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лекарственных средств и медицинских изделий

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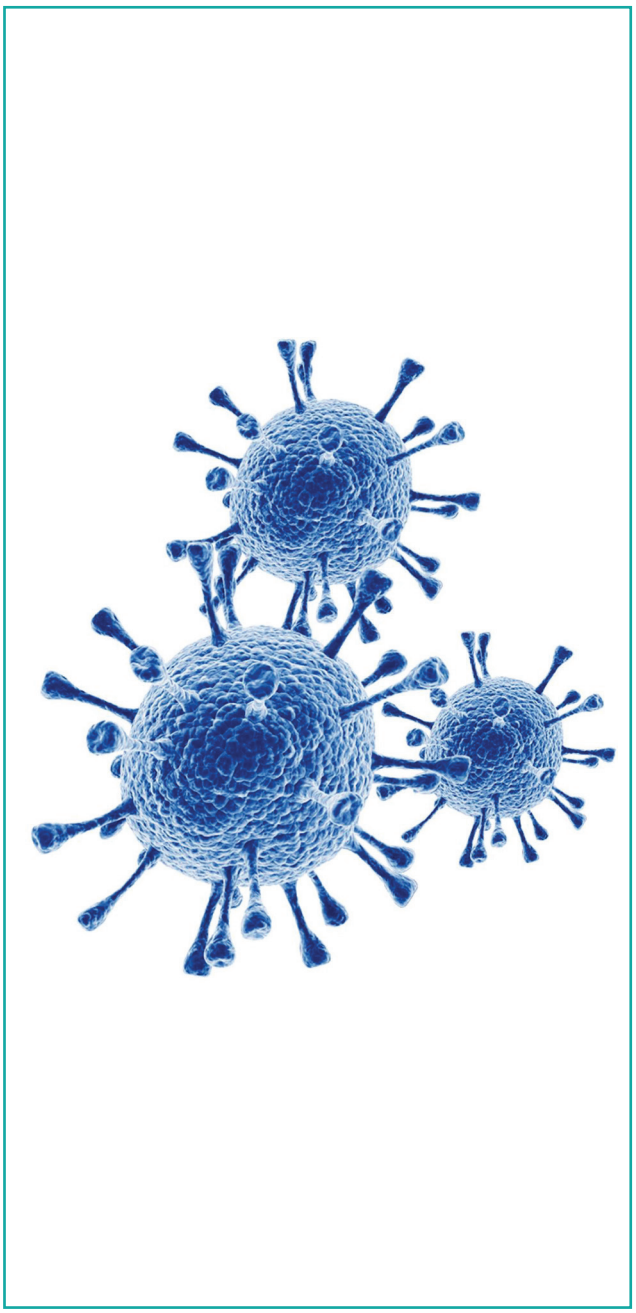
NEGATIVE SIDES OF AZITHROMYCIN USAGE IN TREATMENT OF SARS-COV-2

Resume: *COVID-19 in Kazakhstan, before the release of the last treatment Protocol (on July 9, 2020), was considered to be a nosological unit that causes complications in the respiratory system (pneumonia). Hence, as in the whole world, it was treated against pneumonia and Azithromycin was claimed to be a good and safe macrolide that works effectively in the treatment against pneumonia. However, further research has shown that there are many cardiovascular complications, and Azithromycin has cardiotoxic properties (already described in the prescription). At this time, Kazakhstan was experiencing uncontrolled purchase of medicines by the population (including Azithromycin), which demonstrates the existing danger for the general population. This paper, thereby, will argue, that it is important to cautiously prescribe and use Azithromycin during the treatment of the novel coronavirus.*
Keywords: *Covid-19, cardiac involvement, antiviral therapy, Kazakhstan*



INTRODUCTION

The contemporary world witnessed an time of history, filled with an outstanding pressure on the medicine and challenges to the healthcare systems of all states.

This crisis is caused by the spread of a novel type of coronavirus SARS-CoV-2, first case of which was recorded in December 2019 in China, and rapidly spread globally, leading to a global-scale pandemic.

Being officially named pandemic by the World Health Organization on March 11, 2020, by October 8, 2020, the number of registered cases reached 36,449,681, as well as 1,061,520 deaths associated with the virus worldwide. Kazakhstan, in no terms is an exception, as despite the downshift in the transmission rate, there have been 108,454 cases confirmed with 1,746 fatalities.

