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New alternative for treating COVID-19 in Ecuador



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SUMMARY

In Ecuador there are more than 4,000 confirmed cases of coronavirus, and Guayaquil reports the highest number of infected and 450 deaths in the entire country. And according to medical experts estimate that those who died in the following months will reach between 2,500 and 3,500 due to COVID-19 only in the province of Guayas. The epidemic began in Wuhan, China, and spread rapidly throughout the country and later throughout the world. The WHO warns that COVID-19 is the "public enemy number 1" and potentially more powerful than terrorism, which is why I declare the pandemic. The objective of the present investigation is to determine the benefit of the use of clarithromycin, N-acetylcysteine, Viusid and Tea in patients infected with COVID-19. The treatment was administered to twelve infected patients and their contacts. There are treatments used in various countries of the world with different results, and, given the very serious situation in Ecuador, I share my personal experience with excellent benefits.

Keywords: COVID-19. Coronavirus. Pandemic treatment.

INTRODUCTION

Coronaviruses (CoV) were traditionally considered as non-lethal pathogens for humans, and are mainly responsible for causing around 15% of common colds. However, in this century, we have witnessed two highly pathogenic human coronaviruses on separate occasions—SARS-CoV and MERS-CoV—which caused outbreaks originating in China in 2003 and Saudi Arabia in 2012, respectively. These coronaviruses soon spread to many other countries, demonstrating horrible morbidity and mortality rates. As such, the current COVID-19 pandemic is the third coronavirus outbreak in recorded human history.

In summary, the beginning of this pandemic that is now sweeping the world has its origins in cases of pneumonia that were reported in Wuhan by the Chinese Health Commission, with the first case being reported on 31 December 2019. Seven days later (7 January 2020), the CoV sequence alert was sounded. On 15 January 2020, the first fatality as a result of coronavirus was reported in Wuhan. Meanwhile, the epidemic spread rapidly through neighbouring cities, provinces and countries. On 20 January, it was reported that several members of medical staff had been infected, which suggested that person-to-person transmission was a possibility. On 23 January, lockdown was announced in the city of Wuhan and all forms of public transport were halted. On 24 January, the first clinical study to be carried out on COVID-19 reported that, of the 41 patients who were confirmed as having the coronavirus, only 21 had been in direct contact with the Wuhan seafood market. This was considered to be the source of the infection, with the virus deriving from an unknown animal source [1]. On 30 January, the WHO declared the outbreak to be a global health emergency. At the time of writing, the disease has already spread throughout China and most other countries on the planet, with the WHO declaring it as a pandemic that has led to thousands of infections and deaths. As the situation is rapidly evolving, the final extent

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and severity of the outbreak is yet to be determined [2].

CoVs are a sub-family of large enveloped viruses that contain positive-sense single-stranded RNA. They can be categorised into four genera: alpha, beta, gamma and delta. Of these, it is known that alpha and beta coronaviruses infect humans. The envelope spike (S) glycoprotein binds to its angiotensin-converting enzyme-2 (ACE2) and dipeptidyl peptidase-4 (DPP4) cell receptors for SARS-CoV and MERS-CoV respectively, which leads to membrane fusion. The viral genome of RNA is released in the cytoplasm. After viral genome replication, the genomic RNA accompanied by envelope glycoproteins and nucleocapsid proteins form vesicles containing virions, which then fuse with the plasma membrane to release the virus [3].

SARS-CoV-2 has been shown to infect human respiratory epithelial cells through an interaction between the viral S protein and the angiotensin-converting enzyme receptor in human cells. SARS-CoV-2 therefore has a strong ability to infect humans [4].

