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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Correspondence

Dexamethasone: A boon for critically ill COVID-19 patients?

Dear Editor

As observed at the beginning of other coronaviruses epidemics, such as SARS in 2002 and MERS in 2012 [1], the search of therapeutic interventions has been intense for the coronavirus disease 2019 (COVID-19). The absence of an effective vaccine, treatment regimen, and managemental guidelines for COVID-19 has been responsible for rapid spread and heavy death toll. The COVID-19 associated mortalities in severe forms were mainly attributed to respiratory failure, probably due to lethal pneumonia caused by rampant inflammation [2]. The SARS-CoV-2 infection is characterized by an increase in pro-inflammatory and decrease in anti-inflammatory cytokines resulting in a state of cytokine storm syndrome, which in turn leads to the development of acute respiratory distress syndrome (ARDS), shock, multiple organ failure and subsequent death of the individual [2].

Although the use of corticosteroids has been reported as a routine treatment of COVID-19 to curtail the inflammation associated with injury [2], their use is controversial, and validation through clinical trials is highly warranted. Concerning this, a total of 14 clinical trials were initiated till date to evaluate the safety and effectiveness of the dexamethasone (a corticosteroid) for the management of SARS-CoV-2 infection (https://clinicaltrials.gov/ct2/results?cond=covid-19&term=dexamethasone&cntry=&state=&city=&dist=). Recently, dexamethasone was declared as the world's first treatment proven effective in reducing the risks of death among severely ill COVID-19 patients based on the positive results confirmed by the RECOVERY trial (NCT04381936) conducted by Oxford University. The world's largest clinical trial viz. RECOVERY trial, a randomized, controlled, and open-label trial has begun in March 2020 and aimed to investigate several potential COVID-19 treatments on hospitalized patients [3]. Moreover, dexamethasone has been proven to significantly reduce the mortality risk in COVID-19 patients on ventilation and oxygen by as much as 35% and 20%, respectively. After that, the dexamethasone has been authorized by the UK government for the treatment of critically ill COVID-19 patients. However, no clinical benefits were seen in patients with mild, moderate, and hospitalized COVID-19 patients, not on oxygen or ventilation [4].

The dexamethasone (synthetic pregnane corticosteroid; a cortisol derivative) is a well-known lifesaving drug and commonly used to treat inflammatory and autoimmune conditions (Fig. 1). It is widely used for the treatment and management of rheumatic problems, skin diseases, asthma, many forms of allergies, chronic obstructive lung disease, brain edema, eye pain, as a result of eye surgery and bronchospasm. The mechanism of action of corticosteroids is diverse, with many effects on various body systems. The corticosteroids inhibit the action and expression of many molecules involved in pneumonia associated inflammatory response. Moreover, many molecular mechanisms are associated with corticosteroids and include transactivation by increasing the gene transcription of different anti-inflammatory cytokines [5].

Additionally, the corticosteroids may induce *trans*-expression by decreasing gene transcription of various pro-inflammatory cytokines, chemokines, and adhesion molecules [5]. Moreover, experimental studies revealed a reduced inflammatory response after the administration of corticosteroid in severe community-acquired pneumonia [6]. In this context, the anti-inflammatory effect of the dexamethasone is suggested to probably counter the cytokine storm caused by SARS-CoV-2 infection safeguarding the lungs and subsequently lives, for which detailed investigations are needed.

However, the use of corticosteroids may induce side effects, so the administration of immunoglobulins (IV-IG) and IFN-β simultaneously may help in the management of COVID-19 using corticosteroids. In this context, a clinical trial (IRCT20120225009124N4; https://www.irct.ir/) has already been launched to test the hypothesis of whether early administration of dexamethasone along with IV-IG and IFN-β can reduce the harmful effects of cytokine storm in critically ill COVID-19 patients or not. Moreover, dexamethasone is approved by the FDA as a broad-spectrum immunosuppressant and reported to be about 30 times more active than cortisone with an added advantage of longer duration of action. Furthermore, dexamethasone is suggested to limit the production of inflammatory cytokines and their damaging effect. However, inhibition of T cells functions and blockage of B cells from making immunoglobulins may potentially lead to an increase in plasma viral load, which is a primary concern and needs further investigation [6].

