Short Commentary

Information and Communication Needs in the Administration of Ibuprofen in Covid-19 Patients.

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ABSTRACT

Ibuprofen is a ubiquitous anti-inflammatory drug consumed as an anti-pyretic agent and in the diminution of pain, redness and swelling. There has been an expansive controversy regarding ibuprofen treatment in the exacerbation or aggravation in symptoms of the novel coronavirus, COVID-19. Although, WHO does not recommend non-application of ibuprofen in the treatment and control of COVID-19 symptoms. Currently, there is no perspicuous evidence that ibuprofen aggravates COVID-19 symptoms but a cross-section of opinion recommends paracetamol instead of ibuprofen for COVID-19 symptoms whereas certain studies advocate complete ibuprofen abstinence in the management of COVID-19 symptoms. Previous studies indicate that ibuprofen may exacerbate COVID-19 Symptoms or deteriorate its management because patients have experienced severe thoracic aberrations and prolonged prostrations following the consumption of NSAIDS, such as ibuprofen. It has not been clearly elucidated that ibuprofen consumption per se results in symptom deterioration or illness prolongation, or that anti-inflammatories including ibuprofen may occlude the magnitude of COVID-19 severity and latitude for the interference in certain immune response, as they have not yet been identified with ibuprofen.

Keywords: NSAIDS; Infections; Anti-inflammation; Fever; mortality; Morbidity; Treatment; Drugs

Introduction

The presenting COVID-19 or coronavirus disease 2019 pandemic associated with the etiological agent, the novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2) related to the erstwhile known SARS has emerged in a myriad of increased total morbidity and mortality [1]. Its insidious and non-specific trajectory may culminate in retarded diagnosis and an extended magnitude of self-administration of unnecessary and unwarranted therapeutic regimen.

Ibuprofen is also known as Advil and Motrin is a non-steroidal anti-inflammatory drug, NSAID employed in the treatment of fever, pain, redness and swelling as it prevents the body from the formation of certain substances which may culminate in an inflammatory response and inflammatory pathways [2]. Fever constitutes a prevalent symptom of COVID-19, thus, necessitating anti-pyretics, such as ibuprofen to mitigate the clinical presentations of the disease in infected patients. The speculation that ibuprofen is an untoward treatment regimen was initially stated as SARS-COV-2 was found to bind its target cell *via* ACE2 in the pulmonary system [3]. It was, therefore, proposed that ACE2-stimulating drugs including ibuprofen and ACE inhibitors potentiate the risk in the severity and mortality of the COVID-19 dilemma [4].

It is suggested that ibuprofen augments the risk in the severity and mortality of COVID-19, and therefore, not suitable for any suspected case [5].

Bioinformatics-base

A retrospective cohort study of COVID-19 subjects on ibuprofen evaluated whether ibuprofen utilization in COVID-19 patients was linked with more adverse disease presentation in comparison to paracetamol/acetomophen or without anti-pyretics [6]. A comparison to strict paracetamol consumers depicted no disparities in mortality rates or requirements for respiratory support among subjects on ibuprofen. Thus,

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ibuprofen application was not related to aberrant clinical outcomes versus paracetamol or without any anti-pyretics.

The WHO does not recommend against ibuprofen consumption in COVID-19 treatment and control. Also, it negates the occurrence of untoward impacts in the treatment of the disease with ibuprofen. This contradicts the position that certain anti-inflammatory agents, such as ibuprofen are more likely to exacerbate the viral infection [7]. This hypothesis is not undergirded by any evidence that ibuprofen consumption is associated with untoward consequences in COVID-19.

In this regard, the issue that generated a global interest has been the consumption of non-steroidal anti-inflammatory drugs, NSAIDS and their potential to drive more debilitating illness in COVID-19 subjects. Angiotensin-converting enzyme ACE2 is the SARS-CoV-2 receptor binding site wherefrom the virus permeates the host cell phagocytically [8]. The anecdotal information based mainly on unpublished reports, non-peer reviewed media and speculations are a cause for concern as the trajectory from hypothesis to theory, or from theory to practice may tend towards a protracted mode in drug intake in the expectation of veritable data on the usage of ibuprofen and others. Ibuprofen and acetamophen (paracetamol) are applicable as anti-pyretics with less side effects which have not been indicted in worsening the status of COVID-19 patients.