Treatment for COVID-19

Some countries use various medicinal products to treat coronavirus. In one of its documents, the Spanish Society of Medicine echoes the recommendations of the protocol drawn up for the treatment of COVID-19. Specific antiviral treatment requires medicinal products such as orally-administered lopinavir/ritonavir (informed consent must be obtained). This medicinal product is indicated to help control the infection of human immunodeficiency virus (HIV). It is only administered orally, or in concomitant treatment with interferon beta-1b. In this case Betaferon is recommended, which is indicated for the treatment of multiple sclerosis. Interferons are proteins produced by the body that help it to fight against attacks on the immune system, such as viral infections [5,6].

Lopinavir/ritonavir can also be used in combination with an interferon alfa-2B, such as Intron A, which modifies the response of the body's immune system to help fight against serious infections and diseases.

Another indicated treatment is remdesivir. This drug is indicated for the treatment of Ebola, and three Spanish hospitals are already conducting clinical trials with this medicinal product: the Hospital La Paz, the Hospital Clínic Barcelona and the Hospital Universitario Cruces in Bilbao.

Drugs in a testing phase or those that are not yet proven to be effective against SARS-CoV-2

Besides the drugs mentioned above, many countries point out that "other drugs are being used, with very limited evidence and outside the restrictions set forth in the summary of product characteristics, such as hydroxychloroquine, chloroquine, azithromycin, amoxicillin/clavulanic acid, nitazoxanide, darunavir/cobicistat and tocilizumab (biologic)". Hydroxychloroquine is indicated for the treatment of rheumatoid arthritis, lupus and acute attacks of malaria; chloroquine is indicated for treating malaria and protozoan or helminth infections; and the darunavir/cobicistat combination is indicated for the treatment of HIV [7].

Tocilizumab is indicated for the treatment of rheumatoid arthritis, but certain scientific medical schools and hospitals are conducting studies that test this medicinal product in coronavirus patients who are presenting with high IL-6 values, and claim that it is currently yielding "positive results". Unfortunately retrovirals, biologics and interferons are unattainable for many countries around the world owing to their high cost, with no absolute guarantee of yielding excellent results.

Clarithromycin

Clarithromycin is a macrolide antibiotic drug, approved by the U.S. Food and Drug Administration (FDA) for the treatment of certain bacterial infections, including community-acquired pneumonia, throat infections (pharyngitis), acute paranasal sinus infections and other infections caused by specific types of bacteria. Clarithromycin is also approved by the FDA for the prevention and treatment of mycobacterium avium complex

(MAC) infections, which are another type of bacterial infection.

MAC infections and certain bacterial respiratory diseases (such as community-acquired pneumonia) are opportunistic infections (OIs) that are characteristic of infection by HIV. An OI is an infection that occurs more frequently, or more seriously, in people with immunodeficiency—such as those suffering from HIV—than in people with a healthy immune system [9].

The immunomodulatory effects of macrolides were first reported in patients with diffuse panbronchiolitis in 1998. It was found that immunomodulation with macrolides is independent of antibiotic properties. Its effects include modulating (both increasing and decreasing) the production of inflammatory cytokines, decreasing the hypersecretion of mucus from the airways and blocking the formation of bacterial biofilms and the production of virulence factor. Macrolide therapy has been recommended for chronic obstructive pulmonary disease, cystic fibrosis, non-cystic fibrosis bronchiectasis and severe asthma. In patients with asthma, long-term macrolide therapy has been reported to improve air flow, quality of life and airway hypersensitivity [10].

Periostin is an extracellular matrix protein that is associated with eosinophilic airway inflammation and asthma severity. Periostin can increase type-2 inflammation and the hypersecretion of mucus. It has been reported to be the most robust biomarker for predicting the effectiveness of lebrikizumab, an anti-IL-13 antibody, in the treatment of asthma [11]. Since macrolides also affect type 2-dominated inflammation in asthma, we hypothesise that macrolide therapy may lessen IL-13-induced periostin production and inflammatory gene expression in human lung fibroblasts.

Clarithromycin suppresses the production of IL-13-induced periostin in human lung fibroblasts, partly through the inhibition of STAT phosphorylation [12]. This suggests a new mechanism of clarithromycin's immunomodulatory effect on airway inflammation and fibrosis in asthmatic people, and as we know, it is an atopic disease.

