Review Article

Overview of Viral Infections Induced Oxidative Stress and its Management by Using Antioxidant

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ABSTRACT

Virology is the study of viruses, including the structure of viruses, the method of viral replication that is a lytic or lysogenic cycle in bacteria, and the interaction between the host and the virus, and finally, they produce infectious disease in that host. The frequent cause of viral infection is common in people of all ages, but their spectrum of illness is varied. Those people who have suppressed or deficient immune systems have a higher risk of severe viral infectious disease. Not only for human beings but they also can infect most organisms such as bacteria, fungi, vertebrates, plants, blue-green algae etc., When viral infection occurs produces two types of damage in cells that is direct cell damage and indirect cell damage. Direct cell damage from cell energies is diverted, macromolecular synthesis is affected, interferon defense mechanisms are inhibited, etc., And indirect cell damages from viral genomes are integrated, in host genome induction of mutation occurs, inflammation occurs, etc., Oxidative stress will be produced during cell damage that time antioxidants are very important for normal homeostasis of cells and organisms, because oxidative process in infected cell which promotes viral replication, induce cell apoptosis, and decrease cell proliferation. In this review, I concluded that when oxidative stress occurs leads to an increase in the production of free radicals that relative to oxygen and nitrogen species cause delays in the cellular process during wound healing, and the cells are infected by viruses frequently, so one of the treatment is taking proper antioxidant which helps to restore the reducing condition of infected cells.

Keywords: Virology, Cell damage, Integrated Viral Genome, Oxidative Stress, Cell Damage, Cell Death.

INTRODUCTION

In the 19th century, the first viruses were identified. The tobacco mosaic virus was identified by Ivanovsky and Beijerinck and the foot and mouth disease virus were discovered by Loeffler and Frosch and Walter Reed and the U.S. Army discovered the pathogenesis of yellow fever virus[1]. Tumor viruses, bacteriophages, influenza viruses, mumps viruses, and many arthropod-borne viruses are identified at the end of the 1930s[2]. A major outbreak produced in West Africa which originated in a rural region of Guinea in 2014-2016 due to Ebola Virus[3], the outbreak of the Ebola virus produced multiple cases then it reached other countries including Senegal[4], Nigeria[5], the United Kingdom[6], and United States[7,] etc., 26,648 cases and 11,017 documented death is produced in West Africa due to Ebola virus outbreak and the genomic sequencing also applied for providing information which helps to contain the outbreak[8,9]

Covid-19 and the immune-boosting by antioxidants

From Wuhan City in China, the Coronavirus disease (COVID-19) was first reported in late 2019 then it almost spread all over the countries globally and was declared a pandemic. In India, more than 57 thousand death cases and 3 million positive cases were reported. People with underlying medical treatment such as diabetes, cardiovascular diseases, and some diseases, and also people who are over 60 years old, are affected easily and the rapid spread of disease and also have a high mortality rate in the susceptible population finally to a global lockdown. The transmission of coronavirus from an infected person aerosol droplet through surface contact and then followed by touching the eyes, mouth, and nose, and they also affect newborns through transmission and also by fecal transmission[10,11,12].

Mechanism to Infect

They come under the family of Coronaviridae and their subfamily is Coronavirinae. Coronaviruses are enveloped viruses, and they possess sense single-stranded RNA also the genome size of these coronaviruses ranges from 26-32 Kb[13]. By its spike (S) glycoprotein, these Coronaviruses bind to angiotensin-converting enzyme 2 (ACE2) receptors on the cell. Domains S1 and S2 these two domains are present in the S protein. The receptor binding domain is called when S1 binds to the peptidase domain of ACE2, membrane fusion that is catalyzed by S2 releases the genetic material into the cells[14]. After entry into the cell for synthesis of structural protein, RNA acted as a template, and the structural proteins such as replicate, spike membrane, envelope, nucleoprotein, and also some non-structural proteins[15]. These viruses produce severe stages but may vary between individuals depending upon the medical condition and the immune status of individual

people, and their symptoms are fever, dry cough, headache, sore throat, fatigue dyspnoea etc[11].

