Annals of Pharmacology and Toxicology

Review Article
Published: 11 Dec, 2020

Antimicrobial Resistance and Second Wave of COVID-19: Will It Impose Management Protocols Deviation?

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Abstract

Antibiotics are widely used therapeutic agent in treatment of different infectious diseases either bacterial or fungal. Misuse of antibiotics and other social factors are of the main factor for emerging antibiotics resistant pathogenic stains. It was proven that the high mortality rates increased healthcare economical costs and reduced productivity are highly associated with antibiotic resistance. Currently, COVID-19 infection is at its first wave peak in some countries as American ones, at the same time an emerged second wave started in other countries as European countries which may last for further period of time globally. Investigations showed that healthcare systems are using antibiotics in management of all SARS-CoV-2 infections even if they are mild in symptoms although only 10% to 15% of the infected SARS-CoV-2 cases showed secondary bacterial infection due to difficulty in differentiation between viral and bacterial infection leading to antibiotic misuse. Besides, overwhelmed healthcare systems and lack of proper infection control measures are aggravating the emergence of antibiotic resistance, therefore, proper training for healthcare workers increased public awareness with infection prevention is an important contributing factor for diminishing emergence of antibiotic resistance and might impose protocol deviations in the next wave of COVID-19.

Keywords: COVID-19; Antimicrobial resistance; Secondary infection; ICUs; Azithromycin

Introduction

Antibiotics are considered as one of the principle methods in medicine used in reduction and prevention of infectious diseases, for this reason, a varieties of antibiotics have raised in the period from 1930 to 1960 and this period of time was ended due to continuous failure for innovation of new antibiotics facing the rapid emergence of antibiotic resistant pathogenic strains. It is worthy to mention that, the main reasons of antibiotics resistance are due to increased use and misuse of antibiotics in healthcare facilities, community, and animal sector, overpopulation, poor sanitation, and substandard sewerage systems [1]. From the economic point of view, it was recorded in 2006 that nearly 50,000 American citizens in USA died due to pneumonia and sepsis, adding about 8 billion American dollars to the USA economical cost [2]. The total economic losses estimated to be about 20 billion American dollars, while diminished productivity losses estimated to be about 35 billion American dollars per year due to antibacterial resistance in healthcare facilities [3].

Antimicrobial resistance means that microorganisms undergo specific pathway changes in order to bypass the mechanism of actions of antimicrobial agents against them resulting in ineffectiveness of medication. Resistant microorganisms to most antimicrobials are known as superbugs and resistance is considered a major issue to be concerned with as a resistant infection may be pandemic causing high rates of mortality with increasing healthcare costs for individuals and community as wells [4]. Natural resistance being an intrinsic expressed in the species or as a result of induced resistance in which naturally occurring genes in the bacteria are only expressed to resistance after antibiotic exposure through genetic material transformation, transposition, and conjugation, and/or mutations in chromosomal DNA. Antimicrobial resistance mechanisms can be classified into four categories which are limiting drug uptake, modifying a drug target, inactivating a drug, and active drug efflux [5]. In the USA more than 2,000,000 individuals are infected every year with resistant microorganisms and 23,000 at least die due to these infections [6]. Methicillin resistance is the main remarkable sign of antimicrobial resistance in both *Staphylococcus aureus* and coagulase-negative staphylococci which can be taken as an indicator for multidrug resistance [7]. Antibiotics development has been declined due to the high cost for presenting a new molecule to

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Received Date: *16 Nov 2020*
Accepted Date: *07 Dec 2020*
Published Date: *11 Dec 2020*

Citation:
Raslan M, Eslam MS, Sara AR, Nagwa AS. Antimicrobial Resistance and Second Wave of COVID-19: Will It Impose Management Protocols Deviation?. Ann Pharmacol Toxicol. 2020; 1(1): 1001.

