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Review Article

MISUSE OF ANTIBIOTICS AND OTHER DRUGS IN COVID PANDEMIC

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Abstract:

The COVID-19 outbreak, caused by the severe acute respiratory syndrome corona virus 2, has been detected in December 2019 in Wuhan, China, and is accompanied by significant degrees of morbidity and mortality. Antibiotic resistance (AMR) threatens to wreak havoc on healthcare system and the impact of globalization, and COVID-19 is intended to keep it at bay for the time being. During the COVID-19 crisis, a wide range of antimicrobial medicines were promoted as viable treatments. While both industrialized and industrializing nations have seen a rise in antimicrobial medication usage, use and abuse have been significantly more prevalent in developing countries. Antibiotic resistance is still a concern since microorganisms that cause resistant infections develop in hospitals and medical institutions, placing all patients at risk, complicating the care of COVID-19. Improper prescriptions, a lack of care management policies and needless self-administration by the general population are examples of these. Antibiotics seem to be more motivated to abuse and misusing antibiotics than to keep them safe and take them only when prescribed. Almost all of the substantial antibiotic usage in COVID-19 patients is inevitable. Patients having lung viral infections are more likely to develop subsequent bacterial infections, which lead to higher disease severity and death. Immediately crucial components of any AMR mitigation approach are increased spending in education and increased public knowledge of AMR. More studies are needed to better understand the health risks and rate of co-infection in COVID-19 patients in order to promote a decrease in any unnecessary antimicrobial prescribing.

KEYWORDS: Antibiotic, Azithromycin, Hydroxychloroquine, Remdesivir, Covid-19.

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INTRODUCTION¹

In December 2019, the novel corona virus disease 2019 (COVID-19) emerged in Wuhan, Hubei Province, China. It rapidly spread and many cases were identified in multiple countries, posing a global health problem. Here, we report the first patient cured of COVID-19 infection in Changsha, China, and the symptoms, diagnosis, treatment, and management of this patient are all described in this report. A 57-year-old woman developed cough and fever after returning to Changsha from Wuhan on January 9, 2020. She tested positive for COVID-19 infection, a diagnosis which was supported by chest CT. The patient was treated with lopinavir and ritonavir tablets and interferon alfa-2b injection. A low dose of glucocorticoids was used for a short period to control bilateral lung immune response, and this patient avoided being crushed by cytokine storms that might have occurred. The clinical condition of this patient improved, and a COVID19 assay conducted on January 25, 2020 generated negative results. This patient recovered and was discharged on January 30, 2022. Currently, there are numerous reports on COVID-19 infections focusing on the disease's epidemiological and clinical characteristics. This case describes the symptoms, diagnosis, treatment, and management of a patient cured of COVID-19 infection, which may serve as reference for future cases, while further studies are needed.

MISUSE OF ANTIBIOTICS AND OTHER DRUGS IN COVID -19²

With the pandemic on our minds, why should we care about antimicrobial resistance (AMR)? Treating severe SARS-CoV-2 infections, physicians often prescribe prophylactic antibiotics. In many countries antibiotic courses are even prescribed to non-hospitalized patients. The rationale behind the decision to deploy prophylaxis is simple: Without antibiotics, the risk of a bacterial infection is drastically increased. Secondary bacterial infections establish easily in patients who suffer from a viral induced infection of the lungs, due to a plethora of reasons, including an altered immune response, reduced clearance of mucus and increased attachment of bacteria to epithelial cells. Such infections further reduce the rate of survival.

Studies summarising published clinical reports show that 60% to 70% of COVID-19 patients had received antibiotics. Depending on the country and the healthcare setting, a maximum of 20% of patients exhibit secondary bacterial or fungal infections. While this indicates that some patients will require antibiotic treatments, the prophylactic use of such drugs is questionable.

Corona virus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Corona virus 2 (SARS-CoV-2), was first identified as an outbreak of respiratory illness in Wuhan City, China, in 2019. Then, in March 2020, the World Health Organization (WHO) declared COVID-19 a global pandemic. Since then, SARS-CoV-2 has caused worldwide fear because the infection spread quickly between countries and the clinical course ranged from mild to severe inflammatory disease resulting in multi-organ failure and death. Due to that, efforts for repurposing known drugs were the quickest way to help combat the disease. After screening FDA-approved chemical library, a group from France demonstrated that Azithromycin (AZM) exhibited the highest in vitro anti-SARS-CoV-2 activity.

