Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to Editors

Acute respiratory distress syndrome from Covid-19: A perfect storm from free radicals? Proposal for a new treatment

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Dear Editor

The Covid-19 epidemic transformed life in our cities and continues to cause numbers of deaths. Although it often occurs in mild form, cases that develop acute respiratory distress syndrome (ARDS), cardiovascular damage, shock, or multi-organ dysfunction are frequent and indicate a systemic inflammatory response [1].

The inflammatory response is triggered by activation of monocytes and alveolar macrophages, which produce, and release into the extracellular compartment, bioactive mediators including reactive oxygen species (ROS), reactive nitrogen species (RNS), and cytokines. When the production of these mediators exceeds the capacity of tissues to neutralize them, oxidative stress occurs, and is a major contributor to alveolar cell death and endothelial injury. Damage to the vascular endothelium can lead to multi-organ dysfunction [2]. This inflammatory response is common to many diseases, including septic shock [3]. Drugs that combat the cytokine storm (anakinra, tocilizumab) have been proposed for the treatment of Covid-19-related ARDS [4], but other therapeutic strategies need to be explored.

Data from animal studies indicate that ROS and RNS play fundamental roles in the pathogenesis of ARDS [5], and high levels of RNS are involved in the multi-organ failure of septic shock [6]. Nevertheless, drugs that minimize the harmful effects of these species have not been introduced into clinical practice. Methylene blue, an old anti-malarial drug currently used to treat methemoglobinemia, has been used successfully to treat septic shock [7] with minimal adverse effects. It acts effectively as an antioxidant on RNS by lowering the bio-availability of nitric oxide [8], which is the progenitor of strongly oxidative nitrogen-based molecules. Methylene blue also prevents ROS production by inhibiting the action of xanthine oxidase [9].

Based on these data methylene blue appears worth trying to contrast Covid-19-related pneumonia when the first symptoms of ARDS appear. As regards dose, methylene blue was administered at 1–2 mg/kg in a single bolus or lower dose infusion in septic shock patients; methylene blue has a dose-dependent effect on pulmonary vascular resistance, and venous infusion of doses above 2 mg / kg should be prudently avoided [10]. Continuous infusion would allow for titration based on response and result in a lower dose overall. We therefore suggest that, similarly to what was experienced in septic shock [11], a bolus of 1 mg/kg, followed after 2 h by infusion of 0.5 mg/kg/h for four hours would be an appropriate starting point. The earlier the start of treatment, the better the expected result, and taking low-dose methylene blue (120–180 mg/day orally for ten or fifteen days) from the first Covid-19 symptoms could prevent the onset of ARDS and avoid the need for hospitalization.

Authorship

Giulio Scigliano: conception and design of the study, drafting of article, analysis and interpretation of data, final approval of the version to be submitted.

Giuseppe Augusto Scigliano: acquisition of data, analysis and interpretation of data, final approval of version to be submitted.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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