the market, an average investment of US $800 million and 10 years or longer is required for new antibiotic development. Besides, the risk of post-approval adverse events as incidence of liver toxicity caused by trovafloxacin within a year after its release [8]. It is worthy to mention that, pharmaceutical companies are focusing on medications for the treatment of chronic diseases which showed much superiority to antibiotics due to that most antibiotic treatments courses are from 5 to 14 days and then discontinued, moreover, antibiotics are intended to be the last choice for use by the patients and prescribed by physicians in order to slow emergence of antibiotics resistance [8]. In 2019 there are only four new antibacterial drugs approved, namely; cefiderocol, lefamulin, and combinations of imipenem/cilastatin/relebactam, and pretomanid/bedaquiline/linezolid representing about 8.33% of 48 approved drug molecules [9]. Resistant organisms are called (ESKAPE micro-organisms) including; *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterococcus faecium*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Enterobacter* species which cause a remarkable morbidities and mortalities [10]. Different risk factors are associated with emergence of antibiotic resistance of different reasons and different mechanisms including; Methicillin-Resistant *Staphylococcus aureus* (MRSA) due to use broad spectrum antibiotics, the presence of decubitus ulcers and prosthetic devices. Also, *Vancomycin-resistant Enterococci* (VRE) results from prolonged hospitalization and treatment with glycopeptides or broad-spectrum antibiotics. Additionally, spreading of gram-negative resistant bacteria due to urinary catheterization, excessive use of antibiotics and contamination of humidifiers and nebulizers. Also, Penicillin-Resistant Pneumococci (PRP) due to overcrowding, tracheotomies', and excessive use of penicillin's for viral respiratory infections. Finally, Multidrug-Resistant Tuberculosis (MDRTb) because of poor compliance, convergence of immunosuppressed patients, delayed diagnosis or treatment, poor or inadequate ventilation and isolation facilities [11]. Development of antibiotics resistance resulted from self-medication, misuse of antibiotics, and people ignorance about information regarding antibiotics instruction for administration, dosage, and side effects which are considered from the potential reasons of incorrect treatment and microbial resistance leading to increased morbidity [12]. Studies indicate that self-medication is mainly prevalent in low economic status communities, for that reason, many developing countries are suffering from poor health care facilities and sometimes quite expensive imposing self-medication as an easy and necessary medical choice. Besides, the absence of dispensing rules of prescription and OTC medications lead to the ease of availability of prescribed drugs in patients hand out of physicians control and thus antibiotic misuse [13]. Severe illness increased hospital admission, risk of complications, and mortality rate resulting from infection with antibiotic-resistant pathogens. In addition, an estimate recorded that about 25,000 people in Europe die on annual basis as result of antibiotic-resistant infection and an estimated cost of about 9 billion Euros per year in Europe resulted from complications related to antibiotic resistance [14]. It was remarked that a significant increase in antibiotics use had occurred during the first wave of Coronavirus-19 pandemic even in those patients treated from initial symptoms of COVID-19 viral infection. Data from Asia showed that 70% of COVID-19 infected patients received antibiotic treatment despite the fact that lower than 10% of those patients are proved to have bacterial infection [15]. It is well known that COVID-19 originated from China and spread widely to vast majority of countries worldwide, moreover, the estimate number of infections by 30th of august 2020 was 24,854,140 with total number of deaths 838,924, and graphical data showed that in African region the number of recorded infections are in its declining way, indicating the end of the first wave of COVID-19. In the American region, graphical data showed that infection number are still at the peak which means that these countries are in the mid of the first COVID-19 wave. In European countries graphical data showed finalization of first wave and beginning of the second CVOID-19 wave indicating that this pandemic is not yet ended which may last for longer time and become more intense unless otherwise protective and restrictive measures taken [16].

Since COVID-19 pandemic seems to be extended in the future for unknown and unexpected period of time and so the first wave might be followed by other waves. What we are highly concerned about is the increasing incidence of antibiotics misuse with increasing emergence of antibiotic resistance, especially, that most of the therapeutic protocols used included antibiotics as a standard treatment.