CARDIAC INVOLVEMENT DURING COVID-19

One of the common health issues associated with the development of the COVID-19 is the acute lung injury, which leads to an increased level of morbidity and mortality. However, recent studies demonstrate that the COVI-19 virus leads to cardiac complications, especially myocardial injury and arrhythmic complications [1]. Although the arrythmogenic effects of the novel coronavirus have not been reported with scientifically proven data, it is recommended to conduct cardiovascular observations, especially, among the patients with the history of CVD-related illnesses and in the cases of severe COVID-19 levels.
The most frequently reported cardiac issues among COVID-19 patients is acute cardiac injury (appr. 8-12% of all patients), which is associated with the increasing levels of troponins. The direct myocardial injury rooted in the results of the systemic inflammation and involvement of cardiomyocytes is considered to be the process leading to the cardiac injury, The data on other CVD in COVID-19 is currently not enough to make conclusions. However, it has been numerously reported that the history of CVD increases the chances of worse outcomes among the COVID-19-positive patients [1-4].
The CVD history among the patients with the COVID-19 is considered as a factor for worse outcomes, which is possibly rooted in the acute myocardial injury of mixed genesis, Acute coronary syndrome, decompensation of hypertension, chronic heart failure. The consideration also includes the pathogenetic processes laying under myocardial issues in COVID-19, the results of systemic inflammation, the direct effects of COVID-19, as well as cardiotoxic connection to the antiviral treatment and imbalance in oxygen needs and its delivery. The increase of troponin levels, in turn, leads to the rising need of mechanical ventilation and 5-times increase of mortality [3,5,6]. Hence, the patients with the history of CVD are notably greater in numbers in the intensive care, and demonstrate higher rates of mortality[7-9]. Several existing research highlighted cardiac presence for COVID-19, in comparison to respiratory. Notable number of patients suffered acute myocardial injury, associated with the increasing levels of serum troponin I [1,5,6].
In the beginning of April 2020, the mortality rate was reaching 5% [10]. However, the experts claim that mortality rates have a potential to change over time due to the tendency of higher transmittance rate and increasing mortality, partially due to the mutation of the pathogen [11-14].

AZITHROMYCIN

The ongoing healthcare crisis has led to the strive of finding medicines in order to improve the prognosis of the disease. This resulted in a 'rivalry' between two opposing ideas: one of using only scientifically approved and tested methods of medication against the COVID-19 infection and treatment of its complications, and the one of employing new treatment without the availability of strong evidence, based on intuition or pre-clinical findings [2].
The discussion of the prescribing guidelines, as wells as the review of the existing evidence about the antibacterial properties in the cases of community-acquired pneumonia (CAP), along with immunomodulating and antiviral actions as a basis for the prescribing azithromycin are included in detail. The major risks of the prescribing azithromycin lay in its torsadogenic potential, particularly, together with hydroxychloroquine or chloroquine, which is as well mentioned.
The major factor arguing for the azithromycin's efficacy is connected to its antibacterial function. While there was no research demonstrating the direct evidence of the drug's effectiveness in the COVID-19 treatment, its proponents claimed that the antibacterial capabilities of the described drug make it effective in the CAP treatment, occurring among the COVID-19-infected people. However, there is no universal agreement of this idea, as there is not enough telling evidence of the immunomodulating and antiviral properties of this drug, which also was not specifically derived from the COVID-19 patients.
The acceptance of azithromycin in the treatment of the COVID-19 is rooted in the French study, although the conclusive research data on its effectiveness has been limited [15]. However, the aforementioned study from France raises a certain number of questions. The research was conducted with a limited number of

people (as only 6 patients received azithromycin, while no randomization process was not applied to the study, the grouping of the patients was conducted by doctors on a subjective basis). The additional data was also published, which according to the French researchers highlight the effectiveness of the described drug in the treatment of the COVID-19 [16]. However, considering the limited availability of data on the azithromycin's effectiveness (both containing hydroxychloroquine/chloroquine and not) in the SARS-CoV-2 treatment or as a first-line agent for CAP, it is necessary to consider the existing risks. Certain macrolides are, in fact, arrhythmogenic, for instance, erythromycin [17-19]. While azithromycin is often called to be one of the most safe macrolides [20,21], the information on its connection to arrythmia's increasing risks is conflicting. During the pre-clinical research, the azithromycin's influence on the arrhythmia was tested on different animal models, including guinea pigs, rabbits and dogs, demonstrating that the drug is not connected with torsades de pointes (TdP) or initial afterdepolarization, even though it increases QT interval and the possible length of monophasic action [22-25].

