

Application of Methylene Blue -Vitamin C-N-acetyl Cysteine for Treatment of Critically Ill COVID-19 Patients, Preliminary Report of a Phase-I Clinical Trial

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Abstract

Introduction: COVID-19 is a global catastrophic event that causes severe acute respiratory syndrome. The mechanism of the disease remains unclear, and hypoxia is one of the main complications. There is no currently approved protocol for treatment. The microbial threat as induced by COVID-19 causes the activation of macrophages to produce a huge amount of inflammatory molecules and nitric oxide (NO). Activation of macrophages population into a pro-inflammatory phenotype induces a self-reinforcing cycle. Oxidative stress and NO contribute to this cycle, establishing a cascade inflammatory state that can kill the patient. Interrupting this vicious cycle by a simple remedy may save critical patients' lives. **Methods:** Nitrite, nitrate (the metabolites of NO), methemoglobin, and prooxidant-antioxidant-balance levels were measured in 25 ICU COVID-19 patients and 25 healthy individuals. As the last therapeutic option, five patients were administered methylene blue-vitamin C-N-acetyl Cysteine (MCN). **Results:** Nitrite, nitrate, methemoglobin, and oxidative stress were significantly increased in patients in comparison to healthy individuals. Four of the five patients responded well to treatment. **Discussion:** NO, methemoglobin and oxidative stress may play a central role in the pathogenesis of critical COVID-19 disease. MCN treatment seems to increase the survival rate of these patients. Considering the vicious cycle of macrophage activation leading to deadly NO, oxidative stress, and cytokine cascade syndrome; the therapeutic effect of MCN seems to be reasonable. Accordingly, a wider clinical trial has been designed. It should be noted that the protocol is using the low-cost drugs which the FDA approved for other diseases.

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