Discussion

Reported facts on patients infected with COVID-19 indicated that those patients who are hospitalized at the Intensive Care Units (ICUs) are experiencing concurrent comorbidities and are at higher risk to bacterial infections. Upon investigating COVID-19 mortalities it was found that 50% of mortalities were associated with a bacterial or fungal secondary infection indicating that those co-infections are one of the main factors affecting death rates of severely infected patients with SARS-CoV-2 [17]. It was found that antibiotics consumption rate is very high reaching 94% to 100% in healthcare facilities which were much higher than the reported incidence of secondary infection which was found to be 10% to 15%. Moreover, health care facilities are overcrowded during SARS-CoV-2 pandemic and some of them reported 50% more patient hospitalization than usual [17]. A study review on COVID-19 patients demonstrated that 72% of COVID-19 hospitalized patients received antibiotic treatment and that only 8% of those patients showed to have secondary bacterial or fungal infection [18]. It was reported by the WHO that macrolide antibiotic including azithromycin is being widely used with Hydroxychloroquine in therapeutic protocols of COVID-19 treatment [19]. Piperacillin and tazobactam combination considered as the most commonly prescribed antibiotic for ICU patients, also, combination of β-lactam antibiotics and macrolide antibiotics or fluoroquinolones were reported to be used in COVID-19 management therapeutic protocols [20]. A recent study was conducted in 88 countries included hospital ICUs showed that 70% of ICUs hospitalized patients received a minimum of one antibiotic drug as a prophylactic measure or as a treatment, despite the fact that 54% of those patients had a doubt about or demonstrated an evidence of bacterial or fungal infection [21]. Some healthcare professionals confessed that differentiation between COVID-19 and pneumonia from bacterial origin is a difficult thing, indicating that some COVID-19 patients without bacterial infections are undergoing unneeded antibiotic treatment [22]. Aggravating of COVID-19 patient's illness as a result of multi-resistant pathogen secondary infections should be taken in consideration. Antimicrobial stewardship should be encouraged in order to reduce mortality rates in infected patients, and avoid multi-resistant bacterial infections especially in ICUs patients [23]. Many aspects should be taken in consideration to avoid such emerging threat from antimicrobial resistant microorganism especially in the CVOID-19 pandemic in even the 1st or the next waves. Proper training for healthcare workers is an essential to aware them how to differentiate between signs and symptoms of CVOID-19 and any secondary bacterial of fungal

infection. This in turn will reduce or eliminate the unneeded use of antibiotics. Implementation of tightly strict measures to prevent and control infection in healthcare systems. Reduction in COVID-19 testing time by improving and developing a better tool and testing methods in order to reduce the need to start prophylactic antibiotic treatment in those suspected patients [24]. COVID-19 massively affected public awareness of infection control. It is obvious that people are taking care of correct implementation of hand-washing procedures and committed to social distancing to prevent infection. Healthcare systems worldwide have applied a strict and improved measures. Application of such interventions will probably affect infectious agents' levels and antimicrobial resistance which means a remarkable improvement in global health [25].

Conclusion

It can be concluded that antibiotic resistance in the highly expected coming second COVID-19 wave might increase the incidence of mortality rates for patients as a consequence of multi-resistant secondary infections. Misuse of antibiotics, besides the overwhelmed healthcare services, and lacking of social awareness of infection prevention is all contributing factor for increased antibacterial resistance. Thus, proper and well organized professional high-quality training for healthcare workers and implementation of strict infection control measures are highly recommended. Moreover, increasing public awareness is a basic requirement that aid in avoiding the exacerbation of antibacterial resistance and increasing mortality rates.