Specifically, researchers examined the total sales volume of all antibiotics as well as the individual sales volume for azithromycin. The latter was studied because some countries experienced a spike in azithromycin sales early in the pandemic after observational studies suggested the antibiotic could help treat COVID-19 (subsequent studies disputed the claim).

MISUSE OF CHLOROQUINE AND HYDROXYCHLOROQUINE IN COVID -19³

Chloroquine and hydroxychloroquine are currently authorised for treating malaria and certain autoimmune diseases. In addition to side effects affecting the heart, they are known to potentially cause liver and kidney problems, nerve cell damage that can lead to seizures (fits) and low blood sugar (hypoglycaemia). HCQ is looked upon as the wonder drug or miracle drug that showed antiviral property to aid in management of COVID-19 patients. CQ reduces fever and lung lesions and prolongs the progression of the disease, while HCQ in combination with azithromycin can reduce viral load in COVID-19 patients. Azithromycin enhances the capacity of HCQ in lowering viral load. CQ also reduces pneumonia exacerbations and duration of symptoms. Even though the MOA of CQ and HCQ is the same, HCQ is more effective over CQ. Healthcare professionals are recommended to closely monitor patients with COVID-19 receiving chloroquine or hydroxychloroquine and to take into account pre-existing heart problems that can make patients more prone to heart rhythm issues. They should carefully consider the possibility of side effects, particularly with higher doses, and exercise extra caution when combining treatment with other medicines such as azithromycin that may cause similar side effects on the heart.

MISUSE REMDESIVIR (IV) IN COVID -19⁵

Remdesivir is an antiviral medication that targets a range of viruses. It was originally developed over a decade ago to treat hepatitis C and a cold-like virus called respiratory syncytial virus (RSV). Remdesivir wasn't an effective treatment for either disease. But it showed promise against other viruses. Researchers tested Remdesivir in clinical trials during the Ebola outbreak. Other investigational medications worked better, but it was shown to be safe for patients. Studies in cells and animals suggested that remdesivir was effective against viruses in the coronavirus family, such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). Remdesivir works by interrupting production of the virus. Corona viruses have genomes made up of ribonucleic acid (RNA). Remdesivir interferes with one of the key enzymes the virus needs to replicate RNA. This prevents the virus from multiplying. Researchers began a randomized, controlled trial of the antiviral in February 2020 to test whether remdesivir could be used to treat SARS-CoV-2, the corona virus that causes COVID-19. By April, early results indicated that remdesivir accelerated recovery for hospitalized patients with severe COVID-19. It became the first drug to receive emergency use authorization from the U.S. Food and Drug Administration (FDA) to treat people hospitalized with COVID-19. The final results showed that the antiviral treatment was beneficial, consistent with the preliminary findings. Patients who received remdesivir were quicker to recover, which was defined as being medically stable enough to be discharged from the hospital. The study also suggested that remdesivir treatment may prevent patients from progressing to more severe respiratory disease. Those treated with remdesivir were less likely to need high levels of respiratory support. Remdesivir appeared to most benefit patients who were receiving supplemental oxygen.

MISUSE OF STEROIDS IN COVID-19^{6,7}

One of the treatments for a COVID-19 infection is steroids. This is done under the supervision of medical staff. Experts have now said that irregular or prolonged use of steroids can cause infections in an individual. These infections could include Bacterial and Fungal infections like Black fungus and White fungus. Since most patients that have contracted COVID-19 die due to inflammation of the lungs and severe organ failure, steroids are said to help them. They are administered to those who have an oxygen saturation level of less than 94% and a respiration of more than 24 per minute. Unfortunately, many individuals have started to misuse the steroid medication. Steroids are said to help reduce

inflammation in an individual's body, which can be caused by illnesses. They don't cure any condition, per say. Inflammation is a normal body response when an individual's immune system is fighting an infection. But when this inflammation goes beyond normal and starts affecting our own body's cells, then steroids could be helpful in controlling it.

Taking steroids during the first stages of a COVID-19 infection is not advised at all and is not needed. Prolong steroid usage and steroid misuse can lead to a weakened immune system. As per experts in India, in most cases, steroids should only be given for the duration of 5-10 days. In fact, it was steroid misuse that was considered the reason behind the rise in Black and White Fungus cases in the country. Furthermore, long term use of steroids can also result in increased glucose levels which are the reason behind the bacterial and fungal infections caused by them.

