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Edaravone: A potential treatment for the COVID-19-induced inflammatory syndrome?

We read with great interest the recent article by Zhong et al. titled "Efficacy and Safety of Current Therapeutic Options for COVID-19 – Lessons to Be Learnt from SARS and MERS Epidemic: A Systematic Review and Meta-analysis [1]," which is the most complete review of randomized control trials and cohort studies of potential pharmacotherapies for COVID-19 we have seen. However, after completing their thorough meta-analysis, the authors were not able to identify any particular drug or drug combination they could recommend for the treatment of COVID-19. This conclusion speaks to the need for venturing beyond the relatively short list of drugs that have been re-purposed for COVID-19 because of their efficacy in other viral infections.

In severe cases of COVID-19, an excessive and unregulated release of certain pro-inflammatory cytokines and chemokines can occur, producing an inflammatory syndrome that elicits significant systemic inflammation, multiple organ damage and failure and death [2]. It has been hypothesized that therapeutic interventions that significantly attenuate this severe, injurious inflammatory response could decrease the incidence of organ damage and mortality. Currently, there are no effective treatments for the COVID-19-induced inflammatory syndrome. We suggest that edaravone be considered for such use either alone or in combination with one or more anti-viral drugs, such as Lopinovir/Ritonavir.

Edaravone is given intravenously to treat amyotrophic lateral sclerosis and acute phase cerebral infarction. Edaravone is a lipophilic compound that penetrates readily into numerous tissues and organs and has significant anti-oxidant and anti-inflammatory efficacy [3]. The systemic administration of edaravone produces protective effects against inflammation and injury in animal models of chemical-induced injury to the lungs, kidneys, intestines, pancreas, brain and liver [4]. Edaravone also decreases the levels of 1) certain cytokines (IL-2, IL-6, IL-1β, TNF-α) and chemokines (IL-8, MCP-1, MIP-1a, 2,5); 2) reactive oxygen species and nitric oxide and 3) hepatic AST and ALT, in various animal models [4].

Edaravone's efficacy could be determined by identifying individuals 18 years of age or older who have laboratory – confirmed (using real time RT-PCR) COVID-19 and are diagnosed with severe COVID-19 (based on the criteria of Chen et al. [5]), for a double-blind, randomized placebo-controlled trial. A 60 mg i.v dose of edaravone would be administered once daily in one hour for 10 days to individuals in the test group, while control participants would receive an i.v. placebo solution. All patients should receive the best supportive care. The primary efficacy point would be mortality and clinical improvement would be evaluated as previously described [6]. Edaravone can produce contusion, gait disturbance and headache and patients should be closely monitored for hypersensitivity reactions. Edaravone can be used in patients with mild to moderate hepatic impairment and renal impairment is not expected to significantly alter edaravone exposure. Finally, edaravone has not been reported to produce immunosuppression.

In conclusion, we hypothesize that edaravone, if given in a timely manner, would decrease organ damage, clinical complications and mortality in severe cases of COVID-19. If edaravone decreases mortality and produces significant clinical improvement, its efficacy should be tested in infectious diseases that produce an overexuberant inflammatory response, such as Ebola.

Declaration of Competing Interest

None of the authors has any declaration of interest.

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