References

1. Aslam B, Wang W, Arshad MI, Khurshid M, Muzammil S, Rasool MH, et al. Antibiotic resistance: A rundown of a global crisis. Infect Drug Resist. 2018;11:1645-58.
2. Guidos RJ. Combating antimicrobial resistance: Policy recommendations to save lives. Clin Infect Dis. 2011;52(Suppl 5):S397-S428.
3. Ventola CL. The antibiotic resistance crisis: Part 1: Causes and threats. PT. 2015;40(4):277-83.
4. What is antimicrobial resistance? Online Q&A. 2017.
5. Reygaert WC. An overview of the antimicrobial resistance mechanisms of bacteria. AIMS Microbiol. 2018;4(3):482-501.
6. Centers for Disease Control and Prevention (CDC) Antibiotic resistance threats in the United States. 2013.
7. Akova M. Epidemiology of antimicrobial resistance in bloodstream infections. Virulence. 2016;7(3):252-66.
8. Conly J, Johnston B. Where are all the new antibiotics? The new antibiotic paradox. Can J Infect Dis Med Microbiol. 2005;16(3):159-60.
9. Andrei S, Droc G, Stefan G. FDA approved antibacterial drugs: 2018-2019. Discoveries (Craiova). 2019;7(4):e102.
10. Boucher HW, Talbot GH, Bradley JS, Edwards JE, Gilbert D, Rice LB, et al. Bad bugs, no drugs: No ESKAPE! An update from the Infectious Diseases Society of America. Clin Infect Dis. 2009;48:1-12.
11. Rao GG. Risk factors for the spread of antibiotic-resistant bacteria. Drugs. 1998;55(3):323-30.
12. Michael CA, Dominey-Howes D, Labbate M. The antibiotic resistance crisis: Causes, consequences, and management. Front Public Health. 2014;2:145.
13. Rather IA, Kim BC, Bajpai VK, Park YH. Self-medication and antibiotic resistance: Crisis, current challenges, and prevention. Saudi J Biol Sci. 2017;24(4):808-12.
14. Llor C, Bjerrum L. Antimicrobial resistance: Risk associated with antibiotic overuse and initiatives to reduce the problem. Ther Adv Drug Saf. 2014;5(6):229-41.
15. Jeremy HSU. How COVID-19 is accelerating the threat of antimicrobial resistance. BMJ. 2020;369.
16. Coronavirus Disease (COVID-19) weekly epidemiological update data as received by WHO from national authorities, as of 10 am CEST 30 August 2020.
17. Rossato L, Negrão FJ, Simionatto S. Could the COVID-19 pandemic aggravate antimicrobial resistance? Am J Infect Control. 2020;48(9):1129-30.
18. Rawson TM, Moore LSP, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, et al. Bacterial and fungal co-infection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. Clin Infect Dis. 2020.
19. Clinical management of COVID-19 Interim Guidance. Geneva: World Health Organization. May 27, 2020.
20. Beović B, Doušak M, Ferreira-Coimbra J, Nadrah K, Rubulotta F, Belliato M, et al. Antibiotic use in patients with COVID-19: A 'snapshot' Infectious Diseases International Research Initiative (ID-IRI) survey. J Antimicrob Chemother. 2020;75(11):3386-90.
21. Vincent JL, Sakr Y, Singer M, Martin-Loeches I, Machado FR, Marshall JC, et al. Prevalence and outcomes of infection among patients in intensive care units in 2017. JAMA. 2020;323(15):1478-87.
22. Antimicrobial resistance in the age of COVID-19. Nat Microbiol. 2020;5:779.
23. Rossato L, Negrão FJ, Simionatto S. Could the COVID-19 pandemic aggravate antimicrobial resistance? Am J Infect Control. 2020;48(9):1129-30.
24. Getahun H, Smith I, Trivedi K, Paulin S, Balkhy HH. Tackling antimicrobial resistance in the COVID-19 pandemic. World Health Organization. 2020;98(7):441-508.
25. Sundin A. Considerations for AMR in the COVID-19 pandemic. JPIAMR. 2020.