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The Challenges of COVID-19 Treatment in Older Patients and Potential Drug Interactions

Yaşlı COVID-19 Hastalarında Tedavinin Güçlükleri ve Potansiyel İlaç Etkileşimleri

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COVID-19, araştırmaların ileri yaş, erkek cinsiyet ve komorbiditenin daha şiddetli hastalık ve ölüm riski ile ilişkili olduğunu bildirdiği yeni bir koronavirüs hastalığıdır. Ne yazık ki, herhangi bir potansiyel tedavinin COVID-19 teşhisi konan hastalarda sonuçları iyileştirdiğine dair yeterli destekleyici kanıt yoktur. Şu anda en popüler potansiyel tedavi seçeneklerinden biri hidroksiklorokindir. Ancak hidroksiklorokin, QTc uzaması ile birlikte olası torsades de pointes riski, hipoglisemi, nöropsikiyatrik etkiler, retinopati gibi ciddi yan etkilere (<% 10) neden olabilmektedir. Bu nedenle, hidroksiklorokin tedavisi sırasında dikkatli izlem gereklidir ve COVID-19'u tedavi etme potansiyeline sahip güvenli ve etkili ilaçların geliştirilmesine acil ihtiyaç duyulmaktadır.

Anahtar kelimeler: COVID-19, ilaç etkileşimleri, hidroksiklorokin, yaşlı, polifarmasi

COVID-19 is a new Coronavirus disease that researchers have reported older age, male gender, and comorbidity are associated with a higher risk of severe disease and mortality. Unfortunately, there is no sufficient supporting evidence that any potential therapy improves outcomes in patients diagnosed with COVID-19. Currently, one of the most popular potential treatment options is hydroxychloroquine. However, it also has serious adverse effects (<10%), including QTc prolongation with a possible risk of torsades de pointes, hypoglycemia, neuropsychiatric effects, and retinopathy. Therefore, careful monitoring is required during hydroxychloroquine treatment, and there is an urgent need to develop safe and effective drugs to treat COVID-19 potentially.

Keywords: COVID-19, drug interactions, hydroxychloroquine, older adults, polypharmacy

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INTRODUCTION

The COVID-19 virus infection developed into a pandemic in the short span of 3 months up, has become the main agenda topic throughout the world. Regarding the topic, scientists are making an intense effort to minimize the effects of the pandemic. The infection is more severe in its current form, particularly in older adults, males, and those with chronic diseases, such as hypertension, diabetes mellitus, pulmonary disease, cardiovascular disease, even causing death [1]. As known to all, the number of geriatric syndromes, accompanying conditions, and multidrug use due to these comorbidities are common in elderly patients, whereas the ability to maintain homeostasis and functional capacity decline with aging. As a result, elderly patients predispose to new comorbidities and atypical presentations and are vulnerable to adverse drug effects [2]. Therefore, the treatment of COVID-19 infections is getting harder in these patients.

Moreover, since there is no sufficient supporting evidence from clinical trials that any potential therapy improves outcomes in patients with COVID-19, all pharmacological agents used in COVID-19 infection are experimental, and none of which have been approved by the United States Food & Drug Administration (FDA). Currently, the potential treatment options target viral entry, replication, and immune regulatory pathways. Current therapies, including remdesivir, hydroxychloroquine and chloroquine, and interleukin (IL)-6 inhibitors, are being used off-label and evaluated in ongoing clinical trials.

Hydroxychloroquine for the treatment of COVID-19

One of the most popular treatment options for the COVID-19 is hydroxychloroquine, which is used to treat malaria, lupus, erythematosus and rheumatoid arthritis. Hydroxychloroquine is considered a possible antiviral drug by affecting membrane fusion and endocytosis, leading to immunomodulation through cytokine production and inhibition of autophagy and lysosomal activity [3]. However, the results of the studies investigating the safety and effectivity of the drug are conflicting [4,5]. Additionally, it has serious adverse effects (<10%), including QTc prolongation with a possible risk of torsades de pointes, hypoglycemia, neuropsychiatric adverse effects, and retinopathy. ECG monitoring is advised to patients, and reduction in the dose or discontinuation should be considered with QTc >500ms or an increase in QTc >60ms, and caution is suggested if used together with other drugs that prolong QTc [6]. Accordingly, antidepressants, antipsychotics, antibiotics, and antifungals can interact with hydroxychloroquine through QTc prolongation. The potential drug interactions with hydroxychloroquine are [7,8].

- Anticonvulsants including phenytoin, phenobarbital, primidone, carbamazepine induce CYP3A4 and may significantly decrease hydroxychloroquine concentrations, and coadministration is not advised.
- No interaction was reported with sertraline, duloxetine, doxepin, bupropion, which are likely to be safest among antidepressants.
- Rifampicin, ampicillin, azithromycin, clarithromycin, erythromycin, fluoroquinolones, trimethoprim/sulfamethoxazole have potential interaction with hydroxychloroquine.
- Chloroquine and hydroxychloroquine inhibit CYP2D6, which may increase beta-blocker exposure and risk of bradycardia, PR interval prolongation, and atrioventricular block [6]. Calcium-channel blockers also prolong the PR interval. No interaction is expected by angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB). However, diuretics, including hydrochlorothiazide, furosemide, indapamide may cause electrolyte

disturbances and thereby increase the risk of QT prolongation; thus, caution and electrolyte monitoring is needed.

- As hydroxychloroquine may enhance the effects of a hypoglycaemic treatment, a decrease in doses of insulin or antidiabetic drugs may be required.
- Clinically significant interaction is unlikely with statins, clofibrate, and ezetimibe.
- No interaction was reported with commonly used drugs in patients with major neurocognitive diseases, including acetylcholinesterase inhibitors, NMDA Receptor antagonists, sedatives, anxiolytics (GABA receptor agonists).

In the light of current evidence; except in the context of a clinical trial, National Institute of Health (NIH) COVID-19 treatment guidelines recommends against the use of chloroquine or hydroxychloroquine except in a clinical trial and high dose chloroquine (600 mg twice daily for ten days) for the treatment of COVID-19 [9]. As the latest development, the FDA has also revoked the emergency use authorization to use hydroxychloroquine and chloroquine to treat COVID-19 except for clinical trials [10]. Furthermore, the clinicians should be aware that among experimental COVID-19 therapies, chloroquine and hydroxychloroquine may have a negative effect on the course of the disease due to their potential drug interactions in older adults. Therefore, the studies' results should be interpreted with caution because there are big differences in the studies regarding the severity of the disease, sample size, viral loads, and treatment regimens of the patients. Many drug classes such as antidepressants, anticonvulsants, antihypertensives have the potential to interact with hydroxychloroquine. Accordingly, careful monitoring of older patients is required during hydroxychloroquine treatment.

CONCLUSIONS

There is an urgent need to develop safe and effective drugs to treat COVID-19 potentially. During this time, attention should be paid to the older adults' treatment regimens, and health care professions should be vigilant for potential adverse drug reactions.

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