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Antibiotic Therapy and Offstage about Covid-19 Vaccination

Mahira Amirova[1*], Lala Huseynova[2], Sabrin Azim[3], Svetlana Nagiyeva[4], Muthiah Lovely[5], Gulnara Dashdamirova[1], Ban Almudarris[3], Farah Saed[3]

[1]Biochemistry Department, Azerbaijan Medical University, Baku, Azerbaijan
[2]"Kepro" Clinics, Baku, Azerbaijan
[3]Health Sciences Department, City University College of Ajman, Ajman, UAE
[4]Family Medicine Department, Azerbaijan Medical University, Baku, Azerbaijan
[5]Prosthodontic Department, College of Dentistry Ajman University of Science and Technology, Ajman, UAE
Email: *gerayelmira@gmail.com

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Abstract

In this overview, we discuss the impact of antibiotic therapy on the COVID infection, the complications after vaccination, possible causes of adverse events, and ways to protect against pandemic infection, as well as try to dispel myths about COVID. Antibiotics are necessary only in case of secondary infection, but overlapping with bacterial infection mainly occurs after hospitalization, and the vast majority of infections were caused by the *Acinetobacter baumannii* strain. Commonly used antimicrobial disinfectants are chlorhexidine derivatives; due to their frequent use, microorganisms have become resistant to them, and in addition, chloroquine has no clinical benefit in the treatment of COVID-19. Virus escapes from the immune response due to multiple mutations in the receptor-binding domain, or the N-terminal end, which are the sites responsible for antibody binding and virus neutralization. The COVID infection itself is characterized by a rather powerful suppression of immunity. For this reason, the use of antibiotics in the absence of a secondary infection layer leads to greater suppression of the immune system and an aggravation of the process, which often ends up fatally. Immune dysregulation predisposes to the development of severe COVID-19. A decrease in the number of leukocytes gives an unfavorable prognosis for the severity of the COVID infection course. The main reason for the death cases after vaccination seems to be an increase in blood clotting, which is observed not only among the population over 60 years old, but also amid young people.

Keywords

Chloroquine, Co-Infection, COVID-19, SARS-CoV-2, Secondary Infection, Mutation, Mythbusters, Vaccination

1. Introduction

1.1. Increasing Resistance to Antibiotics Nowadays

The COVID-19 pandemic has paralyzed life across the planet [1]. According to our observations, due to its life-threatening nature, the COVID-19 infection not only seriously undermined the health of the working-age population, but also caused the breakdown of family relationships, leading to psychological disorders and depression. The seriousness of the situation required the distribution of free rapid tests in different countries to help stop disease outbreaks [2]. The symptoms described in COVID-19 usually overlap with other respiratory infections. Some of the specific symptoms described, such as anosmia, are used to confirm the diagnosis of COVID-19; other clinical signs such as fever, persistent cough, diarrhea, fatigue, abdominal pain and loss of appetite can further confirm this diagnosis [3]. According to Tucker M.E., even after recovering from COVID, patients have experienced the following symptoms for a long time: chronic fatigue, headache, muscle and joint pain, and sometimes allergies; they develop fatigue in 78% of cases and cognitive dysfunction in 55%; 45% of the recovered needed a sparing work schedule, and 22% could not work at all [4].

Antibacterial cleaners often contain quaternary ammonium compounds, which are also widely used for sanitization in the context of SARS-CoV-2, to disinfect surfaces in hospitals, homes and food service establishments, in cleaning sprays and wipes. On March 26, 2021, the World Health Organization published very useful information destroying the myths about COVID-19 [5]. It is acknown that hydroxychloroquine has immunosuppressive and anti-autophagic effects; it suppresses immune function by inhibiting the processing and presentation of antigens and the production of cytokines; it also increases intra-lysosomal pH, disrupting autophagic protein degradation, resulting in the accumulation of ineffective autophagosomes unable to destroy even tumor cells, let alone COVID-19. The clinical data indicate that this antibiotic has not reduced the number of deaths among patients hospitalized with COVID-19, nor has it helped people with mild form of illnesses. It claims that since the antibiotics work only against bacteria, not viruses, and COVID-19 is caused by a virus, ergo antibiotics do not prevent or cure COVID-19. According to the World Health Organization, although antibiotics should not be used to prevent or treat COVID-19, however, if you are hospitalized due to COVID-19, bacterial co-infection, mainly observed after hospitalization may be the reason for treating you with antibiotics. Estrada A.D. and co-authors [6] examined the effect of antibiotic use on survival in 13,932 COVID patients. Their data on SARS-CoV-2

indicate that the risk of bacterial co-infection is minimal on admission but increases during hospitalization. The authors reported very low rates of co-infection and absence of most respiratory pathogens in patients with SARS-CoV-2 prior to hospitalization.