A UK-based trial to determine the side effects and the efficacy in a defined ibuprofen formulation that depicts as being more effective than standard ibuprofen for the treatment of severe acute respiratory syndrome, ARDS, a complication of COVID-19 has been suggested for treatment due to its easy accessibility and diminished economic burden [9]. There is no evidence that ibuprofen aggravates COVID-19 infection but resultant gastric side effects from ibuprofen promote acetamophen/paracetamol usage for symptom mitigation at the immature stages of the disease. There is no extant evidence on the effects of ibuprofen or any NSAID consumption in acute healthcare derangement, diminutive quality of life or dissipated long-term prognosis in COVID-19 patients.

Since human pathogenic coronaviruses, SARS-CoV and SARS-CoV2 usually bind to their target cells via ACE2 expressed by epithelial cells of the intestinal, pulmonary, renal and cardiovascular systems, ACE2 expression is significantly elevated in T1DM and T2DM patients treated with ACE inhibitors and ARBs culminating in an unprecedented upregulation of ACE2 [3,10].

Ibuprofen and thiazolidine issues are also experienced in elevatyed ACE2 [11]. It is suggested that the expression of ACE2 is elevated in diabetic patients , and that applicable treatment of diabetes using ARBs and ACE inhibitors augments ACE2 expression. Thus, the resultant augmented ACE2 expression induces COVID-19 susceptibility or infection. It is proposed that since there is no evidence that anti-hypertensive calcium channel blockers predispose to elevated ACE2 expression or functionality, they may constitute optional treatment modulation in cardiovascular disease, diabetes or hypertension as to obviate the high risk of debilitating COVID-19 infection [4, 11]. At this stage, there is no extant evidence to undergird an augmented risk of SARS-CoV-2 or COVID-19 infection via the consumption of ibuprofen.

Discussion

The entire human population faces a novel coronavirus pandemic with grave and expansive issues due to paucity or deficiency of appropriately defined drugs and absence of accelerated modalities against the pandemic [12] with its concomitant morbidity and mortality rates. Speculations are rife as to the etiology of the accelerated outbreak, the pathophysiology and accelerated mortality associated with COVID-19. It is suggested that there is synergism of SARS-CoV-2 RNA replication and ibuprofen intake in patients with elevated frequency of expansive morbidity and mortality. This may indicate that ibuprofen is inextricably-linked in cooperativity and synergism with severe acute respiratory syndrome coronavirus 2, SARS-CoV-2 on patient mortality [13]. Ibuprofen also inhibits the functionality of Cox1 and Cox2 enzymes converting arachidonic acid to prostaglandins following the formation of certain intermediate substrates [14,15]. PGE2 and PGI2 prostaglandins drive the infected cells and immune system protectively against infection. Thus, utilization of ibuprofen, a non-steroidal and anti-inflammatory drug in COVID-19 subjects is attributable to cell defence mechanism intervention.

Ibuprofen is a nitrogen radical scavenger [16] that influences viral infection in viral genome

derangement [17]. There are other indications of ibuprofen antagonistic impact on nitric oxide synthetase isoforms [18]. Ostensibly, dimunition in the formation of nitrogen radicals in coronavirus infected cells result in elevated viral RNA load [13].

Conclusion

The discrepancies in the presentations of ibuprofen and other NSAIDS in the veritable aspect of the treatment and control of COVID-19 infection and symptoms are attributable to certain limitations which include the potential for recall bias associated with a retrospective study which may be obviated due to short-term span of the studies, non-formulating of a particular treatment over the other, and availability of medical information predominantly from medical chart review.

Armchair scientists and researchers have tended to misrepresent, mislead and omit veritable bioinformatics-base regarding the functionality of ibuprofen in COVID-19 symptoms and patients due to ACE2 cell surface binding for the attachment and replication of the novel coronavirus with possible inextricable linkage between chronic disease patients and subsequent COVID-19 infection. Pertinent future research is necessary to elucidate the optimum treatment and control of COVID-19 symptoms and infection.

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