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ABOUT COVER

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LETTER TO THE EDITOR

Therapeutic potential of N-acetyl cysteine during COVID-19 epoch

Ajita Kapur, Munish Sharma, Geetanjali Sageena

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Abstract

N-acetyl cysteine (NAC) is a promising drug for prophylaxis and treatment of coronavirus disease 2019 (COVID-19) based on antioxidant and anti-inflammatory mechanisms. Further studies with cautious approach are needed to establish the benefits and risks before considering NAC as an adjuvant treatment for COVID-19.

Key Words: N-acetyl cysteine; COVID-19; Coagulopathy; Therapeutic potential; Prophylaxis; Treatment

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Core Tip: Risk of coagulopathy is noteworthy in coronavirus disease 2019 (COVID-19) and cerebral hemorrhage could be a potential risk in COVID-19 patients receiving N-acetyl cysteine (NAC). Results of well-designed randomized controlled trials should be awaited before NAC becomes a common practice for prophylaxis and treatment of patients with COVID-19.

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TO THE EDITOR

The impact of coronavirus disease 2019 (COVID-19) pandemic resulting in substantial mortalities and morbidities has driven the quest to accelerate the treatment options for containment of this public health emergency. We read with interest the review by Dominari *et al*[1]. The authors have reviewed the pharmacology, efficacy, and safety of N-acetyl cysteine (NAC) as an adjuvant therapy of COVID-19. NAC is a nutraceutical precursor of vital antioxidant glutathione. Based on a broad range of antioxidant and anti-inflammatory mechanisms, NAC seems to be a promising drug to attenuate the risk of developing COVID-19, and in high doses might play an adjuvant role in the treatment of severe COVID-19 and alleviate its fatal complications[2]. We agree with author's insight that NAC is a worthy candidate to be evaluated for COVID-19; however, we consider that a cautiously optimistic approach is required to assess the risk-benefit profile of this medication in the current scenario.

Patients with COVID-19 suffer from coagulopathy and prolonged prothrombin time (PT)[3]. Hypercoagulation due to elevated D dimer and fibrinogen could lead to ischemic stroke in COVID-19 patients. Though less common, intracerebral haemorrhage resulting from consumption coagulopathy related to fibrinogen depletion has been reported in more than 10% of COVID-19 patients with stroke [4].

As documented in the review, adverse effects from NAC could vary from mild gastrointestinal symptoms to severe anaphylactoid reactions[1]. Abnormal hemostatic activity, such as anticoagulant and platelet-inhibiting properties with increased bleeding risk, has been documented in patients receiving NAC[5]. NAC interacts with human vitamin K epoxide reductase at the same binding site and causes interruption in the vitamin K reduction pathway. A recent study warns regarding prolonged use of NAC in COVID-19 patients and suggests the monitoring of international normalized ratio, PT, and partial thromboplastin time. In addition, considering the lipophilicity, and hence, easy passage of NAC through blood brain barrier, this study cautioned about the risk of cerebral hemorrhage in COVID-19[6].

The possible benefits of NAC in COVID-19 seem to outweigh the risks, but an important issue plaguing the usefulness of NAC is its uncertain efficacy in mild cases[7] and potential of unregulated use in the current scenario where there are limited drugs available for the management of COVID-19. Hence, as is rightly stressed upon by the author[1], before the use of NAC in COVID-19 spreads, further research is warranted to avoid another failure story[8]. Clinical trials are already underway to establish efficacy of NAC in COVID-19[9,10], and recent review by Wong *et al*[11] (2021) elaborated the potential role of NAC as adjunctive remedy for COVID-19[11]. However, there is no in vivo research to specifically examine its effects in COVID-19.

A retrospective cohort study of hospitalized patients with moderate or severe COVID-19 pneumonia documented lower risk of progression to serious respiratory failure in patients treated with NAC[12]. However, we would like to emphasize that the results of the randomized controlled trials should be awaited before incorporating NAC to improve prognosis and clinical outcomes in the treatment of COVID-19.

FOOTNOTES

Author contributions: Kapur A designed the editorial; Kapur A, Sharma M, and Sageena G wrote the manuscript; All authors gave final approval for publication.

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