KAZAKHSTAN

Currently azithromycin is included in the official treatment protocol of COVID-19 in Kazakhstan, thereby, after its release, the citizens were buying uncontrollably, which led to shortage of the drug [26]. Prior to the release of the aforementioned treatment protocol, the novel coronavirus was treated as a separate nosological unit influencing the respiratory system of a human, while the pneumonia was named as one of the distinguishing features. Nevertheless, the aforementioned facts, and the newly discovered factors based on the experience of the treatments, allowed us to reconsider the disease and include adjustments in the treatment. Furthermore, during the maximal numbers of fatalities, the purchase of medicines among the population was not under control [27-29], including azithromycin, since the control could not be properly executed under an unprecedented pressure on the healthcare system of the country In addition, in Kazakhstan, the number of cases of pneumonia with symptoms similar to COVID-19, but negative PCR results has increased. It was decided to introduce separate statistics (starting 1st August) and to date, 34193 cases have been identified [30]. So in the treatment of this disease in the protocol of treatment for pneumonia, azithromycin is used and recommended by the Ministry of Health[31]. In this regard, it is also worth paying attention, since the results of laboratory tests may not be accurate, but at the moment PCR confirmation is the main criterion for the exhibition of the diagnosis of COVID-19 in Kazakhstan [26].

CONCLUSION

In sum, the final picture and understanding of the discussed drug's effect on a patient's health will be available only after the release of official data, thereby, for now, it is important to cautiously prescribe and use azithromycin. It is vital to keep in mind the negative interaction of certain antiviral and cariological medicines, thereby, the drugs employed in the treatment of the coronavirus must be considered in terms of cardiotoxicity and intra-drug relations. The special emphasis is needed to be put on patients prescribed the medicines that tend to prolong the QT interval and leading to ventricular tachycardia TdP.

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НЕГАТИВНЫЕ ЭФФЕКТЫ ИСПОЛЬЗОВАНИЯ АЗИТРОМИЦИНА В ЛЕЧЕНИИ SARS-COV-2

Резюме: COVID-19 в Казахстане до выхода последнего протокола лечения (9 июля 2020 г.) считался нозологической единицей, вызывающей осложнения со стороны дыхательной системы (пневмония). Следовательно, как и во всем мире, его лечили от пневмонии, а азитромицин был заявлен как хороший и безопасный макролид, который эффективно работает при лечении пневмонии. Однако дальнейшие исследования показали, что существует множество сердечно-сосудистых осложнений, а азитромицин обладает кардиотоксическими свойствами (уже описанными в рецепте). В это время в Казахстане происходила бесконтрольная закупка населением лекарств (в том числе азитромицина), что свидетельствует о существующей опасности для населения в целом. Таким образом, в этой статье утверждается, что важно с осторожностью назначать и использовать азитромицин во время лечения COVID-19.
Ключевые слова: COVID-19, поражение сердца, противовирусная терапия, Казахстан

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SARS-COV-2 ЕМДЕУДЕ АЗИТРОМИЦИНДІ ҚОЛДАНУДЫҢ ЖАҒЫМСЫЗ ӘСЕРЛЕРІ

Түйін: Қазақстандағы COVID-19, емдеудің соңғы хаттамасы шыққанға дейін (2020 жылы 15 шілдеде) тыныс алу жүйесінде асқынулар тудыратын нозологиялық бөлімше болып саналды (пневмония). Демек, бүкіл әлемдегідей, ол пневмонияға қарсы емделді және азитромицин пневмонияға қарсы емдеуде тиімді жұмыс істейтін жақсы және қауіпсіз макролид деп мәлімделді. Алайда, одан әрі жүргізілген зерттеулер жүрек-қан тамырлары асқынуларының көп екендігін көрсетті және Азитромициннің кардиоуытты қасиеттері бар (рецептте сипатталған). Осы уақытта Қазақстанда дәрі-дәрмектерді бақылаусыз сатып алу басталды (оның ішінде Азитромицин де бар), бұл қарапайым халық үшін бар қауіпті көрсетеді. Осы құжатта коронавирусты емдеу кезінде азитромицинді сақтықпен тағайындау және қолдану маңызды екендігі айтылады.
Түйінді сөздер: COVID-19, жүрекке қатысу, вирусқа қарсы терапия, Қазақстан.