



Effectiveness of the Use of Dexamethasone in Treatment of Coronavirus Infections: A Systematic Review

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Abstract

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BACKGROUND: WHO declared the coronavirus disease (COVID)-19 outbreaks as a worldwide pandemic in March 2020. More than 1,500,000 confirmed cases have been diagnosed in more than 130 countries and regions, estimated to cause 93,000 deaths so far recorded on April 10, 2020. There is no vaccine or antiviral treatment for coronavirus.

METHODS: The literature sources from the research were obtained by searching for national and international journals. The journal is indexed in Google Scholar, PubMed, Science Direct, e-books, and others. Five journals were obtained, including a literature review, systematic review, and randomized controlled trials (RCT) discussing the use of dexamethasone in COVID-19 therapy, Middle East respiratory syndrome, and severe acute respiratory syndrome.

RESULTS: A study from Oxford University compared 2100 COVID-19 patients who received low and moderate potential dexamethasone at a dose of 6 mg/day for 10 days with 4300 COVID-19 patients who only received standard treatment for coronavirus infection. The results obtained in patients using ventilator mortality decreased from 40% to 28%, and patients using oxygen, the mortality rate decreased from 40% to 20%. The dexamethasone RCT study can reduce the death rate of 1 in 3 COVID-19 patients who received mechanical ventilation therapy and 1 in 5 patients who received oxygen therapy without mechanical ventilation but did not reduce patients' mortality rate who did not receive therapy oxygen.

CONCLUSION: The use of dexamethasone with oxygen therapy and mechanical ventilation can reduce mortality patients with COVID-19.

Introduction

Coronavirus (CoV) is an RNA virus of 120–160 nm particulate size. This virus infects mostly wildlife, including bats and camels. CoV is contagious with six types: Alphacoronavirus 229E, alphacoronavirus NL63, OC43 beta CoV, HKU1 beta-CoV, severe acute respiratory syndrome-CoV (SARS-CoV), and Middle East Respiratory CoV Syndrome (Middle East respiratory syndrome [MERS]-CoV) [1], [2].

In December 2019, due to an unknown virus, some patients in Wuhan, Hubei, China, were diagnosed with secondary pneumonia. From December 31, 2019, to January 3, 2020, there was a significant increase in cases marked by 44 cases reported. This disease has spread in separate provinces in China, Thailand, Japan, and South Korea for <1 month [3], [4].

The sample studied shows the etiology of a new type of CoV. The name of this disease was originally the 2019 novel CoV (2019-nCoV). The WHO

revealed a new name on February 11, 2020, CoV Disease (COVID-19), which was caused by the CoV-2 (SARS-CoV-2) extreme acute respiratory syndrome virus [5], [6].

In March 2020, the WHO proclaimed the COVID-19 epidemic a global pandemic. In more than 130 countries and regions, more than 1,500,000 confirmed cases are diagnosed, expected to cause 93,000 casualties as recorded on April 10, 2020 [7].

SARS-CoV-2 can cause various symptoms, including fever, fatigue, dry cough, myalgia, and difficulty breathing. There is evidence that SARS-CoV-2 variations have been produced from humans by respiratory outlets triggered by cough and sneezing [8]. There is no vaccine or antiviral treatment for CoV. Therefore, it is imperative to determine the treatment plan as soon as possible for the COVID-19 outbreak [9], [10], [11].

Dexamethasone is a corticosteroid preparation. Corticosteroids have an outstanding inhibitory effect on inflammatory factors and are typically used

as an alternative treatment for viral pneumonia. Glucocorticoids are steroid hormones with anti-inflammatory properties that block pro-inflammatory genes encoding cytokine, chemokine, cellular adhesion molecules, inflammatory enzymes, and inflammatory process receptors [12].

Dexamethasone was shown to be the first drug to prevent CoV deaths in more than 430,000 patients worldwide, based on a randomized controlled clinical trial (randomized controlled trials [RCT]) study in the United Kingdom. Dexamethasone can decrease mortality by around one-third in patients with CoV infection ventilators in these tests [13], [14], [15]. Based on these problems, we are interested in conducting a literature review on the effectiveness of using dexamethasone in the treatment of CoV infections.

Methods

This literature uses the method of literature review. Sources from the research were obtained by searching for national and international journals. The journal is indexed in Google Scholar, PubMed, Science Direct, e-books, and others. Five bulletins were obtained, including a literature review, systematic review, and RCT discussing the use of dexamethasone in COVID-19 therapy, MERS, and SARS.

Results

In a recovery trial study in March 2020 conducted at Oxford University, a RCT tested various potential therapies. The research compares 2100 patients receiving low to moderate potential 6 mg a day dexamethasone for 10 days, with 4300 patients getting normal CoV treatment only. The findings found

that dexamethasone had the most extraordinary effect relative to mildly ill people in seriously ill patients who used ventilators. The results of using dexamethasone in patients using a ventilator can reduce the risk of death from 40% to 28%. Dexamethasone also has an effect on patients taking oxygen therapy but not on the ventilator; an increase in mortality decreased from 40% to 20% [16].

Based on studies conducted by Chen *et al.*, corticosteroids were administered to 401 SARS patients, in which there were 152 patients in the critical category. The results showed that corticosteroids reduced mortality and treatment time in acute SARS patients. Dose offered for <7 days is low-moderate (to 0.5–1 mg/kg body weight or equivalent of methylprednisolone) [17].

Built upon the RCT dexamethasone report, the mortality rate was reduced by 1 in 3 COVID-19 patients receiving mechanical ventilation and by 1 in 5 COVID-19 patients receiving oxygen therapy without mechanical ventilation, but mortality rates were not reduced in those without oxygen therapy [18], [19].