N-acetylcysteine

N-acetylcysteine is a mucolytic that has been rediscovered as an antioxidant thanks to the appearance of new experimental and clinical studies that point towards certain added benefits.

Out of these additional properties, which distinguish it and set it apart from other mucolytics, its antioxidant capacity stands out above all. This property allows it to counteract the oxidative imbalance that has been discovered at the origin of important diseases such as chronic obstructive pulmonary disease (COPD), pulmonary fibrosis and heart attack, as well as in situations in which oxidative stress is induced, such as the application of radiological contrast media where it acts as a protector, helping to prevent kidney damage. It also has an anti-inflammatory and lung structure remodelling effect [13].

Bronchial mucus is produced by goblet cells and serous cells, and is stored until a secretion signal is released. Excess mucus increases the chances of complications developing in patients with COVID-19, with oxidative stress playing a role in the pathogenesis and progression of lung diseases. Reactive or oxyradical species cause structural changes in the essential components of the lungs, resulting in irreversible damage to both the parenchyma and the walls of the airways. Based on in vitro and in vivo evidence, N-acetylcysteine has been shown to protect the lungs against toxic agents by enhancing the lung defence mechanisms through its direct and indirect antioxidant properties, as a result of being a precursor to the synthesis of glutathione (GSH). Glutathione is an important antioxidant found in the lung which has a protective effect against internal and external toxic agents.

Some drugs, such as paracetamol, have been shown to deplete glutathione S-transferase from the lung. This places the patient at a disadvantage against the coronavirus, as he/she will not be able to fight against the avalanche or storm of cytokines produced by the virus, and the anorexia that further reduces the availability of one of the most powerful antioxidants that the body possesses: glutathione. This explains the importance of the use of N-acetylcysteine in these patients.

One of the recent studies in the field of respiratory diseases, the Bronchitis Randomized on NAC Cost-Utility Study (BRONCUS), has proven the capacity of N-acetylcysteine (NAC) in preventing the development of flare-ups of chronic obstructive pulmonary disease. The results of this macro trial, with 3 years of follow-ups, which was carried out across 10 European countries, were presented at the European Respiratory Society's conference held in Vienna in 2011 [14].

Viusid

Viusid is a nutritional supplement with recognised antioxidant and immunomodulatory properties which have beneficial effects on cirrhosis-related clinical outcomes such as survival, disease progression and the development of hepatocellular carcinoma (HCC). This study evaluated the safety and efficacy of Viusid in patients with HCV-related decompensated cirrhosis [15].

Viusid (Laboratorios Catalysis, Madrid, Spain) is a nutritional supplement that contains different molecules (ascorbic acid, zinc and glycyrrhizic acid) with recognised antioxidant and immunomodulatory properties. Glycyrrhizin (0.033 g), the supplement's most important active substance, is known to have an immunomodulatory, antiviral and biologic effect. It has also demonstrated different anti-inflammatory properties (such as the increased production of IL-10: a potent anti-inflammatory cytokine that inhibits the syntheses of many pro-inflammatory proteins), as well as an anti-apoptotic effect, hepatocyte proliferation and the stabilisation of cell membranes in the liver.

Recent data suggest that Viusid improves oxidative stress through the reduction of lipid peroxidation products, and that it has an immunomodulatory effect on cytokine secretion through increased production of IFN- γ and IL-10, decreased production of IL-1 γ , stabilised tumour necrosis factor and secretion in HCV patients in whom previous antiviral treatments have failed [16].

Tea

Tea is consumed by many people around the world. In general, tea is divided into six different categories: white tea, green tea, yellow tea, oolong tea, black tea and pu'er tea, depending on the degree of fermentation. Tea contains abundant phytochemicals such as polyphenols, pigments, polysaccharides, alkaloids, free amino acids and saponins [17]. Drinking tea is considered to be safe for humans, with very few reports existing on the serious adverse effects of drinking tea.

