

Letter to the Editor

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Magnesium Sulfate: A Potential Adjuvant Treatment on COVID-19

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COVID-19 has currently become a major global health problem. Due to novelty and high morbidity and mortality, there are some important medical challenges to achieve proper management and treatment of the disease. Different pharmaceutical categories have been candidate for viral or cytokine phase control, and in this regard many clinical trials are underway to obtain evidences and acceptable results (1). One of these compounds is magnesium (Mg) sulfate which may have potential therapeutic effect on the cytokine phase of COVID-19. Mg compounds have long been used in practice under various indications and purposes as supplemental compounds, electrolyte regulation and also prevention of drugs side effects. In addition, the effectiveness of Mg sulfate in controlling asthma attacks, gynecological cases and pre-natalogical problems has also been proven. Herein we briefly reviewed immunomodulatory and respiratory effects of Mg and its potential benefits in COVID-19 treatment. Mg sulfate can be used both systemically and by inhalation, but nebulizer route has potential effect on rapid onset of action on respiratory system and reduced incidence of systemic side effects (2). To the best of our knowledge, in COVID-19 patients, as other viral infections, airway hyper-reactiveness can be overrepresented (3). In this regard ventilation improvement and reducing of airway resistance should be considered. Some bronchodilators, such as β 2-agonists and anti-muscarinic agents used to relieve these symptoms. Another option has provided for hospitalized patients, is nebulized Mg sulfate. It has been suggested in the literature that Mg sulfate can cause bronchodilation in asthmatic patients by various mechanisms, including by inhibition of calcium influx into the cytosol, prevention of acetylcholine secretion, inhibition of histamine release; and finally, by β 2-receptor

affinity enhancement, increases bronchodilator effect of β 2-agonists (4). On the other hand, according to some researches, low Mg level is associated with increased inflammatory response. *in vitro* studies showed that short-term exposure to Mg sulfate without affecting on viability and function of phagocytes, diminished cytokine gene and protein expression, and consequently could reduce production of TNF- α and IL-6 from neonatal monocytes (5). Moreover, Mg sulfate can reduce the level of interleukin 1 β , that is a potent pro-inflammatory cytokine (6). Another study of the anti-inflammatory effect of Mg compounds showed that neutralized Mg ions can convert THP-1-derived macrophages to the M2 phenotype (anti-inflammatory macrophages), thereby reduce the production of inflammatory cytokines and enhance the secretion of anti-inflammatory cytokines. As well as, according to *in vitro* and *in vivo* studies, Mg sulfate significantly reduces baseline level along with LPS-stimulated cytokine production (5, 6). Altogether, given that the cytokine phase of COVID-19 plays a very significant role in patient morbidity and mortality, therefore proper management and control of this stage of the disease is important on rescuing patients. It seems that, administration of Mg compounds as an adjuvant treatment may improve this condition of disease. Our preliminary experiences indicated the potential positive effects of Mg sulfate on the improvement process in covid-19. However, in order to achieve more accurate and reliable results, adequate randomized clinical trials are needed. It should be considered that intravenous administration of this drug can be performed only in the intensive care unit (ICU) and or under close observation, but the Inhaler form does not require close monitoring. Moreover, oral Mg supplementation in outpatients may also reduce the inflammatory response in COVID-19.

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