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**Therapeutic Potential of N-acetyl cysteine during COVID-19 epoch**

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

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## **Abstract**

N-acetyl cysteine (NAC) is recognized as a promising drug for prophylaxis and treatment of COVID-19, based on antioxidant capacities and anti-inflammatory mechanisms. NAC thus represents a potential additional treatment option to improve prognosis in patients with COVID-19. Still, its clinical effectiveness needs further investigations to establish efficacy, safety benefits and risks associated before considering NAC as an adjuvant treatment for COVID-19.

**Key Words:** N-acetyl cysteine; COVID-19; coagulopathy

Kapur A, Sharma M, Sageena G. Therapeutic Potential of N-acetyl cysteine during COVID-19 epoch. *World J Virol* 2021; In press

**Core Tip:** Risk of coagulopathy is noteworthy in COVID-19 and cerebral haemorrhage could be a potential risk in COVID-19 patients receiving 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.

## **TO THE EDITOR**

The impacts of COVID-19 emergency resulting in substantial mortalities and morbidities has driven the quest for rethinking, to accelerate the options for adjunctive treatment with existing anti-COVID19 therapies. We read with interest the review by Dominari *et al* <sup>[1]</sup> The authors have reviewed the pharmacology, efficacy and safety of N-acetyl cysteine (NAC) as an adjuvant therapy of COVID-19. 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. <sup>[2]</sup> We agree with author's insight that NAC is a worthy candidate to be evaluated for COVID-

19, however; we consider that a cautious 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. [3] Hypercoagulation due to elevated D dimer and fibrinogen could lead to ischaemic 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% patients of COVID-19 with stroke. [4]

As documented in the review, adverse effects from NAC could vary from mild gastrointestinal symptoms to severe anaphylactoid reactions. [1] Abnormal haemostatic activity viz. anticoagulant and platelet-inhibiting properties with increased bleeding risk has been documented in patients receiving NAC. [5] NAC interact with human vitamin K epoxide reductase, in the same binding site and cause 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 (INR), prothrombin time (PT) and partial thromboplastin time (PTT). 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 of limited drugs available for the management of COVID-19. Hence as rightly stressed upon by the author [1] before the popularity of use of NAC in COVID -19 spreads in desperation for search of a magic drug, 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]. We would like to emphasize that the results of the trials should be awaited before incorporating NAC to improve prognosis and clinical outcomes in the treatment of COVID-19. However, there is explicitly no *in vivo* research to examine plausible effect of NAC in coronavirus disease. A recent study by Wong *et al* (2021) elaborated the potential role of N-

acetylcysteine, as it has garnered a capable adjunctive remedy for COVID-19 being a nutraceutical precursor of vital antioxidant glutathione [11].

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### PRIMARY SOURCES

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- 2** Carl J. Fossum, Bethany F. Laatsch, Harrison R. Lowater, Alex W. Narkiewicz-Jodko et al. "Pre-Existing Oxidative Stress Creates a Docking-Ready Conformation of the SARS-CoV-2 Receptor-Binding Domain", ACS Bio & Med Chem Au, 2021 12 words — 2%  
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