Furthermore, many studies have indicated that tea and its bioactive components possess multiple health benefits. These include anti-oxidation, anti-inflammation, immunoregulation, anti-cancer properties, cardiovascular protection, anti-diabetic and anti-obesity properties and hepatoprotection [18]. Various technologies, including the recently-developed nanotechnology, have been adopted to improve the bioavailability of tea's polyphenols. Moreover, adverse effects of tea have been rarely reported. Therefore, the combination of tea's health and safety properties justifies its consumption by humans, with a view to potentially preventing and controlling certain acute and chronic diseases such as respiratory and digestive diseases, obesity and cancer [19].

Saponins are another bioactive component found in tea and tea extracts, which generally possess anti-oxidant, immunoregulatory, anti-carcinogenic and cardiovascular protective effects. In addition, tea saponins are generally considered to be safe compounds that have anti-fungal and insecticidal properties. In fact, they are widely used in agriculture and the food industry [20].

Methodology

Twelve patients confirmed as having COVID-19 were managed on an outpatient basis at their homes between 16 March 2020 and 2 April 2020 in the city of Machala, El Oro Province, which is two-and-a-half hours

away from the Guayas Province (which has reported the highest number of infections and deaths). These included four doctors, two nurses and six patients, all aged between 35 and 65 years old. All of these people live in the same city. The first six patients developed the disease in a hospital setting, with the other six being infected in the community.

As far as the signs and symptoms are concerned, the majority only presented with muscle pains, headache, fever and hyporexia. A doctor and a nurse presented with a cough with whiteish-yellowish expectoration and 90% saturation, requiring admission in a hospital unit for 8 hours before going back to their home to self-isolate.

The information recorded includes the patient's demographic data, medical record, contact history, potential co-morbidities, symptoms, signs, laboratory, test results, chest x-ray and a 10-day treatment regimen. The latter was based on three sachets of viusid every day, clarithromycin 500 mg every 12 hours, acetylcysteine 600 mg every day and acetaminophen 1 g every 8 hours. This was complemented with 4 cups of hot tea every day. All treatments were taken orally.

Besides self-isolating, the people with whom the infected patients had been in contact were given 1 sachet of viusid to take every day, in addition to clarithromycin 500 mg. This treatment regimen was continued for 10 days. They also drank hot tea 3 times a day and took N-acetylcysteine when necessary.

RESULTS

Two patients (a doctor and a nurse) presented with respiratory compromise, exhibiting cough and reduced oxygen saturation of 90%. These patients needed to be admitted to a hospital unit for 8 hours. The chest x-ray showed an interstitial pattern with small consolidation at the base of the right lung in the doctor. Bilateral pulmonary infiltrates, meanwhile, were observed in the nurse's x-ray results. As the CT scanner was damaged, this procedure could not be performed.

When they were checked and monitored by officials of the Ministry of Health, their improvement was established at 95% (at the time of writing). The patients are due to undergo a coronavirus test in 15 days' time. However, all patients will remain in self-isolation at home.

All individuals who came into direct or indirect contact with the infected patients evolved satisfactorily, with no complications arising.

DISCUSSION

The use of clarithromycin, N-acetylcysteine, Viusid and tea was shown to be effective in the aforementioned patients, based on the scientific evidence of the benefits of each of its components. Given the safety of these treatments, they can be used in people of all ages within the established pharmacological dosing limits. Medicine is evidence-based and observations will certainly be made, which will be welcomed. However, I would like to encourage you to use the aforementioned treatment as a new alternative in the face of this pandemic that is wiping out mankind.

Protection of people and animals

The authors declare that no experiments were conducted on humans or animals for this study.

Data confidentiality

The authors declare that no patient data appear in this article. Right to privacy and informed consent.

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Conflict of interests:

The authors declare that there are no conflicts of interest.

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