

Title	Summary of evidence: Use of corticosteroids in Covid-19 patients.
Identification code	03192020LB
Requesting Area	COVID-191. Keralty Public Health Crisis Committee
Name	COVID-191. Keralty Public Health Crisis Committee
Date of response	19 03 2020

Question:

1. Is the use of corticosteroids indicated as an adjuvant therapy in patients with respiratory tract infection due to coronavirus COVID-19?

Methodology:

A fast-systematic search was performed. (Fast Systematic Search Manual. Institute of Clinical Global Excellence. 2019)

Terms of search: COVID 19, corticosteroids, glucocorticoids

Types of studies: clinical practice guidelines, literature systematic reviews, meta-analysis, clinical trials and other primary studies.

Source of information: PubMed, Cochrane Library, BMJ Best practice

Background:

The role of corticosteroids in the treatment of severe viral respiratory infections is controversial with respect to the risks and benefits in critically ill adult patients. Cochrane’s February 2019 systematic review, which included 21 observational studies, found that the adjuvant corticosteroid therapy is associated with a higher mortality rate in patients with influenza infection. Despite this, the evidence was low in quality and insufficient to determine the effectiveness of the corticosteroids in these patients (1).

Recently, corticosteroids have been used in some patients with COVID-19 without effective results and their use is not recommended (2). The WHO (as well as other pneumonia international guidelines) do not recommend standard use of systemic corticosteroids for viral pneumonia or acute respiratory distress syndrome unless they are indicated for another reason (2). At the moment, a randomized clinical trial that investigates the use of corticosteroids in patients with COVID-19 is in progress (3).

Summary of evidence:

1. Characteristics of evidence:

15 documents were found. Seven documents were excluded (4 did not include the population, two did not include the intervention in study, among these there was a systematic review and a ECA protocol). The remaining 8 documents were analyzed in complete text (three letters to the editor, four reviews and a descriptive study) (2,4,10).

Identification --- Records identified in the data bases (N-15) ---PubMed 13, Cochrane Library: 1, BMJ Best practice: 1

Screening: Screened records: n=15

Excluded records: PubMed: 6, Cochrane Library: 1

Eligibility: Complete text evaluated articles – n:8 – Included records- PubMed: 3 letters, 4 reviews, 1 descriptive.

Excluded articles in complete text with justification: n=0, type of study: 0, population=0

Included: included studies: n=8

Findings:

- To date, the available evidence about the use of corticosteroids in patients with COVID-19 is controversial.
- Some authors agree not to recommend corticosteroids for the treatment of patients with COVID-19 in a mild or early stage. The early use of corticosteroids could delay the elimination of the virus and increase the mortality risk.
- The February 2020 consensus of the Chinese Thoracic Society suggests to follow the four basic principles for the use of corticosteroids in critical patients with 2019-nCoV pneumonia:
 1. The benefits should outweigh the risks, and this must be determined carefully before the use of corticosteroids.
 2. The corticosteroids should be used with caution in critical patients with 2019-nCoV pneumonia
 3. For patients with hypoxemia, due to underlying diseases or who use corticosteroids regularly for chronic diseases, the additional use of corticosteroids should be cautious.
 4. The dose should be low to moderate (< 0,5-1mg per day of methylprednisolone or its equivalent) and the duration of the treatment should be short (< 7 days).

Once the previous findings were discussed with the leaders of the Intensive Care Units of Clinica Universitaria Colombia and Clinica Reina Sofia, and taking into account the actual state of evidence, the following recommendations are proposed with respect to the use of corticosteroids in intensive care unit adult COVID-19 patients:

Expert recommendations:

1. The use of systemic corticosteroids in adult ICU patients with COVID-19 and Adult Respiratory Distress Syndrome (ARDS) in an early phase is not recommended due to the fact that corticosteroid may increase the risk of mortality.
2. The use of systemic corticosteroids in adult ICU patients with COVID-19 and Adult Respiratory Distress Syndrome (ARDS) in a late phase with pathologic lymphoproliferative response without bacterial infection is left to consideration of the clinical team. In the case that the clinical team decides to use corticosteroids, the experts suggest to start with an infusion of methylprednisolone at a dose of 0.5-1mg/kg/day for 7 to 14 days (5,11,12).

References:

1. Lansbury L, Rodrigo C, Leonardi-Bee J, Nguyen-Van-Tam J, Lim WS. Corticosteroids as adjunctive therapy in the treatment of influenza. *Cochrane Database of Systematic Reviews* 2019, Issue 2. Art. No.: CD010406. DOI:10.1002/14651858.CD010406.pub3. Available from: <https://www.cochranelibrary.com/es/cdsr/doi/10.1002/14651858.CD010406.pub3/full#CD010406-abs-0001>
2. BMJ Best practice. COVID-19. Last updated: Mar 12, 2020. Available from: <https://bestpractice.bmj.com/topics/en-gb/3000168/pdf/3000168/COVID-19.pdf>
3. Zhou YH, Qin YY, Lu YQ, et al. Effectiveness of glucocorticoid therapy in patients with severe novel coronavirus pneumonia: protocol of a randomized controlled trial. *Chin Med J (Engl)*. 2020 Mar 5 [Epub ahead of print]. Abstract
4. Zhou W, Liu Y, Tian D, Wang C, Wang S, Cheng J, et al. Potential benefits of precise corticosteroids therapy for severe 2019-nCoV pneumonia. *Signal Transduct Target Ther*. 2020 Feb 21;5:18. doi: 10.1038/s41392-020-0127-9.
5. Shang L, Zhao J, Hu Y, Du R, Cao B. On the use of corticosteroids for 2019-nCoV pneumonia. *Lancet*. 2020 Feb 29;395(10225):683-684. doi: 10.1016/S0140-6736(20)30361-5.
6. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet*. 2020 Feb 15;395(10223):473-475. doi: 10.1016/S0140-6736(20)30317-2.
7. Fu Y, Cheng Y, Wu Y. Understanding SARS-CoV-2-Mediated Inflammatory Responses: From Mechanisms to Potential Therapeutic Tools. *Viol Sin*. 2020 Mar 3. doi:10.1007/s12250-020-00207-4.
8. Xu K, Cai H, Shen Y, Ni Q, Chen Y, Hu S, et al. [Management of corona virus disease-19 (COVID-19): the Zhejiang experience]. *Zhejiang Da Xue Xue Bao Yi Xue Ban*. 2020 Feb 21;49(1):0. Chinese.
9. Arabi YM, Fowler R, Hayden FG. Critical care management of adults with community-acquired severe respiratory viral infection. *Intensive Care Med*. 2020. Feb;46(2):315-328. doi: 10.1007/s00134-020-05943-5.
10. Ling Y, Xu SB, Lin YX, Tian D, Zhu ZQ, Dai FH, et al. Persistence and clearance of viral RNA in 2019 novel coronavirus disease rehabilitation patients. *Chin Med J (Engl)*. 2020 Feb 28. doi: 10.1097/CM9.0000000000000774.
11. Meduri GU, Bridges L, Shih MC, Marik PE, Siemieniuk RAC, Kocak M. Prolonged glucocorticoid treatment is associated with improved ARDS outcomes: analysis of individual patients' data from four randomized trials and trial-level meta-analysis of the updated literature. *Intensive Care Med*. 2016;42(5):829-40.
12. Meduri GU, Siemieniuk RAC, Ness RA, Seyler SJ. Prolonged low-dose methylprednisolone treatment is highly effective in reducing duration of mechanical ventilation and mortality in patients with ARDS. *J Intensive Care*. 2018 Aug 24;6:53. doi: 10.1186/s40560-018-0321-9.