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The Use of Interleukin-6 Inhibitors in Patients with Coronavirus Disease 2019 Who Develop Acute Kidney Injury

Chia Siang Kow[1], Syed Shahzad Hasan[2], Dinesh Sangarran Ramachandram[3]

[1]Department of Pharmacy Practice, International Medical University, Kuala Lumpur, Malaysia
[2]Department of Pharmacy, School of Applied Sciences, University of Huddersfield, Huddersfield, UK
[3]School of Pharmacy, Monash University Malaysia, Selangor, Malaysia

Corresponding author: Chia Siang Kow ✉ chiasiang_93@hotmail.com

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Dear Editor,

We compliment Çalışkan et al.[1] for reporting their retrospective investigation on the clinical profiles and outcomes of hospitalized patients with coronavirus disease 2019 (COVID-19) and comorbid kidney disease, including those with acute kidney injury (AKI). We believe the reporting of this retrospective study is of utmost importance since the researchers have not given the much-deserved attention to COVID-19-related AKI compared to other COVID-19-related outcomes such as the requirement for mechanical ventilation and admission into the intensive care unit. Nevertheless, we believe the study raises the opportunity for ongoing discourse on evolving evidence-based care in this population.

Based on the findings of the retrospective study,[1] the mortality rate in patients with COVID-19 and AKI was much higher than their counterparts with stage 5 chronic kidney disease on dialysis—46% in the former vs. 24% in the latter. The same pattern was observed for the requirement for mechanical ventilation, in which 50% of patients with COVID-19 and AKI required ventilatory support, whereas only 22% of their counterparts with stage 5 chronic kidney disease on dialysis required ventilatory support.

Therefore, in order to prevent clinical deterioration, patients with COVID-19 and AKI should be administered proven disease-modifying therapies for COVID-19, such as interleukin-6 (IL-6) inhibitors.[2] Notably as reported by the authors,[1] there were only 3.1% of patients with AKI who received tocilizumab (an IL-6 inhibitor). Indeed, higher proportions of patients with COVID-19 and AKI were prescribed with azithromycin (29.6%) and remdesivir (20.4%), which have been notoriously associated with AKI and with doubtful benefits in patients with COVID-19.[1]

Interleukin-6 inhibitors have been proven to reduce all-cause mortality in patients with COVID-19, based on the prospective meta-analysis performed by The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group (pooled odds ratio = 0.86; 95% CI 0.79-0.95).[3] However, in addition to their mortality benefits, many may have overlooked their benefits in terms of preventing clinical deterioration in patients with COVID-19 and AKI. According to

the aforementioned prospective meta-analysis,[3] the use of IL-6 inhibitors in patients with COVID-19 was also associated with significantly reduced progression to kidney replacement therapy or death (pooled odds ratio = 0.79; 95% CI 0.71-0.88), and such beneficial clinical outcome is especially important for patients with COVID-19 who develop kidney impairment.

The ability of IL-6 inhibitors to reduce progression to kidney replacement therapy in patients with COVID-19 may be related to the inhibition of oxidative stress and apoptosis in kidney tissue via blockade of the activation of nuclear factor kappa B. Therefore, we believe the use of IL-6 inhibitors should be more widespread in the eligible patients with COVID-19 and AKI, considering their kidney protective effects. In addition, to prevent the occurrence of dose-related side effects, clinicians should also be mindful of the requirement to adjust the dose of medications used in patients with COVID-19 who develop AKI.[4]

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Author's Response

Yaşar Çalışkan, Krista Lentine

Department of Nephrology, Saint Louis University, St. Louis, MO, USA

Corresponding: Yaşar Çalışkan ykcaliskan@yahoo.com

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Dear Editor,

In this single-center cohort study of coronavirus disease 2019 (COVID-19) in patients with kidney disease hospitalized in the first surge of our local pandemic (3/19/2020 to 7/31/2021), we observed high rates of respiratory failure, kidney replacement therapy needs, and mortality, especially in those with acute kidney injury (AKI).[1] Kow et al[2] point out the potential benefits of interleukin-6 (IL-6) inhibitors in the treatment of patients with COVID-19 and AKI, based on a prospective meta-analysis performed by The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, which was published in August 2021, after our first-surge study was completed.[3] Treatments for COVID-19 have evolved over the pandemic, and our cohort study describes the experience during the first surge of the pandemic when IL-6 inhibitors were not broadly used in patients with COVID-19. Given the rapidly changing landscape of COVID-19 incidence, vaccination, and treatment approach, understanding the key drivers of COVID-19 outcomes and best treatment options in patients with comorbid kidney disease is a challenging but critically important topic. Ongoing studies and dynamic management recommendations are needed as knowledge of the optimal care of COVID-19 in patients with comorbidity and high-risk profiles continue to evolve.

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