

Effectiveness of Dexamethasone for Acute Respiratory Distress Syndrome (ARDS) due to Coronavirus: A Systematic Review

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Abstract: Estimates have suggested that up to 12% of patients hospitalized with COVID-19 have required invasive mechanical ventilation, with the majority developing acute respiratory distress syndrome (ARDS). Corticosteroids are the most potent anti-inflammatory drugs. The therapeutic mechanism of corticosteroids might base on attenuating the action of many cytokines that participated in the inflammatory reaction associating severe CAP. However, the clinical and efficacy of dexamethasone in COVID-19 patients are currently unclear, so research is needed to know the effectiveness of dexamethasone therapy in patients with COVID-19. This research uses a structured analysis focused on preferred reporting items for systematic reviews and meta-analyses (PRISMA) in order to classify all existing literature with appropriate keywords. The database using PRISMA (Preferred Reporting Items for Systematic Reviews & Meta Analyses) for instruments and used flowcharts based on the 2009 PRISMA checklist and based on inclusion and exclusion criteria, we found that dexamethasone resulted in a significant increase in the number of ventilator-free days (days alive and free of mechanical ventilation) over 28 days in patients with COVID-19 and moderate or severe ARDS.

Keywords: SARS-CoV-2; COVID-19; Dexamethasone

1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a major health concern since the World Health Organization declared coronavirus disease 2019 (COVID-19) a pandemic on 11 March 2020. COVID-19 is the disease caused by the SARS-CoV-2 virus which is ribonucleic acid viruses. The viruses may infect in human especially in respiratory, gastrointestinal, hepatic, and central nervous systems. The incidence of SARS-CoV-2 first appeared in Wuhan, China and then spread throughout the world with a rapidly increasing incidence which from the latest WHO data showed in 3 months COVID-19 has been infected 209 countries and every day there are approximately 5,798 people infected with COVID-19 and a very high mortality rate of 62,773 people who have died with high morbidity as well as 1.133046 people who have been diagnosed with COVID-19.⁽¹⁻⁴⁾

Based on the latest data from John Hopkins University, shows the first place is USA with an incidence of 7.191.061 people, second place in India with an incidence of 6.225.763 people, third place in Brazil with an incidence of 4.777.522 people. Indonesia ranks 23rd with a total of 287.008 cases.⁽⁵⁾ Based on the latest data from the Republic of Indonesia Ministry of Health, the highest number of COVID-19 cases in Indonesia is in DKI Jakarta with a total of 72.577 cases, the second place in East Java with a total of 43.450 cases, the third is Central Java with a total of 22.205 cases. While on the island of Sulawesi the first ranks is South Sulawesi with a total of 15.501 cases.⁽⁶⁾

The pressures of a global pandemic make healthcare workers around the world are prescribing drugs off-label for which there is only very low quality evidence. Despite global efforts to identify effective interventions for the prevention and treatment of covid-19, which have resulted in 2342 trials completed or underway, evidence for effective treatment remains limited.⁽⁷⁾

Estimates have suggested that up to 12% of patients hospitalized with COVID-19 have required invasive mechanical ventilation,^(8,9) with the majority developing acute respiratory distress syndrome (ARDS).⁽¹⁰⁾ Diffuse alveolar damage with hyaline membranes,⁽¹¹⁾ hallmarks of ARDS, have been found on pulmonary histological examination of patients with COVID-19. Furthermore, an uncontrolled inflammatory state is frequent with COVID-19 and may contribute to multiorgan failure in these patients.^(12,13)

Corticosteroids are the most potent anti-inflammatory drugs. The therapeutic mechanism of corticosteroids might base on attenuating the action of many cytokines that participated in the inflammatory reaction associating severe CAP. In addition, with the proposition of critical illness-related corticosteroid insufficiency (CIRCI), corticosteroids replacement therapy has been gradually accepted in critical illness, such as septic shock and ARDS. Based on researched from Horby et al, said that in patients hospitalized with Covid-19, the use of dexamethasone resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone.^(14,15)

However, the clinical and efficacy of dexamethasone in COVID-19 patients are currently unclear. Given this background, the present review investigates the effectiveness of dexamethasone therapy in patients with Acute Respiratory Distress Syndrome (ARDS) due to Coronavirus by applying a systematic review of the literature currently available. The main objective is to investigate whether there is a clinical necessity, or therapeutic justification, for the use of dexamethasone in patients with COVID-19.

