



CODEN [USA] : IAJPB

ISSN : 2349-7750

## INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

<http://doi.org/10.5281/zenodo.4008282>
Available online at: <http://www.iajps.com>

Review Article

### “DEXAMETHASONE ADJUNCTIVE STANDARD CARE IN REDUCING MORBIDITY AND MORTALITY RATE IN SEVERE COVID-19 PATIENTS: A SHORT REVIEW”

<sup>1\*</sup>Mehshikhes, Ruqayah K

<sup>1</sup>Almaarefa University, Pharmacy College, Riyadh, Saudi Arabia

\*Mouwasat Hospital, Pharmacy Department, Qatif, Saudi Arabia

Article Received: June 2020

Accepted: July 2020

Published: August 2020

**Abstract:**

**Introduction:** Corticosteroids have been used for acute respiratory distress (ARDS) for more than 50 years. Recently, corticosteroids, specifically Dexamethasone, used in critically ill COVID-19 patients for respiratory support in which some evidence showed significant improvement in their condition's outcome.

**Method:** Search had been conducted until August 21, 2020 through looking for keywords, COVID-19 and dexamethasone, via PubMed, Cochrane Library, and MedRxiv. We reviewed all kinds of studies published lately from January 2020 to August 2020.

**Results:** The preliminary findings of Recovery Trial are indicating benefits related to severe COVID-19 patients' mortality rate and their hospitalization duration. Another study showed reduction in C- reactive protein and length of study. A Spanish trial is ongoing conducted on similar patients' criteria to evaluate the mortality rate and hospitalization duration.

**Discussion:** Giving Dexamethasone beside standard care showed significant results on COVID-19 mechanically ventilated patients. However, practitioners should take precaution in patient selection and patients who need Dexamethasone and patients who do not in order to prevent any adverse effects e.g. hyperglycemia and allergic reactions.

**Conclusion:** Dexamethasone is still controversial when it comes to COVID-19 patients. Yet, it might be considered for ARDS patients with careful monitoring. We suggest more trials to prove the effect.

**Keywords:** COVID-19, Coronavirus, Dexamethasone, ARDS, Corticosteroids

**Corresponding author:****Mehshikhes,**

Qatif 31911, Saudi Arabia

Roqaya91@gmail.com

+966545834478

QR code



Please cite this article in press Mehshikhes et al, *Dexamethasone Adjunctive Standard Care In Reducing Morbidity And Mortality Rate In Severe Covid-19 Patients: A Short Review.*, Indo Am. J. P. Sci, 2020; 07(08).

**INTRODUCTION:**

Steroids were frequently used during SARS-COVID-2 along with other medications to reduce acute respiratory distress syndrome (ARDS)<sup>1</sup>. Since December 2019, the whole world restricted due to COVID-19 (Corona virus) spread. The pharmacotherapy studies still ongoing and there is no effective medication can be used solely to eradicate COVID-19. Many of the studies indicated that Dexamethasone, a synthetic glucocorticoid which has immunosuppression and anti-inflammatory actions<sup>2</sup>, can decrease the morbidity and mortality rate in severe COVID-19 patients. This is because critically ill patients develop acute respiratory distress syndrome (ARDS) due to excessive inflammatory response as a result of cytokine storm. Anti-inflammatory drugs like corticosteroids can be used to effectively reduce the effect of this cytokine storm and lung dysfunction<sup>3</sup>.

**Inclusion Criteria:**

COVID-19 patients from all ages  
Severe COVID-19 patients  
COVID-19 Intubated patient  
COVID-19 with ARDS condition patients

**Exclusion Criteria:**

Dexamethasone as anti-emetic treatment for COVID-19 patients  
Single Case report  
Non-English studies  
Pregnant COVID-19 women

**METHOD:**

We conducted a vast search on PubMed, Cochrane Library, and MedRxiv database with the following keywords: Covid-19, Dexamethasone, with a Boolean inter-position of "AND" was made up from January 1, 2020 till August 21, 2020. Furthermore, all the articles were carefully analyzed and presented in the text.