Long Term side effects of steroid usage

- Weakened immune system
- Increased risk of diabetes
- High risk of bacterial and fungal infections
- Disturbed sleep and irritability
- Bone and muscle weakness
- Increased risk of cardiovascular diseases
- Kidney damage

MISUSE OF IVERMECTIN IN COVID-19^{9,10,11}

The WHO essential medicines list provides recommendations for minimum medicine needs for a basic health-care system, which includes ivermectin as an Anthelmintic, ant filarial, and ant ectoparasitic treatment.

There has been a groundswell of opinion across several countries that ivermectin might be useful in reducing the symptoms of and mortality due to COVID-19, with many citing meta-analyses that infer positive effects

However, these conclusions appear to be unreliable. On March 31, 2021, WHO advised that ivermectin should only be used within clinical trials and not as part of routine clinical practice.

COVID-19 (CORONAVIRUS): LONG-TERM EFFECTS⁸

Most people who have corona virus disease 2019 (COVID-19) recover completely within a few weeks. But some people — even those who had mild versions of the disease — continue to experience symptoms after their initial recovery.

These people sometimes describe themselves as "long haulers" and the conditions have been called post-

COVID-19 syndrome or "long COVID-19." These health issues are sometimes called post-COVID-19 conditions. They're generally considered to be effects of COVID-19 that persist for more than four weeks after you've been diagnosed with the COVID-19 virus.

Older people and people with many serious medical conditions are the most likely to experience lingering COVID-19 symptoms, but even young, otherwise healthy people can feel unwell for weeks to months after infection. Common signs and symptoms that linger over time include:

- Fatigue
- Shortness of breath or difficulty breathing
- Cough
- Joint pain
- Chest pain
- Memory, concentration or sleep problems
- Muscle pain or headache
- Fast or pounding heartbeat
- Loss of smell or taste
- Depression or anxiety
- Fever
- Dizziness when you stand
- Worsened symptoms after physical or mental activities

ORGAN DAMAGE CAUSED BY COVID-19

Although COVID-19 is seen as a disease that primarily affects the lungs, it can also damage many other organs, including the heart, kidneys and the brain. Organ damage may lead to health complications that linger after COVID-19 illness. In some people, lasting health effects may include long-term breathing problems, heart complications, chronic kidney impairment, stroke and Guillain-Barre syndrome — a condition that causes temporary paralysis.

Some adults and children experience multisystem inflammatory syndrome after they have had COVID-19. In this condition, some organs and tissues become severely inflamed.

BLOOD CLOTS AND BLOOD VESSEL PROBLEMS

COVID-19 can make blood cells more likely to clump up and form clots. While large clots can cause heart attacks and strokes, much of the heart damage caused by COVID-19 is believed to stem from very small clots that block tiny blood vessels (capillaries) in the heart muscle.

Other parts of the body affected by blood clots include the lungs, legs, liver and kidneys. COVID-19 can also weaken blood vessels and cause them to

leak, which contributes to potentially long-lasting problems with the liver and kidneys.

PROBLEMS WITH MOOD AND FATIGUE

People who have severe symptoms of COVID-19 often have to be treated in a hospital's intensive care unit, with mechanical assistance such as ventilators to breathe. Simply surviving this experience can make a person more likely to later develop post-traumatic stress syndrome, depression and anxiety.

Because it's difficult to predict long-term outcomes from the new COVID-19 virus, scientists are looking at the long-term effects seen in related viruses, such as the virus that causes severe acute respiratory syndrome (SARS).

Many people who have recovered from SARS have gone on to develop chronic fatigue syndrome, a complex disorder characterized by extreme fatigue that worsens with physical or mental activity, but doesn't improve with rest. The same may be true for people who have had COVID-19.

MANY LONG-TERM COVID-19 EFFECTS STILL UNKNOWN

Much is still unknown about how COVID-19 will affect people over time, but research is ongoing. Researchers recommend that doctors closely monitor people who have had COVID-19 to see how their organs are functioning after recovery.

Many large medical centres are opening specialized clinics to provide care for people who have persistent symptoms or related illnesses after they recover from COVID-19. Support groups are available as well. It's important to remember that most people who have COVID-19 recover quickly. But the potentially long-lasting problems from COVID-19 make it even more important to reduce the spread of COVID-19 by following precautions. Precautions include wearing masks, social distancing, avoiding crowds, getting a vaccine when available and keeping hands clean.

