



Gluthione Enrichment as a Possible Prevention and Treatment for COVID-19

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In this global pandemic situation of corona virus disease (COVID-19) outbreak arises due to rapid spread of Novel Corona Virus (SARS-CoV-2), I would like to draw your kind attention and point out to the possibility of application of a set of known drugs to prevent and treat COVID-19. My three decades experiences as a Scientist in the field of Cancer Biology, particularly in multidrug resistance (MDR), dealing with phase II detoxification, immunology and reactive oxygen species (ROS) impel me to place such an observation before your erudition and able leadership/consideration.

Objective: Considering very high rate of serious illness and mortality due to COVID-19 in senior people and those with comorbidity, the urgent need is to identify effective drugs for the treatment and prevention. Without going into the detail of the mechanistic aspect of the virus (SARS-CoV-2) attack, I point out to one aspect of viral invasion and the possibility of prevention and treatment through known drugs.

Background: Corona virus (SARS-CoV-2), with its minute virion size (50–200 nm in diameter) enters into the human body by using its spike protein (ACE2) and protease (TMPRSS2) and binds to cellular receptors (ACE2 receptor) and then starts rapid multiplication in the lung tissue leading to breathing difficulty and death^[1]. For its rapid growth the virus attacks the immune system, overpowers the defense mechanism and creates the so called 'cytokine storm'^[2].

Virus causes severe oxidative stress that leads to destruction of the phase II detoxification pathway, the major component of body's Innate Immune System. The function of this detoxification system is governed by glutathione (GSH, reduced form) and some related en-

zymes^[3,4]. The thiol compound GSH (gamma-glutamyl cystein glycine, a ubiquitous tripeptide), the major antioxidant that controls various biological processes like removal of free radicals, mitochondrial activity, apoptosis, immune response and even antiviral action. The amount of cellular GSH level also varies with age, sex and other disease features of the body^[5].

Role of cellular Gluthione (GSH):

Studies including ours^[5, 6,7,8] disclosed that cellular glutathione deficiency (due to decreased biosynthesis or increased depletion) leads to oxidative stress, immune dysfunction, viral attack and cancer^[5-8]. Recent biomedical literature also highlights that GSH deficiency is the most accepted explanation of higher COVID-19 infection among aged population and in persons suffering from comorbidity (diabetes, cardiac or pulmonary diseases^[5,9]) Endogenous GSH progressively decreases with age and thus cells in elderly people (particularly in lung tissue) are more susceptible to oxidative damage caused by environmental factors and viral attack. Evidences disclose that the effect of glutathione deficiency, as seen in many chronic diseases, causes severe oxidative damage in COVID-19 patients^[9, 10]. Oxidative damage thereby exacerbates inflammation in lung and airways leading to acute respiratory distress syndrome

(ARDS), multi organ failure and death^[11]. Levels of cellular GSH is higher in female population than in males that may be the reason of prevalence of COVID-19 attack more in males^[13].

The new drugs and the possibility:

Recent clinical findings also disclose that patients with moderate-to-severe COVID-19-infection have lower levels of glutathione, higher ROS levels, and greater ROS/GSH ratio than patients with a mild illness^[12]. Thus coronavirus (SARS-CoV-2) cannot actively replicate in patients having higher levels of cellular glutathione; the lower viral load is manifested by milder clinical symptoms^[11, 12, 13]. Ample evidences thus support the proposition that glutathione may be a promising drug for etiological treatment of SARS-CoV-2 infections^[12-15].

COVID 19 patients have lower level of cellular GSH compared to healthy individuals and therefore, glutathione replenishment may be an effective therapy. In this regard I propose that:

- The prescribed dose of Glutathione may applied to treat COVID-19 patients
- The precursor of glutathione is N-acetylcysteine (NAC) and so oral administration in required doses of NAC may be a suitable drug. Oral administration dose of NAC is 60mg/kg^[14].
- Intravenous injection of NAC may be given in patients with serious illness.
- Intravenous injection of reduced glutathione (GSH is highly bioavailable) may be given in patients with serious illness.

v. Glutathione in combination with vitamin C is available as cheap product in the market.

Additional advice:

i. Patients should consume lot of pure vegetables, fruits, dairy products containing high amount of glutathione. (Some GSH containing vegetables are mushrooms, asparagus, avocado, cabbage, Brussels sprouts, spinach, broccoli, garlic, onions, tomatoes, cucumber, almonds, and walnuts.

ii. Patients should be advised to take glutathione supplements (if available in pure form).

iii. Exercise should be included in the daily routine of COVID-19 patients as yoga and exercise reduces oxidative stress and increases glutathione.

Conclusion: Reduction of oxidative stress could be an effective approach for the prevention and treatment of COVID-19. As most of the cofactors (aging, diabetes, hypertension, cardiovascular disease) of COVID-19 are associated with low levels of cellular GSH, I propose the increase of cellular GSH as a new approach to treat COVID-19. Oral glutathione, glutathione precursors (N-acetyl cysteine) may represent a novel treatment approach for addressing oxidative stress, cytokine storm syndrome and respiratory distress in patients with COVID-19 pneumonia.

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