REVIEW PAPER

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N ACETYL-L- CYSTEINE AND ITS IMPORTANCE IN TODAYS WORLD

Medical Science

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ABSTRACT

Vaccines are of utmost importance in preventing viral transmission especially among young people who are considered as carriers or spreaders of COVID -19.Yet again NAC an old drug with new approaches has undergone another milestone in medical world. It is a precursor of reduced glutathione. Its use to loosen thickening mucus in acute respiratory distress syndrome is well known and paracetamol intoxication can be contained by the high dose of intravenous NAC. It is a soluble thiol, a free radical scavenger, a GSH supplier, anti- inflammatory reaction participant. Thiols block the angiotensin converting enzyme-2 thus preventing penetration of SARS-CoV-2directly into cells.

KEYWORDS

thiols, L-Cysteine, Glutathione, antioxidant,

COVID- 19

COVID -19 caused by SARS-Cov-2 causes multisystem organ dysfunction leading to high mortality and morbidity. ARDS is the major cause of death in Covid-19 patients due to dysregulated host immune responses due to viral infection [1].Though new vaccines are used to contain its spread ,its use in young volunteers produce neutralizing antibodies but not so effective in the elderly showing an age related immune response.

The use of NAC in COVID-19 patients has been fruitful because of its anti- inflammatory and immune- modulating behaviour. IL8 detected early in infected patients [3]attracts neutrophils rapidly at sites of inflammation in the lungs that produce cytokines, enzymes elastase , ROS by oxidative burst, release DNA to form neutrophil extracellular traps-NETs traps[4].A large neutrophil release is caused by large amounts of proinflammatory cytokines creating: "cytokine storm." – which has Reactive Oxygen Species (ROS).Neutrophils produce ROS radicals mainly superoxide radicals (O_2)

Neutrophil elastase (NE) degrades clotting factors and complement proteins and as a result pulmonary haemorrhage is seen in Covid-19 patients [2] It degrades local plasminogen thus impairs fibrinolysis leading to intravascular coagulation and pulmonary embolism usually occur in ICU patients. Suppression of NE production by stabilising neutrophils or inhibiting neutrophil activation by IL-8 antibody can combat acute lung injury[5,6]

Cellular immunity by way of oxidant –antioxidant balance is required by host to fight viral infection. Antioxidant like glutathione (GSH) is required to balance decreased glutathione (GSSG) in cells caused by increased ROS that inhibits T cell apoptosis. Reduced glutathione restores normal functions of immune cells reducing incidence and severity of pneumonia due to this virus infection[2]

NAC is an immunomodulating agent, a precursor of glutathione can also boost immune system suppress viral replication and reduce inflammation .NAC can improve compromised cell immunity and prevent development of certain respiratory viral diseases[7]

Can NAC administration benefit Covid-19 patients?
NAC offers the following to combat Covid-19

1. Antiviral functions of NAC inhibit NF-kB activation in human lung epithelial cells[8]
2. It reduces the production of IL-8 and thus chemotactic migration of monocytes[9]
3. NAC inhibits replication of other viruses HIV [10] and respiratory syncytial virus (RSV) [11].Guthappa suggested that NAC may bind to Cys-145 thus inhibit Mpro activity and viral replication. It can be the first line drug for SARS –Cov-2due to its structural characteristics.

Immune Modulating properties of NAC.

1. NAC can replenish GSH redox balance in neutrophil which supress NFkB activation, cytokine production and chemotactic signals. [13]
2. Studies show NAC lowered rates of oxidative burst and chemotaxis, supresses elastase release from neutrophils also reduces monocyte chemotaxis.[14]
3. Without affecting phagocytosis and bacterial killing function of neutrophils.[15]
4. NAC can increase GSH and block T- cell apoptosis via Fas antigen/fas ligand lethal signal.[16]
5. In higher doses, NAC increases GSH in lymphocytes during chronic inflammatory disease.[17]
6. It can reduce pneumonia and also significantly reduce TNF and MDA improving oxidative stress. [18]
7. It improves lung function to reduce mortality rate[19]As it is a powerful scavenger of OH- prevents pulmonary oedema and respiratory failure[20,21,22,23] suggesting high concentration enough prolonged use of NAC could help treat virus caused pneumonia and mediated sepsis.it can reduce viral replication and remove pneumocyte damage decrease immune responses in COVID -19 patients. So significance of NAC mediated treatments should be emphasized as part of a multimodal approach for home care COVID-19 patients .

CONCLUSION:

NAC is an inexpensive, dietary supplement, FDA approved many years ago .A holistic approach develops good immune system and a right antioxidant balance. Yoga and meditation are positive approaches to life de-stressors that maintain redox balance of glutathione, for persons treated at home and NAC is a good supplement given IV to patients in ICU along with antivirals. It can supress viral replication and improve outcomes if timely used with other antiviral agents and can reduce hospital admission rate, mechanical ventilation and mortality.

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