Cytokine Storm

The immune systems have various mechanisms which are responsible for various pathogens. Through the activation of the inflammatory pathway, the host immune system response increases, by anti-viral immune response that can produce severe diseases if remains uncontrolled[16]. In the inflammatory process, cytokines are very important, and they are produced by several immune cells which include dendritic cells, macrophages, natural killer cells, and also adaptive T and B lymphocytes. When viral infection occurs the activation of innate immune response helps to produce pattern recognition receptor (PRRs) which helps to identify the different molecular structures that are the same as the invading virus, and these are referred to as pathogen-associated molecular patterns (PAMPs). The PRRs trigger the inflammatory response against the virus when binding PAMPs with PRRs they cause the activation of some signaling pathways and also the activation of transcription factors. Then the transcription factor which stimulates the expression of genes helps to produce some products these are the stages involved in virus attack for human immune response[17].

Pro-Inflammatory Cytokines

In innate immune response of most important of pro inflammatory cytokines are three. These three pro-inflammatory cytokines play a very important role that is IL-1, IL-6, and TNF-α. During innate immune response, some major sources of these cytokines are tissue macrophages, endothelial cells, mast cells, and epithelial cells. Cytokine storm is referred to as different pro-inflammatory cytokines such as IL-6, IL-1, TNF-α, and interferon these are sudden acute increases in circulating level. These ultimately lead to deleterious effects on human tissue which causes destabilization to occur in between the endothelial cell-to-cell interactions, vascular barrier damage, capillary damage, diffuse alveolar damage, death may occur[18].

Pathogenesis

The pathogenesis of infection can be classified into two phases based on suggested available evidence. Phase 1: This is an asymptomatic phase, in this phase with or without a detectable virus. Phase 2: is a symptomatic phase, in this phase presence of high viral load [13]. When the virus enters the airway epithelium they are readily binding to angiotensin-converting enzyme 2 receptors by S protein by the cellular transmembrane protease, serine 2. After their entry, they first inhibit the innate interferon immune response of the host, but their mechanism is not completely understood that is how to modulate the host interferon response. And also other evidence is suggests that they inhibit the downstream signaling pathway of interferon α/β as well as they also inhibit the type 1 interferon[19].

Replication

When the virus binds to the downstream signaling it produces degradation that occurs in RNA adopter molecules, that is inhibiting interferon regulatory factor, tumor necrosis factor, and mitochondrial antiviral signaling proteins[20]. The virus-inhibiting signal transducer also modulates transcription 1 phosphorylation, when the virus interferes with interferon signaling[21], it also modulates the host type 1 interferon response by the viral protein which also includes structural and non-structural proteins. These impairment causes viral replication in cells, after replication, they produce inflammation by the activation of monocytes, macrophages, etc., and these conditions are said to be Cytokine Storm and finally produce hyper inflammation in tissues and tissue fibrosis and pneumonia due to high reaction of pro-inflammatory cytokines [13,19,22].

Oxidative Stress

For inhibiting host immune response signaling and also producing inflammation by the presence of free radical components that are reactive oxygen species and reactive nitrogen species. In this reactive oxygen species play a vital role in damaging cells by CoVs through oxidative stress[23]. Due to an imbalance of free radicals and antioxidants, oxidative stress will be produced at that time deregulation of signaling and redox signaling[24]. Due to the viral infection, there is the inability to neutralize the free radicals by antioxidants finally produces oxidative stress. This again causes cell damage, alters the functions of nucleic acid, protein denaturation, DNA damage, lipid peroxidation, and cell death may also occur[25,26,27], which increases the production of reactive oxygen species, causing the release of cytokine expression and makes acute lung injury produced[28]

Acute Lung Injury

The body's antioxidant defense system can be changed by RNA viruses, and they also affect enzyme molecules such as superoxide dismutase, and antioxidant molecules are reduced such as carotenoids, ascorbic acid, and glutathione[29,30,31]. Phospholipid oxidation due to oxidative stress produces the main triggering factor in SAARS-induced acute lung injury due to the activation of pulmonary macrophage signaling[20]. Due to acute lung injury, hypoxia is produced which causes myocardial infection in the presence of reactive oxygen species by coronavirus disease 2019[32]. Mitochondria have an important function such as energy production, their mechanism and functions are strictly maintained for responding to environmental conditions and energy requirement[33].

