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EDITORIAL: A New Promising Strategy in the Treatment of COVID-19

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We have recently proposed a new strategy in the treatment of COVID-19; i.e. to make use of antihypoxic agents (1). Based on this hypothesis, we showed (one) mechanism of action dexamethasone as an effective anti-COVID-19 drug in the clinic (2). We proposed other drugs such as Magnesium sulfate (3) or Edaravone (4) and some medicinal plants with high antihypoxic activities such as *Crataegus spp*. (5), *Eryngium caucasicum* (6), *Sambucus ebulus* (7), *Allium sativum* (8), *Juglans regia* (9), and *Lemon Beebrush* (10), or *Cantharellus cibarius* (11) are good candidates for the treatment of COVID-19.

COVID-19 is currently affecting millions of lives worldwide. Many studies indicate that an elevated level of inflammatory cytokines and pro-inflammatory factors are associated with both increased severity and mortality of the disease. Recently a group of researchers showed using topoisomerase 1 inhibition will suppress the lethal inflammation induced by this virus. The therapeutic efficacy of two doses of Topotecan, an FDA-approved topoisomerase 1 inhibitor, has been reported recently. This drug suppresses infection-induced inflammation in hamster and mouse models (12). Topotecan treatment for four days after infection reduces morbidity and rescues mortality in animals. These results support the potential of topoisomerase 1 inhibition as an effective therapy against severe SARS-CoV-2 infection. Topotecan and its derivatives (such as Irinotecan) are inexpensive drugs available in most countries. Of course, larger clinical trials are needed to evaluate the efficacy of topoisomerase 1 inhibitors for COVID-19 in humans. Several studies have shown that levels of inflammatory molecules in COVID-19. Increased levels of interleukin-6 and fibrin degradation products have been correlated with the risk for death from COVID-19. Therefore, the increased systemic inflammation that occurs during the progression of disease provides a biological rationale for combating hyper-inflammation to reduce the severity of the disease. Therefore, the efficacy of cytokine blockers and anti-inflammatory molecules were tested against COVID-19 (13). But, inhibition of single cytokines such as interleukin 6 or granulocyte-macrophage colony-stimulating factor was not sufficient (14). because many pathways are involved in triggering the inflammatory process. Also, levels of cytokines are the age-dependent and clinical history of patients. It has been previously shown that topoisomerase 1 is required to fully trans activate infection-induced genes and thus controls the inflammatory gene programs during many viral and bacterial infections (15). It has been predicted that this strategy could be useful for future pandemics. Now, based on a newly published paper, topoisomerase 1 inhibitors have the potential for inhibition of COVID-19 infection.

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