1.2. The Most Common Secondary Infections in COVID-19, Frequency of Occurrence

Antibiotics are increasingly being used as a component of COVID-19 treatment regimens, even in the absence of a diagnosis of bacterial infection; this inappropriate use of antibacterial agents is expected to lead to the emergence of new resistances in the future. It is understood that the prevalence of bacterial infection can vary from country to country, the time after the onset of symptoms at which samples are taken. The vast majority of scientists declare that bacterial co-infection is rare among patients with COVID-19, but despite this, antibiotics are widely used in COVID treatment. It is pertinent to note here that concomitant bacterial infections are less common than secondary infections. Reported bacterial infections in COVID-19 patients include *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Haemophilus influenzae*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *and Acinetobacter baumannii* [7], which cause common fatal resistant to antibiotics infections. In a study of nearly 1400 COVID-19 patients, only 2.7% were diagnosed a bacterial co-infection that occurred concurrently with viral infection [8]. Another study found that only 5.1% (5 out of 99) of COVID-19 cases had co-infections, mainly *Acinetobacter baumannii* and *Klebsiella pneumonia* [9].

In a larger study by Zheng *et al*. (Zheng *et al*. 2020) in January 2020, it was reported that among the 1001 patients included in the study, only 4 (0.4%) were found to be co-infected with SARS-CoV-2 and influenza virus. Blasco M.L. *et al*., after examining 183 patients with COVID-19, also claime that patients with COVID-19 pneumonia were infrequently infected with other respiratory infections [10]. Wang P. *et al*. found that among 1400 COVID-19 patients, only 2.7% were diagnosed coexistence of bacterial infection with viral one [11]. Additionally, in a study by Yu Jie *et al*., only approximately 5% of COVID-19 cases were associated with co-infections, with *Acinetobacter baumannii* and *Klebsiella pneumoniae* leading the way [12]. By the way, *Acinetobacter baumannii* repeatedly leading to complications of Iraq and Afghanistan western veterans' injuries received the ironic nickname "Iraqibacter".

Several studies from Wuhan have shown that in the case of SARS-CoV-2 infection, the bacterial infection rate is <10%: only four cases were reported among 41 patients (9.8%). A study in Italy showed that the rate of co-infections was even less than 5%. Mentor A.B. *et al*. also reported that a January 2020 study at the China Department of Adult Infectious Diseases confirmed bacterial co-infection rate among patients hospitalized with COVID-19 was just 1% [13]. According to this author, another study from two hospitals in China found that

95% of COVID-19 patients received antibiotic regimens, although secondary bacterial infection was found in only 15% of them. In a study from the UK, blood cultures in early 2020 were positive only in 3.2% of cases during the first 5 days of hospitalization, but after hospitalization the rate increased to 6.1%, showing that hospitalization is the cause of the bacterial infection layering on COVID-19. It was revealed that in respiratory samples a pathogenic bacterium can be identified in 34.8%. All examined by Sharifipur E. [14] patients had the following bacterial infections: *Acinetobacter baumannii* in 90% and *Staphylococcus aureus* in 10% of cases. Estrada A.D. and co-authors (Estrada A.D., 2021) state that the overall mortality rate among COVID patients was about 20.7%, but it increased even more after antibiotic use (87.8%). The antibiotics were started after the detection of elevated inflammatory markers and/or infiltration on the X-ray. Nevertheless, the patients receiving antibiotics required frequent respiratory support and were more likely to be transferred to intensive care units. Higher mortality was observed after the use of all antibiotics, except for macrolides, which are characterized by a higher survival rate. It is acknown that macrolide antibiotics are one of the safest groups of antimicrobial drugs and are well tolerated by patients, since they exhibit minimal cases of hemato- and nephrotoxicity and the adverse drug reactions observed in other classes of antimicrobial drugs [15]. Summing up the above and taking into account the opinion of a majority of scientists [6] [13], we can state: if the use of antibiotics is still unavoidable, there is promising evidence that azithromycin is a potential treatment for COVID-19.

