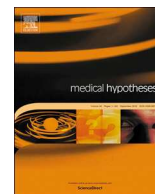




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## N-acetylcysteine: A potential therapeutic agent in COVID-19 infection



### ARTICLE INFO

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### ABSTRACT

COVID-19 is an overwhelming pandemic which has shattered the whole world. Lung injury being the main clinical manifestation, it is likely to cause COPD (chronic obstructive pulmonary disease) and ARDS (acute respiratory distress syndrome). The possible cause behind this might be redox imbalance due to viral infection. Elevation in Glutathione (GSH) levels by administration of its promolecule might be effective. N-acetylcysteine is one such drug with potency to scavenge Reactive Oxygen Species, least side effects, and an effective precursor of glutathione. Consequently we hypothesize that N-acetylcysteine along with the conventional treatment may be treated as a potential therapeutic solution in cases of COVID-19 patients.

### To the Editor,

Studies revealed that COVID-19 patients with critical condition demonstrated lower glutathione levels, with a high concentration of reactive species thus showing high ROS/GSH ratio as compared to the patients with mild symptoms. GSH depletion in cells amplifies the viral replication cycle [1,2] which could be a possible cause of augmented SARS CoV-2 infections in these patients. Histological examination of lung samples from COVID-19 patients showed pulmonary edema and hyaline membrane formation, indicative of acute respiratory distress syndrome (ARDS) [3,4]. The toxicity of severe lungs injury is supposed to be due to free radicals generation together with deteriorating innate immunity and activation of transcription factors [5]. Experimental and clinical studies confirmed the role of GSH against inflammatory pathologies of the lungs by attenuating Oxidative Stress [6]. This suggests that endogenous glutathione depletion may be a possible consequence of progression of COVID-19 patients from mild to severe illness. Supplementation of glutathione directly is difficult due to its short half life and impermeability to many biological membranes, thus its precursor N-acetyl-cysteine could be used to elevate its intracellular levels.

N-acetylcysteine is the promolecule to cysteine, a potent precursor of glutathione, enhancing the intracellular sulphhydryl pool as a powerful antioxidant. NAC liquefies mucus by opening disulfide bonds in mucoprotein, reduces viscosity of bronchial and lung secretions and recovers oxygen saturation in the blood. NAC directly inactivates reactive electrolytes and free radicals non-enzymatically and maintains oxidant/ antioxidant balance in cells. At doses more than 1200 mg, it acts as an antioxidant by reducing the formation of pro-inflammatory cytokines, such as IL-9 and TNF- $\alpha$  and also shows vasodilator property by increasing cyclic GMP levels and contributing to the regeneration of endothelial-derived relaxing factor. A placebo controlled study by

Zhang et. al., [7] has investigated the antioxidant properties of NAC in exacerbations of chronic obstructive pulmonary disease. NAC also protects against H9N2 swine influenza virus-induced acute lung injury (ALI) thus dictating its therapeutic importance in ALI caused due to influenza virus. Studies also revealed that NAC treatment in ARDS patients can improve the outcome of the patients by rising total thiol molecule and anti-oxidant molecules [8]. This shows the potential benefits of using NAC as therapeutic agent in these patients.

There is substantial evidence to support our hypothesis that N-acetyl-cysteine has a potential to be used as a therapeutic agent in the treatment of COVID-19 patients. It is a drug with potency to scavenge Reactive Oxygen Species (ROS), least side effects, and an effective precursor of glutathione. Our hypothesis is worth proving in well designed clinical studies that may benefit in the treatment of COVID-19 patients.

### Prior presentation

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### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**Abbreviations:** COVID-19, Corona virus disease 2019; GSH, Glutathione; NAC, N-acetylcysteine; ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; ALI, acute lung injury

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.110133>.

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