DOI: 10.1111/jce.14894

LETTER TO THE EDITOR

WILEY

Atrial fibrillation and flutter in patients hospitalized for COVID-19: The challenging role of digoxin

To the Editor,

We read with interest the article by Peltzer et al.[1] referring to the occurrence of atrial fibrillation and flutter (AF/f) in patients hospitalized with coronavirus disease (COVID-19). An incidence of 16% was observed, while 60% of this arrhythmia was of new onset. The manifestation of AF/f was followed by high morbidity and mortality, which were further aggravated when markers of cardiac injury and inflammation were present, suggesting an imminent cytokine storm. The study was retrospective; thus, information regarding the therapeutic treatment of AF/f was missing. However, in an illustrated paradigm, the treatment consisted of the administration of amiodarone and digoxin. Digoxin and digitalis are the main clinical representatives of cardiac glycosides (CGS), in uninterrupted use for more than a century, prescribed for controlling heart rate in AF/f. Although beta-blockers and calcium antagonists seem to obtain preference temporarily, CGS remains of undisputed value when AF/f coexists with low blood pressure and heart failure. Of notice, in the study by Peltzer et al., a large number of patients were under vasopressor support, preventing the use of beta- blockers and calcium antagonists.

For years, the clinical application of CGS was justified by their ability to suppress Na,K-ATPase membrane pump, with secondary modulations of Na^+, K^+, and Ca^{2+} intracellular concentrations. Accumulation of Na^+ and Ca^{2+} with parallel K^+ depletion were considered suitable to explain the dromotropic, chronotropic, and inotropic properties of CGS.[2] However, a recent investigation in the field of oncology revealed unexpected characteristics of CGS related to their ability to transform Na,K-ATPase[3,4] into a signaling transducer, capable of suppressing complex intracellular protein machinery.[5] By this action, significant anticancer, antiviral, and anti-inflammatory effects were obtained in vitro and in vivo. When this data was tested during the Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome coronavirus (SARS-CoV) endemics, the results were more than promising. CGS administration compromised the whole viral cycle, including RNA replication, messenger RNA transcription, host cell translation of proteins, and finally budding of the newly formed viral particles.[6] Similar findings were obtained when CGS were tested in the setting of other DNA and RNA viruses, with implications in COVID-19 infection.[7]

Of further significance were the anti-inflammatory properties of CGS exerted via Na,K-ATPase inhibition. Hyperinflammation and cytokine cascade was suppressed in various experimental observations, including the nuclear transcription factor NF-κB, which, in turn, suppresses a whole series of other proinflammatory factors, such as TNFα, TGFβ, GRO/KC, MCP1, MIP2, IL-1β, and finally interferon IFNγ.[7–10]

To conclude, CGS with their electrophysiological and immunological properties merit a priority in the armor against COVID-19, especially when atrial arrhythmias complicate the in-hospital course.

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Disclosures: None.

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