The breakthrough discovery of dexamethasone as the first drug to save lives is very encouraging. It enlightens the hope to reduce the mortality in critically ill hospitalized patients. Though the drug is found to be effective in only patients on ventilators or oxygen, the overall impact on reducing the mortality will be huge because critically ill patients are the great contributors to the COVID-19 death toll. Furthermore, the comparatively low price and worldwide availability of the drug will contribute to the reduction worries caused by the pandemic. The drug will prove a boon for low and middle-income countries where an effective but expensive drug would be beyond the financial reach of the general population [6]. However, finding effective drugs like dexamethasone will transform the global impact of the COVID-19 pandemic on lives and economies. However, the goal is not yet achieved, and an effective vaccine and treatment are still awaited to counter this pandemic.

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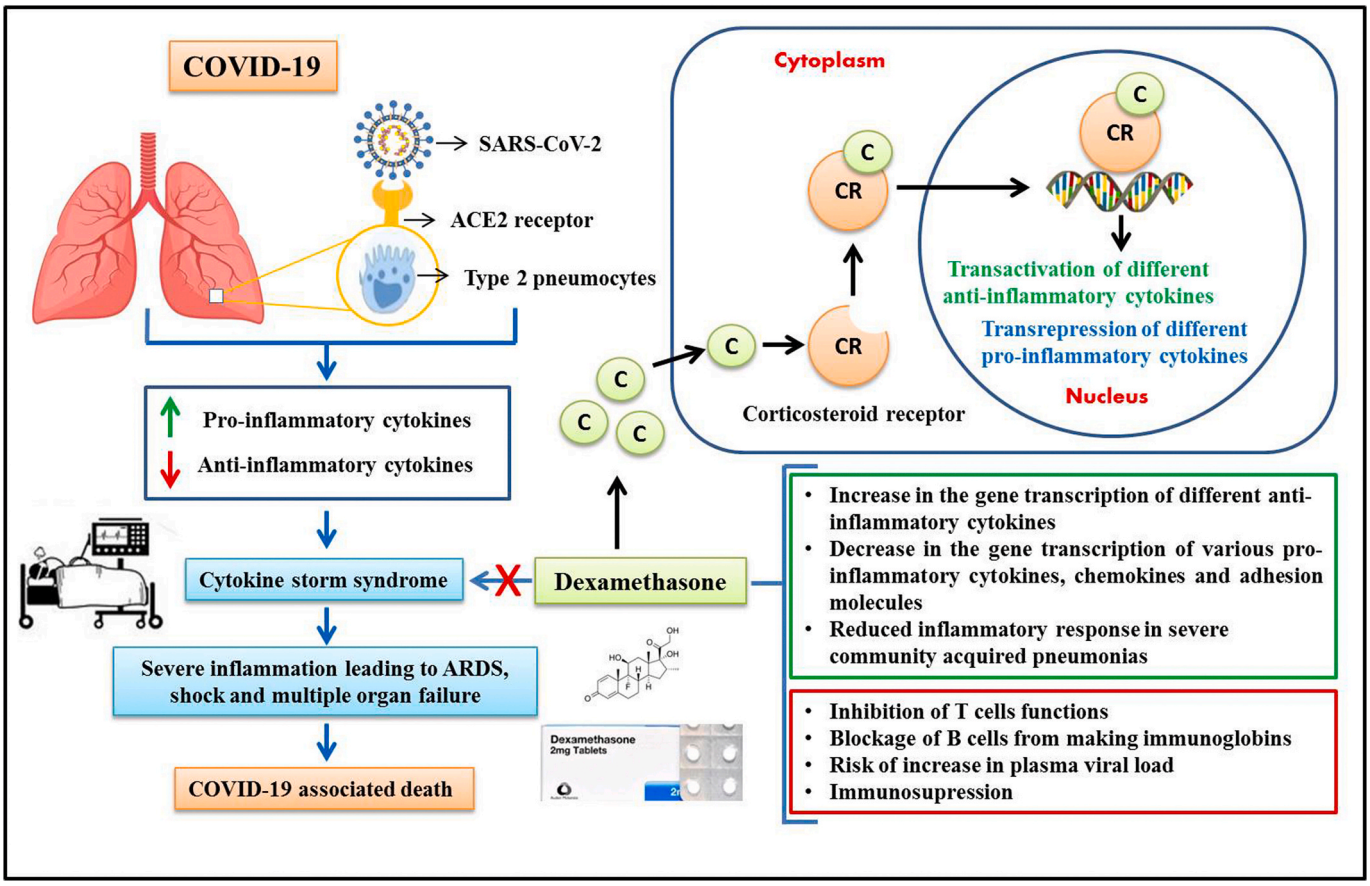

Fig. 1. An overview of dexamethasone and its mode of action in COVID-19 patients.

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CRediT authorship contribution statement

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Declaration of competing interest

We declare that we have no competing interests.

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