Table 1 shows the use of dexamethasone in the preliminary report and some guidelines that have used dexamethasone as a therapy in the treatment of COVID-19.

Discussion

Since the first study was released in December 2019, COVID-19 has gained worldwide interest because of its similarity to SARS-CoV and MERS-CoV in causing fatal respiratory illnesses and possibly contributing to significant human infections and their economic effects. The use of corticosteroid treatment is still under consideration in patients with SARS and MERS that are close to COVID-19 [24], [25].

Corticosteroid therapy of patients with SARS is used regardless of the early anecdotal knowledge,

Table 1: Using dexamethasone

References	Year	Drug	Trial and clinical experience	Dosage
Horby Peters [20]	2020	Dexamethasone intravenous	A total of 2104 patients were assigned to receive dexamethasone and 4321 to receive usual care. Overall, 482 patients (22.9%) in the dexamethasone group and 1110 patients (25.7%) in the usual care group died within 28 days after randomization (age-adjusted rate ratio, 0.83; 95% confidence interval [CI], 0.75–0.93; $p < 0.001$) In the dexamethasone group, the incidence of death was lower than that in the usual care group among patients receiving invasive mechanical ventilation (29.3% vs. 41.4%; rate ratio, 0.64; 95% CI, 0.51–0.81) and among those receiving oxygen without invasive mechanical ventilation (23.3% vs. 26.2%; rate ratio, 0.82; 95% CI, 0.72–0.94) but not among those who were receiving no respiratory support at randomization (17.8% vs. 14.0%; rate ratio, 1.19; 95% CI, 0.91–1.55)	6 mg once daily for up to 10 day
Guidelines CHKD [21], [22]	2020	Dexamethasone intravenous and peroral	Dexamethasone should not be used in COVID-19 (+) patients who are: a) Otherwise healthy and do not require respiratory support Dexamethasone should be utilized in COVID-19 (+) patients with: a) Respiratory support (oxygen or invasive mechanical ventilation) b) An underlying condition requiring chronic steroid treatment, steroids should be continued c) An additional diagnosis where steroid therapy is appropriate	0.15 mg/kg once daily (Max: 6 mg)
Raymond [23]	2020	Dexamethasone	In the RECOVERY trial, dexamethasone was beneficial for participants treated seven or more days into the symptomatic phase, with the onset of hypoxemia. Importantly, there was a non-significant trend ($P = 0.14$) toward possible harm affecting participants without hypoxemia and not on mechanical ventilation. RECOVERY findings, therefore, support use of dexamethasone only for patients with hypoxemia, not those with milder disease. The data do not support the use of dexamethasone or other corticosteroids in the outpatient setting	6 mg/day

and it is comparable of patients with acute respiratory distress syndrome (ARDS) to radiological and histologic observations in essential diseases [26], [27]. In March 2003, the proposed high dose glucocorticoids should be used based on Chinese SARS treatment trials if the patient has a fever for more than three days or if radiological reports are indicative. Persistent pulmonary activity or gradual decline in Bronchiolitis obliterans, the radiographic picture with pneumonia and likeness of the histologic features to those of early ARDS in postmortem studies have prompted doctors in china use corticosteroids in combination with ribavirin for the treatment of SARS. In ARDS and particularly in Bronchiolitis obliterans with organizing pneumonia, corticosteroid therapy with ribavirin has been used with some success in the resolution of fever and lung opacities within two weeks [28].

Recovery trials conducted at Oxford University show that at the dose of dexamethasone tested, steroid treatment benefits may outweigh the potential harm posed. This research did not find any remarkable medication side effects. According to Anthonia, a deformed or hyperactive inflammatory reaction in patients with a ventilator leads to morbidity, mortality, and clear viral effects [13].

The corticosteroid partnership in SARS management may be complicated with acute lung injury (ALI)/ARDS. Excessive systemic inflammation has been identified in ARDS and B emission factors may lead to glucosteroid tolerance, which is related to relative adrenal insufficiency and further degradation of ARDS. Use methylprednisolone, which can be used to solve problems by recovering systemically. The present opinion thus indicates that ARDS steroid therapy can only be done on the basis of relative loss due to systemic inflammation and targeted at increasing systemic inflammation. The length of the steroid depends on the inflammatory length. In summary, appropriate advice for ALI/ARDS steroid administration involves the initialization of a sufficient steroid dosage at a time of relative adrenal insufficiency, discussed in terms of steroid application. Steroids need not, however, be delayed until ARDS continues [17], [29], [30].

Corticosteroids will dramatically reduce the concentrations of interleukin (IL)-8, monocyte protein-1, and induced protein-10 from days 5 to 8 after treatment. In further analysis, IL-10, IL-6, and tumor necrosis factor (TNF) levels were higher than average before intake. Corticosteroid treatment still decreases IL-10 but not IL-6 and TNF. The data show the benefits of steroid therapy in reducing the lungs' reserve response and protection [28], [31].

They observed that corticosteroids, large doses of 2019-nCoV pneumonia such as secondary infections, long-term complications, and extended-release of the virus were likely based on corresponding research. However, severe inflammation and

cytokine-related lung injuries can rapidly cause progressive pneumonia in critically ill patients. Doctors of the Chinese Thoracic Community have formed a consensus of experts on pneumonia corticosteroids 2019-nCoV. Under the expert's agreement on the basics of use with corticosteroids to be discussed;(1) The role of corticosteroids in suppressing the production of dysregulated cytokines patient with pneumonia in 2019-nCoV (2) Corticosteroid must be used with caution in a critically diseased patient with pneumonia in 2019-nCoV; (3) with hypoxia patients [32].

Conclusion

The use of dexamethasone with oxygen therapy and mechanical ventilation can reduce mortality patients with COVID-19.

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