INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH AND ANALYSIS

ISSN[Online] : 2643-9875 || ISSN[Print] : 2643-9840

Volume 3 Issue 09 September 2020

DOI: 10.47191/ijmra/v3-i9-09, Impact Factor : 5.522

Page No : 122 – 123

N-acetyl cysteine (NAC) and COVID-19 treatment: New hopes in old medication

Naser Hatami[1], Navid Kalani[2], Farshid Javdani[1*], Sayyed Reza Ahmadi[3], Seyed Reza Habibzadeh[3], Behzad Shahi[4],Fatemeh Maleki[5], Neema John Mehramiz[6], Mahdi Foroughian[3]

1. Student Research Committee, Jahrom University of Medical Sciences, Jahrom, Iran.
2. Research center for social Determinants of Health, Jahrom University of Medical Sciences, Jahrom, Iran.
3. Department of Emergency Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
4. Department of Emergency Medicine, Faculty of Medicine, Zahedan University of Medical Sciences, Mashhad, Iran.
5. Department of Emergency Medicine, Faculty of Medicine, Birjand University of Medical Sciences, Mashhad, Iran.
6. Department of Psychiatry Neurology. Banner university medical center, Tucson, AZ, USA.

Corresponding Author : Farshid Javdani.
Student Research Committee, Jahrom University of Medical Sciences, Jahrom, Iran.

ABSTRACT

N-acetyl cysteine is seen to improve patients with acute respiratory diseases. The recommended pathways, of it's the effect on pulmonary diseases, are its antioxidant capacity through glutathione synthesis (GSH) and following effects on preventing and controlling cytokine storm. These features make it a good candidate to be evaluated for COVID-19 disease as this disease is causing a cytokine storm.

KEYWORDS:

N-acetyl cysteine, COVID-19, Acute respiratory distress syndrome

INTRODUCTION

Severe acute respiratory coronavirus 2 syndromes (SARS-CoV-2), first identified in Wuhan, China, is responsible for the outbreak of 2019 coronavirus disease (COVID-19), which World Health Organization (WHO) have proclaimed it as a pandemic in March 2020 (1). The symptoms of COVID-19 generally include fever, cough, sore throat, breathlessness, tiredness, malaise, and various other symptoms. While the disease tends to happen in a mild form in most people; it can progress to severe complications as well as pneumonia, acute respiratory distress syndrome (ARDS), and multi-organ failure in some patients with higher age and those with comorbidities. A significant cause of multiple organ dysfunction and high mortality caused by COVID-19 is its severe systemic inflammation in the body, known as cytokine storm (1). Cytokine storm is a systemic inflammatory reaction that can be caused by infection, some medications, and other causes, characterized by a sudden rise in the level of a large number of pro-inflammatory cytokines (2). The Cytokine storm syndrome mostly happens in COVID-19 patients with serious conditions (3). Based on WHO recommendations, various medications could help COVID-19 patients, while yet there is not any specific treatment available. In the 1960s, N-acetyl cysteine (NAC) was introduced as a mucolytic treatment for chronic respiratory diseases (4). While being commonly known as an antidote to acetaminophen overdose, N-acetyl cysteine has several other applications backed by varying pieces of proof. Such therapeutic applications are the product of its ability to support antioxidant and nitric oxide systems in the body during stress, infections, intoxications, and inflammatory conditions (5). Acetyl cysteine makes bronchial mucous less viscous. Cysteine derivatives function in vitro by breaking disulfide bridges between macromolecules, leading to a reduction in viscosity of the mucus (4). It has a well-established safety profile and is still widely used orally as a mucolytic at 600 mg/day dose. In hospital settings, it is also used in patie0nts with the acute Broncho pulmonary disease (pneumonia, bronchitis, tracheobronchitis) as well as a treatment for paracetamol overdose (IV formulation at doses up to 150 mg/kg) and in nebulized forms (5). On the other hand, several types of research have dealt with NAC's antiviral activity (6). NAC helps glutathione synthesis (GSH) function during oxidative stress when there is increased demand for GSH. GSH is a

vital molecule for overcoming oxidative stress by recycling oxidized glutathione back into reduced form with the enzyme glutathione reductase (GR). GSH function decline as age increases and with certain disease conditions as like as type II diabetes mellitus and cardiovascular disease (7). As we see that COVID-19 appears with more severe symptoms in older people (1). Synthesis, and thereby reducing oxidative stress (7). While in certain cases of COVID-19, glutathione reductase (GR) levels were seen to be increased significantly (8). GSH regeneration is known to be an important cornerstone of treatment for cytokine storm syndrome, as Horowitz et al. reported successful treatment of 2 cases of COVID-19 by NAC's effect on cytokine storm (8). Glutathione levels are significantly increased by intravenous NAC therapy in clinical trial studies. Also, clinical responses to treatment, including oxygen supply, lung compliance, and pulmonary edema were seen to get improved by NAC therapy of ARDS patients (8). In a meta-analysis of trials testing NAC efficacy in acute respiratory distress syndrome, NAC shortened the length of ICU stay (9). NAC can inhibit potential cytokine storm-causing pathways followed by complex immunological activations. In patients with COVID 19 pneumonia, NAC may represent a novel approach to treatment for inhibiting cytokine storm in acute respiratory distress syndrome.

ACKNOWLEDGEMENT

We would like to thank the Clinical Research Development Unit of Peymanieh Educational and Research and Therapeutic Center of Jahrom University of Medical Sciences for providing facilities to this work.

FUNDING

None

CONFLICT OF INTEREST

None

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