Antioxidants

An antioxidant that helps to produce improvement in coronavirus disease, is apolipoprotein D- it is a lipocalin, against encephalitis they give a neuroprotective effect stimulated by coronavirus OC43 in mice. This will help to reduce the oxidative stress and regulate inflammation[34,35]

and also treatment with N-acetylcysteine which helps to prevent apoptosis during coronavirus infection[36] and acute lung oxidative injury also regulated by melatonin because of the presence of anti-inflammatory and antioxidant actions, and it is one of the compounds for the treatment of coronavirus[37]. By these studies which compound has good antioxidant actions, they are very useful in the treatment of coronavirus infection.

Influenza Virus and Their Antioxidant Therapy

Influenza is one of the most acute infectious diseases, and they produce huge economic and medical loss, they usually produce infection during the winter season, and they usually or periodically attack all constituents of the population, but their attack is higher in school-age children. After the flu symptoms, they may produce death in a few 48 hours when influenza viral pneumonia can occur, the pandemic-producing influenza A virus infection causes mild upper respiratory tract illness may have fever or not then they followed to produce illness gastrointestinal symptoms are diarrhea, nausea, and vomiting, etc., Then they produce severe illness such as pneumonia finally causes respiratory failure and multi-organ failure, death may also occur [38,39].

Pathogenesis

The influenza virus infection is mainly based on two principles in the human body that are (1) due to viral replication and produces local damage to the lungs in the columnar ciliary epithelium of bronchioles and bronchi which leads to cells of alveolar are damaged at last may cause death due to massive bronchitis[40]. Another one is (2) due to high inflammatory bursts that stimulate the other process which is reactive oxygen species it is one of the major compounds that produce extensive damage on cellular membranes, and also on small vessels, capillaries, and arteries [41,42,43,44].

Respiratory Tract Affecting

Mainly in the lungs, the influenza virus will replicate in the human respiratory tract, in influenza tracheobronchitis is one of the common clinical pictures. The columnar epithelium was filled with edema when acute stage with multifocal destruction and also congestion of submucosa are characteristics identified. At the final stage, cell necrosis will develop due to affected epithelium. By the process seen in larger airways, small and medium-sized bronchioles are affected strongly, due to the destruction of endothelium and alveolar epithelium causing lung injury[40,45]. Influenza virus infection causes lung disorder and may be triggered by, the alveolar space due to viral infection characteristics there is a massive infiltration of leukocytes, that is polymorphonuclear leukocytes are mainly released, development of hypoxia, formation of metabolic acidosis and also partial pressure of CO2 are increased, cytokine-storm a release of cytokines and others and last oxidative stress will also be developed[43,42,46,47].

Oxidative Stress

In influenza virus lungs are the major organ for their target. Reactive oxygen species they include superoxide, hydrogen peroxide, singlet oxygen, and hydroxyl radical[48]. However, due to ROS, they are harmful to cell damage, so various cellular defense measures are needed to control them. Oxidative stress may be defined as an imbalance between free radicals and antioxidants. Due to the oxidation of various host macromolecules, the increased amount of oxidative stress resulting in cellular damage occurs. Phase II cytoprotective and detoxifying enzymes are the important ones, and they act as cellular guardian[49,50,51,52]. So proper management of oxidative stress is important not only for the maintenance of germ-free state in cells but also for the preservation of cellular components or materials. Redox homeostasis in the lungs is very important during influenza virus infection because it links with inflammation-produced cytokine production, cell death, and some other pathologic conditions developed due to increased ROS production.