1.3. Consequences of Frequent Use of Quaternary Ammonium Disinfectants

The authors of one study stated that of 238 *Staphylococcus* isolates in Norway, 50% were phenotypically resistant to quaternary ammonium disinfectants; the authors suggested that this resistance was due to the frequent use of these disinfectants in a routine environment [16]. Studies have also shown that *Staphylococci* strain from surfaces often treated with quaternary ammonium disinfectants are insensitive to them, while *Staphylococci* from other, untreated surfaces remain sensitive to this compound, so the use of quaternary ammonium disinfectants actually increases bacterial resistance, and this fact limits our ability to heal new infections. It is acknown that mostly disinfectants result in cell lysis by affecting membrane permeability, but *Staphylococcus spp*. along with some other gram-positive bacteria have become resistant due to the mutation with consequent development of efflux pumps located on mobile genetic elements such as plasmids [17].

1.4. The Difference in the Body's Response to the Vaccination Leading to Death

Impaired immunity regulation predisposes to the development of COVID-19

severe form. The difference in the immune response to COVID infection may be due to variation in certain host factors, such as the genes, immune system, and metabolic status. It is acknown that the immune system disturbances are classified cause a vulnerability to infections by bacteria, viruses, fungi, as well as protozoa [18]. A decrease in the number of white blood cells gives unfavorable prognosis regarding the severity of COVID infection course. The vaccination is currently seen by some as a possible way to stop the spread of the COVID disease. Concerns over possible side effects of the AstraZeneca COVID-19 vaccine in March led to a halt in vaccinations across Europe as scientists fear it would undermine public confidence in the vaccine [19]. For example, on March 11, the prosecutor of the Sicilian city of Syracuse brought two doctors and a nurse to trial for manslaughter following the sudden death of a naval officer just hours after he was shot by AstraZeneca PLC vaccine. A few days after the Syracuse incident in northern Italy, police seized nearly 400.000 AstraZeneca vaccines after another sudden death following an injection. The lawsuit in Italy preceded the decision of more than a dozen European countries, including Germany, France and Italy, to stop using the vaccine after a blood clotting disorder was reported. The federal state of North Rhine-Westphalia is also loosening rules on who can get vaccines from AstraZeneca, Reuters reported on April 2 [20]. Blood clotting problems have prompted the country to limit vaccinations for people over 60. It is clear today, that most healthcare organizations do not require their employees to be vaccinated. South Africa is also pausing the rollout of Johnson & Johnson's COVID-19 vaccine after the United States federal health agencies have recommended that its use should be suspended due to blood clots [21]. In Azerbaijan, the 25-year-old boy who was preparing for the wedding died after vaccination; and not the bride entered the dressed room of the future newlywed, but the boy's corpse. The mental state of one of the vaccinated was so aggravated that he was trying to commit suicide. He developed a desire for suicide only after vaccination; before the vaccine, he was a practically healthy person. Some vaccinated patients begin to have problems with their limbs, sometimes ending in paralysis. New Zealand announces the death of a woman associated with the Pfizer Covid-19 vaccine. The vaccine manufacturers state that heart inflammation is a "very rare" side effect of Pfizer, as well as Moderna COVID vaccines. Independent COVID-19 vaccine safety monitoring board has reported that myocarditis was probably caused by vaccine [22]. Due to the reasons counted at the beginning of this paragraph, people with impaired immune response get COVID viral infection more severely than others, and vaccination often becomes the reason for their death. If we consider vaccination from this point of view, then it can be called a method of ridding society of sick and susceptible to the disease individuals, *i.e.*, it is a kind of society sanitation through vaccination. It was revealed that severe infection is also associated with genetic defects in interferon production, while timely treatment with interferon gives promising results in these patients [18].