Author, Title & Year	Study Design	Control Group	Treatment Group	Findings
<sup>4,5,6</sup> Horby P et al., 2020 (UK RECOVERY Trial) Phase III	Randomized controlled trial, open label	4321 patients allocated with usual standard treatment	2104 patients allocated with standard care plus Dexa* 6mg OD*, PO* or IV* for 10days or until discharge	Primary outcome: Rate of mortality is 21.6% for TG* vs. 24.6% for CG*  Secondary outcome: Duration of hospitalization is 12days for TG vs. 13days for CG
<sup>7</sup> Selvaraj V et al., 2020	Case series	-	21 moderate to severe hospitalized patients treated with Dexa* alone or beside other medications.	77.98% reduction in CRP* after the initiation of Dexa*. 71.42% reduction in length of hospitalization.
<sup>8</sup> Tomazini B et al., 2020 Phase III	Randomized control trial, open label	Standard tx*	Standard tx* plus Dexa* 20mg IV* for 5days, followed by 10mg IV* for 5days	Terminated
<sup>9</sup> Villar J et al., 2020 Phase IV	Randomized, controlled, open-label, parallel	Standard care	Dexa* + standard care	Ongoing

\*Dexa: Dexamethasone, OD: once daily, PO: oral, IV: intervenes, TG: treatment group, CG: control group, CRP: C-reactive protein, Tx: treatment

**RESULTS:**

*Horby P et al., 2020 (UK RECOVERY Trial):*

Randomized control trial (RCT) conducted on 176 National Health Service (NHS) hospitals in the United Kingdom (UK). It conducted on 15,000 participants so far. The preliminary outcomes have been released on 6,425 patients tested positive with

COVID-19. Participants are at least 18 years old and the mean age is 66.1 years old. They randomized the eligible patients for control group (4321 participants) with standard care and intervention group (2104 participants) with standard care plus Dexamethasone 6mg once daily (orally or intravenous) for 10days. After following up for 28

days, the primary outcome indicates that Dexamethasone patients' mortality rate reduced by 21.6% compared to 24.6% for usual care patients. It is, also, shows that the mortality rate significantly reduced in dexamethasone patients on invasive mechanical ventilation by 35% compared to dexamethasone patients receiving oxygen without mechanical ventilation. However, no evidence shows benefits for those who don't receive respiratory support. In addition, the secondary outcome related to the hospital stay in dexamethasone patients is shorter (12 days vs. 13 days for usual care patients) and greater probability of discharge within 28 days for those are on mechanical ventilation, but it is lower for patients on oxygen supplement. Peer review of this study is ongoing in Phase III.

*Selvaraj V et al., 2020:*

Case series conducted on 21 patients moderate to severe patient evaluated based on several characteristics including, at least 30% increase in C-reactive protein (CRP) level within 36 hours of admission, and escalating oxygen requirement. 61.9% of the patients were male their mean age were  $60 \pm 15.77$  years. Patients have some comorbidities such as, diabetes mellitus (38.09%) and hypertension (61.9%). After initiation of Dexamethasone there was 77.8% reduction in CRP levels. The mean CRP levels at the admission were  $129.52 \pm 72.05$  mg/L (Peak levels were  $185.09 \pm 76.34$  mg/L). At the time of discharge, mean levels were  $40.73 \pm 49.28$  mg/L. Also, 71.42% of patients discharged with a mean length to stay of 7.8 days. However, dexamethasone was discontinued early in one patient because of hyperglycemia.

*Tomazini B et al., 2020 (Brazilian trial):*

The study included 350 patients with moderate to severe ARDS. They randomized participants to control group with standard treatment and treatment group with Dexamethasone 20mg IV once daily followed by 10mg IV once daily. The study has been terminated in Phase III based on Recovery Trial results.

*Villar J et al., 2020 (Spanish trial):*

Randomized controlled trial conducted on 200 hospitalized and mechanically ventilated adult patients due to severe respiratory symptoms by COVID-19. The trial is evaluating the rate of mortality among the patients and the hospitalization duration period. Participants are given Dexamethasone 20mg, IV from day 1 to day 5, and 10mg from day 6 to day 10. The study still ongoing in Phase IV. It should be completed on February 2021.

## DISCUSSION:

Dexamethasone has been showed remarkable progress in particular case with COVID-19, such as ventilated patients, while in other cases, it has no benefits or may be caused harm.

A recent study of a randomized controlled trial, COVID-19 patients who have given Dexamethasone demonstrated benefit over those who solely received standard care. It indicated a reduction in mortality by one- third in mechanical ventilated patients and one- fifth in patients who needed oxygen only <sup>10</sup>. Few months ago, the Infectious Diseases Society of America (IDSA) did not recommend using corticosteroids in their guideline for COVID- 19 patients based on data about previous viruses from the same family (coronaviruses) which showed no benefit of corticosteroids administration. Yet, after the significant outcomes of RECOVERY trial (UK), this guideline was updated to advise giving glucocorticoids (preferably Dexamethasone) for severe COVID-19 patients, but recommended to avoid it for patients without hypoxemia <sup>11 12</sup>. In addition, in a recent RCT study (Keller M et al., 2020) conducted on 2,998 COVID-19 patients, glucocorticoids (no specific drug had mentioned) help those who have elevated CRP, whereas patients with lower CRP may have harmed them <sup>13</sup>.