2. METHOD

Several search strategies are used to identify This systematic review followed PRISMA guidelines (Preferred Reporting Items for Systematic Reviews & Meta Analyses) for instruments and using the flowchart based on the 2009 PRISMA checklist, eliminating articles that are not relevant to the criteria of identification, screening, eligibility, and finally

downloading the article which is relevant. The investigators independently conducted a literature search using NCBI, NEJM, Nature, Wiley and JAMA then use advanced search. The database search was run from 2019 until 2020. All studies reporting information regarding the use of dexamethasone in COVID-19 were included. In PubMed, the following search strategy was used: “dexamethasone AND (COVID-19 OR SARS-CoV-2)”. The strategy was then adapted for the other databases. The researcher found 1467 documents based on full text access for free or paid documents, documents based on publication year (2019-2020). Then reselection the journal by title and abstract into 51 documents, then we find 2 documents that meet the research criteria and then we analyze the document. The document inclusion criteria that we deem appropriate for conducting a systematic review are participants who had a validated diagnosis of COVID-19, irrespective of stage, or severity; intervention: use of dexamethasone; comparison: patients affected by COVID-19 not taking dexamethasone. Studies are excluded if they cannot be accessed, do not have reliable references, are expensive.

3. RESULTS

The researcher identified the database using PRISMA (Preferred Reporting Items for Systematic Reviews & Meta Analyses) for instruments and used flowcharts based on the 2009 PRISMA checklist and based on several criteria such as documents that can be accessed for free or paid full text, in English and published in 2019 until 2020 and following inclusion and exclusion criteria. We obtained 1467 documents, then based on titles and abstracts we obtained 51 relevant studies and 1416 irrelevant studies. Then based on the inclusion and exclusion criteria obtained 2 journals that match the criteria, the study discusses the overall COVID-19 or SARS-CoV-2 disease such as epidemiology, characteristics, pathogenesis, cytokine storm, and anti-viral drugs for COVID-19 or SARS-CoV-2, as well as some mortality and morbidity data from COVID-19. Then 2 studies that were relevant and had eligibility were analyzed systematically.

Based on two randomised controlled trials one have been published in peer reviewed journals, and other only as preprints. Both of the trials were registered, published in English and evaluated treatment in patients admitted to hospital with covid-19. Table 1 presents the characteristics of the included studies.

Tabel 1. Study Characteristics

Study	Publication status, registration No	No of participants	Country	Mean age (years)	Men (%)	Type of care, comorbidities	Severity	Treatments (dose and duration)	Outcomes
Tomazini, Bruno M., et al, 2020 ⁽¹⁶⁾	Published, NCT04327401	299	Brazil	61	63	Inpatient; Hypertension 66%; Diabetes (42%); Obesity (27%); Heart failure	Moderate-Severe (100%)	Dexamethasone (20 mg/day intravenously for 5 days, continued 10 mg/day for 5 days or	Mortality; mechanical ventilation; adverse events leading to discontin

						(0,07%)		until ICU discharge); standard care	uation; duration of hospital stay
Horby 2020; RECOVERY ⁽¹⁵⁾	Published, NCT04381936	6425	UK	66.2	63.6	Inpatient; heart disease (27.3%); diabetes (24.1%); chronic lung disease (21.0%); tuberculosis (0.4%)	NR	Dexamethasone (6 mg/day for 10 days); standard care	Mortality; mechanical ventilation; duration of hospital stay

NR=not reported

Mortality

Two randomised controlled trials including 6724 reported mortality. Tomazini, Bruno M., et al, 2020 found that there was no significant difference in all-cause mortality at 28 days (56.3% in the dexamethasone group vs 61.5% the standardcare group; hazard ratio,0.97;95%CI,0.72 to1.31;P = .85) different with Horby found that 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 to 0.81).^(15,16)

Duration of hospital stay

Two randomised controlled trials including 6724 reported duration of hospital stay. Compared with standard care, duration of hospitalisation was shorter in patients who received dexamethasone (median, 12 days vs. 13 days) and a greater probability of discharge alive within 28 days. The greatest effect regarding discharge within 28 days was seen among patients who were receiving invasive mechanical ventilation at randomization.^(15,16)

Duration of mechanical ventilation

Three randomised controlled trials enrolling 6724 total participants reported duration of mechanical ventilation. The risk of progression to

invasive mechanical ventilation was lower in the dexamethasone group than in the usual care group (risk ratio, 0.77; 95% CI, 0.62 to 0.95). Mechanical ventilation duration 11.2 to 13.8 days for the dexamethasone group vs 12.7 to 15.1 days for the standard care group.^(15,16)

4. CONCLUSION

Based on a systematic review it can be concluded that the dexamethasone have potential effect to increase in the number of ventilator-free days the For Acute Respiratory Distress Syndrome (ARDS) due to Coronavirus by decreasing the duration of hospital stay, duration of mechanical ventilation and mortality.

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