1.5. Multiple Mutations as The Main Factor in the Ineffectiveness of COVID -19 Treatment and Vaccination

As for the cause of ineffective treatment, as well as frequent complications and not uncommon deaths from COVID and vaccine, the basic factor of the virus vitality in the body is its ability to multiple mutations. Mutant forms of the COVID-19 virus have been found in some countries, and Brazil could be taken as the epicenter of yet another devastating wave of COVID-19 infections caused by various virus variants; these options are still rare and have not yet become widespread. In Brazil, they state the fact of the spread of even more dangerous versions of the virus that causes COVID-19 [23]. The study described 11 sequences of SARS-CoV-2, each of which contains changes in the binding domain of the receptor. In each of them, additional changes were found in the N-terminal domain, which were deletions of important antibody binding sites. Besides point mutations, viruses can also lose/gain parts of their genetic code. These insertions and deletions can reshape SARS-CoV-2, allowing it to escape antibodies with affinity to these binding sites. Since there are many antibodies that are being produced for these N-terminal sites, these mutations are likely to make the virus even more resistant. The deletions will further impair the ability of antibodies to capture these viruses and block them from infection. Scientists have also discovered an easily transmitted variant of COVID in UK & Africa with multiple mutations in spike protein [11]; these are B.1.1.7 SARS-CoV-2 of the UK and B.1.351 from South Africa. A mutated virus can easily avoid being destroyed by the host's immune system, since most of the mutations are found in the antigenic supersite in the N-terminal domain or in the receptor-binding domain, which are the sites responsible for binding the virus with antibodies and its neutralization. This B.1.1.7 mutant is resistant to neutralization by most monoclonal antibodies that bind the N-terminal domain of the viral spike protein; due to this, it cannot be neutralized by majority of monoclonal antibodies directed against the spike protein. The N-terminal domain of the spike protein is also relatively resistant to several monoclonal antibodies that bind the receptor-binding domain. Data, first discovered in late 2020 in South Africa, indicated that B.1.1.7 contains eight additional mutations in the spike gene; these include mutations causing two deletions (ΔH69/ΔV70 and ΔY144) in N-terminal domain, one substitution (N501Y) in the receptor-binding domain, and one substitution near the furin cleavage site (P681H). What about mutation B.1.351, compared to the original type SARS-CoV-2, it is much more resistant to neutralization with convalescent plasma (nearly 9 times) and vaccinated serum (approximately 11 times). This is due to the fact that B.1.351 contains 9 mutations in the spike gene in addition to the mutation causing the D614G substitution. The additional mutations include a cluster of mutations, such as for instance mutations leading to Δ242 - Δ244 and R246I in N-terminal domain, 3 substitutions in receptor-binding domain: 417N, E484K and N501Y, and one substitution, namely A701V, next to the furin cleavage site.

1.6. WHO Advice on COVID-19 Prevention

Clinical trials are being conducted to find out if vaccines prevent transmission, and if COVİD in vaccinated becomes asymptomatic, or can they pass the infection on to others. Along with this on 26 March 2021, the World Health Organization published the novelmyth-busters according to COVID-19 [5]:

1) The COVID virus multiplies easily in hot and humid environment, so people should not wear masks while exercising. Sweat wets the masks, making breathing difficult and encouraging the growth of microorganisms.

2) Drinking alcohol increases the risk of contracting coronavirus, because ethanol is poisonous and can lead to unwanted effects.

3) The best way to protect yourself from COVID-19 is to wash hands frequently.

4) Cold weather cannot kill the new coronavirus or other pathogens, because regardless of the ambient temperature, the human body temperature remains at 36.5˚C. The most effective protection is to wash your hands with soap, or with an alcohol solution.

2. Conclusion

In our paper, two key areas regarding COVID-19 are considered by review of the currently available data on the development of COVID and the impact of vaccination. In conclusion, it can be said that the use of antibiotics for covid is rather undesirable, especially in non-hospitalized patients. The widespread use of quaternary ammonium compounds in routine life has led to the emergence of resistant bacteria strains, so it is advisable to abandon them if they are not needed. If, nevertheless, the use of antibiotics is unavoidable, in the COVID-19 era it is preferable to use drugs of the macrolide group. The vaccine does not cure COVID; it is just an attempt to stop desease spread.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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