COVID-19-ASSOCIATED MUCORMYCOSIS.⁹

During the COVID-19 pandemic in India, the Indian government reported that more than 11,700 people were receiving care for Mucor mycosis as of 25 May 2021. Many Indian media outlets called it "black fungus" because of the black discoloration of dead and dying tissue the fungus causes. Even before the COVID-19 pandemic, rates of mucormycosis in India were estimated to be about 70 times higher than in the rest of the world. Due to its rapidly growing number of cases some Indian state governments have declared it an epidemic. One treatment was a daily

injection for eight weeks of anti-fungal intravenous injection of amphotericin B which was in short supply. The injection could be standard amphotericin B deoxycholate or the liposomal form. The liposomal form cost more but it was considered "safer, more effective and [with] lesser side effects". The major obstacle of using antifungal drugs in black fungus is the lack of clinical trials.

A number of cases of Mucor mycosis, aspergillosis, and candidiasis, linked to immunosuppressive treatment for COVID-19 were reported during the COVID-19 pandemic in India in 2020 and 2021. One review in early 2021 relating to the association of Mucor mycosis and COVID-19 reported eight cases of Mucor mycosis; three from the U.S., two from India, and one case each from Brazil, Italy, and the UK. The most common underlying medical condition was diabetes. Most had been in hospital with severe breathing problems due to COVID-19, had recovered, and developed Mucor mycosis 10–14 days following treatment for COVID-19. Five had abnormal kidney function tests, three involved the sinus, eye and brain, three the lungs, one the gastrointestinal tract, and in one the disease was widespread. In two of the seven deaths, the diagnosis of Mucor mycosis was made at post-mortem. That three had no traditional risk factors led the authors to question the use of steroids and immunosuppressive drugs. Although, there were cases without diabetes or use of immunosuppressive drugs. There were cases reported even in children. In May 2021, the BBC reported increased cases in India. In a review of COVID-19-related eye problems, Mucor mycosis affecting the eyes was reported to occur up to several weeks following recovery from COVID-19.

Other countries affected included Pakistan, Nepal, Bangladesh, Russia, Uruguay, Paraguay, Chile, Egypt, Iran, Brazil, Iraq, Mexico, Honduras, Argentina, Oman, and Afghanistan. One explanation for why the association has surfaced remarkably in India is high rates of COVID-19 infection and high rates of diabetes. In May 2021, the Indian Council of Medical Research issued guidelines for recognising and treating COVID-19-associated Mucor mycosis. In India, as of 28 June 2021, over 40,845 people have been confirmed to have Mucor mycosis, and 3,129 have died. From these cases, 85.5% (34,940) had a history of being infected with SARS-CoV-2 and 52.69% (21,523) were on steroids, also 64.11% (26,187) had diabetes.

CONCLUSION:

Overuse of antibiotics or other drugs for covid-19 and use of azithromycin, chloroquine,

hydroxychloroquine, steroids and injection antibiotics in primary care are the major problems of clinical practice in rural areas. There is no reason to explain why antibiotic prescribing in common cold, sore throat or any other common respiratory infection (the most frequent primary care) is so great. In fear of covid-19 many doctors are prescribing antibiotics and other drugs used in treatment of corona when there is no need of that treatment. These misuse is the main reason of antimicrobial resistance. Doctors have to do well and not harm, while respecting the ethical principles of autonomy and justice. This misuse of therapeutic drugs harms people health. We know that we can reduce antibiotic prescribing in many of the infections that are currently unnecessarily treated without compromising our patients' health. By accomplishing this, we will do less harm. Moreover, we know that antibiotics can stop being effective in the short and medium term. The use of the strategies discussed in this paper will help GPs to reduce prescribing of antibiotics. Our duty is to prescribe antibiotics and other therapeutic drugs only when they are necessary, i.e. in less than 20% of the infectious seen in primary care.

ABBREVIATIONS

AMR – Antimicrobial Resistance
 CRP – C - reactive protein
 ICU – Intensive Care Unit
 PCT – Patient Care Technician
 NICE – National Institute For Health And Care Excellence
 DNA – Deoxyribonucleic Acid
 RNA – Ribonucleic Acid
 RCT – Randomized Control Trials
 WHO – World Health Organization
 SARS – Severe Acute Respiratory Syndrome

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