Antioxidants

Enzymes like catalase, superoxide dismutase, vitamin C vitamin E, and glutathione are important antioxidant defense mechanisms that are very important for giving protection from free radicals. A lipid-soluble substance is considered as vitamin E, and they have a hydrophobic tail, and they can accumulate in the lipid membrane of the interior portion. Their mechanism is to act like chain breakers, and then they react with lipid peroxy radical, but their reaction is four times faster than the reaction with adjacent fatty acid side chains. Their main mechanism can prevent oxidative damage[53,54,55,56]. By using passive diffusion they easily pass through the cell membrane because of its lipophilic structure, and then they are allowed to reach the single-plated reticulum and mitochondria, by these mechanisms of action lipid peroxidation and cell damage will be protected by vitamin E. Influenza virus infection produces more free radical that can produce lipid peroxidation in liver, lungs and plasma, and also they decrease the natural antioxidants.

HIV and Antioxidant Defense Pathways

Biology of HIV 1

Type 1 Human Immunodeficiency Virus is called a lentivirus that produces infection in humans, and it can kill human immune systems of important cells that are macrophages, T-helper cells, and dendritic cells, and they produce immunodeficiency syndrome AIDS. AIDS is due to progressive failure of the immune system in humans by HIV-1 infection, and they can produce life-threatening opportunistic infections. Without taking proper treatment when HIV 1 infection occurs and the survival time of the patient is estimated to be 9 to 11 years, for HIV therapy 27 antiretroviral drugs have been approved[57].

Structure of virus

Single-stranded HIV has a positive sense, and they are referred to as an enveloped RNA virus. The genome of HIV carries 9 genes that are that, pol, env, gag, nef, rev, vpu, vif, and over, and they encode 19 proteins, long terminal repeats it is a coding sequence that is to be framed [58,59]. For making new viral particles gag, pol, and env are the three genes that contain information for making new genes. When processing occurs on the pol gene it produces three enzymes that is protease, reverse transcriptase, and integrate. Glycoprotein 160 which is produced by translation of the env gene then they are further processed to the outcome of Gp120 and Gp41. After they enter the target cell, the reverse transcriptase enzyme of HIV by their RNA genome they converted into double-stranded DNA, when they are transported into the cell nucleus chromosomes are integrated and virus-encoded enzymes are activated[58]. Also, by the transcription and translation process, they can produce a new RNA genome and the viral protein then they are released from the cell as viral particles afterward they are ready to produce a new infection cycle.

HIV Infection and their Oxidative Stress

Production of ROS in monocytes is enhanced exhibit in HIV-infected individuals[60]. Loss of HIV 1 replication producing pathogenic effect they needed detoxifying enzyme for the intact function of ROS. A person who has shown HIV 1 with the presence of null-allele polymorphism, and also associated with compensation of functions such as loss of phase II detoxifying enzyme glutathione S-transferase[61], then also producing count goes to lower in CD4 T-cells, then finally produced to increase the viral load of HIV, and enhancement of mitochondrial DNA of 8-oxoG[62]. In HIV-infected cell culture marked increase in ROS level was also detected[63,64], and the oxidative stress rate increased in other tissues and body fluids was detected. That is increased level of 8-oxoG in the nuclear DNA was characterized in HIV-infected persons of brain tissue[65] and also an increasing level of HNE.

Antioxidants' Role in HIV Infected Individual

HIV-infected individuals have oxidative stress which produces apoptosis, decreases the count of CD4+ T-Cells, and also, they are increasing the activity of HIV replication and transcription. During redox impairment, these produce activation of NF-kB. These are due to the significant depletion of antioxidant levels that is vitamins A, C, and E by a recent study. So, to increase oxidative stress from free radicals the antioxidant system is overwhelmed. Also, antioxidant deficiency produces HIV-associated progression, as more rapidly suggested by studies. So proper antioxidant supplement taking may help to suppress the HIV viral loads and immune function will be restored and the progression of AIDS will also be potentially slowed[65].

CONCLUSION

In this article we see about the three types of diseases caused by viruses that are COVID-19, Influenza virus, and HIV, these three diseases have a link with antioxidants and also trigger ROS production. When free radical occurs, antioxidant depletion and oxidative stress finally will be produced. When ROS level increases plays an important role in accelerating and controlling the immune system. So, one of the treatments is taking proper antioxidants during a disease attack so we can slow down the potentially causing progressive disease. If we take proper antioxidants before a disease attack, we can prevent many diseases.

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