-from-the-International-Society-of-Hypertension-on-COVID-19/. Accessed March 5, 2020). Given the retrospective nature of this work, these data need further validation in geographically diverse, prospective, cohort studies. Randomized controlled trials are needed to examine the effectiveness of ACEI / ARB use in hypertension and COVID-19 patients. Previous clinical studies have shown that hypertension is a risk factor for higher mortality in patients with SARS and Middle East Respiratory Syndrome(Morra et al.,2018;Matsuyama et al.,2016).

As a result, increased ACE2 expression can increase infection in the body due to COVID-19.

REFERENCES:
Jin Y, Yung H, Ji W, Wu W, Chen S, Zang W. et al. Virology, Epidemiology, Pathogenesis, and Control of