However, practitioners must be careful before the initiation of Dexamethasone or any corticosteroids. In (Selvaraj V et al., 2020), patients with low CRP did not get any benefits by using Dexamethasone and they may get its adverse effects more often than patients with elevated CRP. Also in the same study, some of the patients who included had diabetes mellitus. As a result, dexamethasone was discontinued early for one patient due to hyperglycemia. Furthermore, in a recent Chinese study (Ling Y et al. 2020), showed that using glucocorticoid in mild patients may delay the virus RNA clearance compared to severe patients <sup>14</sup> which means longer hospitalization duration. Finally, in order to prevent patients from exacerbations of dexamethasone, healthcare giver must weight benefits against risks for every single patient to avoid dexamethasone adverse effects and reduce the mortality and morbidity rate.

## CONCLUSION:

No specific treatment yet had been shown a reduction in COVID-19- related mortality rate barring dexamethasone<sup>15</sup>. Although some studies, which used Dexamethasone for severe COVID- 19 patients, showed progress and positive outcomes, Dexamethasone usage still controversial doubtful. Evidence still insufficient, thus, more randomized control trails are needed to support dexamethasone usage in corona virus.

**Acknowledgment:**

No potential conflict of interest

No financial funding

**REFERENCES:**

- 1- Mattos-Silva, P et al. 2020. Pros and cons of corticosteroid therapy for COVID-19 patients. [ONLINE] Available at: <https://doi.org/10.1016/j.resp.2020.103492>
- 2- Horby P et al. 2020. Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report. [ONLINE] Available at: <https://www.nejm.org/doi/pdf/10.1056/NEJMoA2021436?articleTools=true>
- 3- Abdolahi et al. Trials. 2020. [ONLINE] Available at: <https://doi.org/10.1186/s13063-020-04499-5>
- 4- Horby P et al. (2020). Effect of Dexamethasone in Hospitalized Patients with COVID-19: Preliminary Report. [ONLINE] Available at: <https://doi.org/10.1101/2020.06.22.20137273>
- 5- Horby P et al. 2020. Trial. [ONLINE] Available at: <https://clinicaltrials.gov/ct2/show/study/NCT04381936>
- 6- Lester M et al. 2020. The use of dexamethasone in the treatment of COVID-19. [ONLINE] Available at: <https://doi.org/10.1016/j.amsu.2020.07.004>
- 7- Selvaraj V, Dapaah-Afriyie K, Finn A, Flanigan TP. Short-Term Dexamethasone in Sars-CoV-2 Patients. R I Med J (2013). 2020;103(6):39-43. Published 2020 Jun 19.
- 8- Tomazini BM et al. 2020. COVID-19-associated ARDS treated with DEXamethasone (CoDEX): Study design and rationale for a randomized trial. [ONLINE] Available at: <https://doi.org/10.1101/2020.06.24.20139303>
- 9- Villar, J., Añón, J.M., Ferrando, C. et al. Efficacy of dexamethasone treatment for patients with the acute respiratory distress syndrome caused by COVID-19: study protocol for a randomized controlled superiority trial. Trials 21, 717 (2020). <https://doi.org/10.1186/s13063-020-04643-1>
- 10- Horby P et al. (2020). Effect of Dexamethasone in Hospitalized Patients with COVID-19: Preliminary Report. [ONLINE] Available at: <https://doi.org/10.1101/2020.06.22.20137273>
- 11- Mattos-Silva P et al. 2020. Pros and cons of corticosteroid therapy for COVID-19 patients. [ONLINE] Available at: <https://doi.org/10.1016/j.resp.2020.103492>
- 12- Bhimraj A et al. 2020. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. [ONLINE] Available at: <https://www.idsociety.org/globalassets/idsa/practice-guidelines/covid-19/treatment/idsa-covid-19-gl-tx-and-mgmt-v2.1.0.pdf>
- 13- Marla J Keller, MD, Elizabeth A Kitsis, MD, MBE, Shitij Arora, MD, Jen-Ting Chen, MD, MS, Shivani Agarwal, MD, MPH, Michael J Ross, MD, Yaron Tomer, MD, William Southern, MD, MS, Effect of Systemic Glucocorticoids on Mortality or Mechanical Ventilation in Patients With COVID-19. *J. Hosp. Med* 2020;8:489-493. Published Online First July 22, 2020. doi:10.12788/jhm.3497
- 14- Ling, Yun et al. “Persistence and clearance of viral RNA in 2019 novel coronavirus disease rehabilitation patients.” Chinese medical journal vol. 133,9 (2020): 1039-1043. doi:10.1097/CM9.0000000000000774
- 15- Singh K et al. 2020. Role of corticosteroid in the management of COVID-19: A systemic review and a Clinician’s perspective. [ONLINE] Available at: <https://doi.org/10.1016/j.dsx.2020.06.054>