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Platinum Opinion

The Use of Nonsteroidal Anti-inflammatory Drugs in Urological Practice in the COVID-19 Era: Is “Safe Better than Sorry”?

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The recent emergence of the SARS-coronavirus 2 (SARS-CoV-2) and its rapid spread have led to a global state of emergency, major logistical disturbances in the care of oncological diseases [1], and (at a more minor level) disruption to the care of all common medical conditions [2]. On March 14, 2020, several reports raised concerns about whether nonsteroidal anti-inflammatory drugs (NSAIDs; eg, ibuprofen) could worsen symptoms of COVID-19. The French Health Minister alerted the public about concerns regarding the use of NSAIDs in patients with a fever and/or serological evidence of COVID-19 infection. This warning leads to a misleading statement that in the absence of information about serological status, NSAIDs should be proscribed. This raised concerns among the medical community, given the common use of NSAIDs in urological diseases [3]. NSAIDs are frequently used for pain, fever, and several common urological diseases (eg, simple renal colic) and are part of the perioperative management of urinary tract surgery and for symptom relief after vesical instillations. It is estimated that 30 million people per day worldwide take NSAIDs [4].

There is a sizeable body of literature suggesting that NSAIDs might alter the course of bacterial pneumonia, resulting in more invasive disease and complications and potentially leading to higher rates of admission to hospitals and intensive care units [5]. The balance between the leukotriene and prostaglandin pathways during acute inflammation/infection in humans is not well understood, and COX inhibitors may result either in an enhanced or a reduced bacterial host response. Similarly, concerns have

been raised about the negative effects of NSAID exposure on the clinical course of viral infections. One of the mechanisms of action of SARS-CoV-2 involves binding to target cells through ACE2 protein. ACE2 is promoted by numerous epithelial cells, especially those in the lung and kidney. Fang et al [6] recently reported concerns about the impact of hypertension or diabetes mellitus on COVID-19. Treatments with ACE inhibitors and angiotensin II type-I receptor blockers are used for these diseases and lead to upregulation of ACE2. Similarly, owing to their pharmacological action, NSAIDs could also increase ACE2; it has been hypothesised that ACE2-stimulating drugs increase the risk of developing severe and fatal COVID-19 [6]. Conversely, administration of COX inhibitors significantly ameliorated mortality in an animal model of influenza H5N1 infection [7] and there was no evidence that NSAIDs influenced severe H1N1 mortality in a retrospective human cohort [8]. In addition, NSAIDs might be potential inhibitory factors for SARS-CoV [9] (which shares 99.8% sequence homology at the nucleotide level with SARS-CoV2 [10]) replication, suggesting NSAIDs could have both anti-inflammatory and antiviral activity [9]. However, the exact role of COX inhibitors in the cytokine storm and pyroptosis observed for highly pathogenic human coronavirus has not yet been investigated [10].

The European Medicines Agency (www.ema.europa.eu/en/news/ema-gives-advice-use-non-steroidal-anti-inflammatories-covid-19) and World Health Organization (<https://www.who.int/news-room/q-a-detail/q-a-coronaviruses>) stated on March 18, 2020 that to date there is no scientific evidence that NSAIDs can worsen COVID-19

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and they do not recommend against the use of NSAIDs. According to this statement, physicians should be aware that there are multiple substitute medications for pain relief and fever control that should be prioritised for these conditions. For some urological conditions, NSAIDs have additional benefits not delivered by other medications, such as in glomerular filtration, renal pelvic pressure, ureteric peristalsis, and ureteric oedema in renal colic management.

For these particular cases, we believe that NSAID use for urological diseases should still follow established indications, particularly for all patients without fever or COVID-19 symptoms, but with more caution. This recommendation has also been provided by other specialities covering conditions for which chronic anti-inflammatory medications are prescribed. Nevertheless, physicians should rigorously screen for COVID-19 symptoms and inform patients before prescribing any medication. In the case of any doubt, NSAIDs should be avoided. For example, treatment decisions for renal colic should follow the same rules as during pregnancy and for febrile renal colic.

The entire medical community worldwide and all the international and national agencies are closely monitoring this issue. We should continue to treat our patients with the best standard of care without falling into paranoid practice and stay focused on our main goal: “patients first”.

Conflicts of interest: The authors have nothing to disclose.

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