Outcome of early short-course corticosteroids in hospitalized patients with coronavirus disease-2019 (COVID-19): A report from a Saudi Arabian hospital

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Abstract:
BACKGROUND: The efficacy of corticosteroid use in patients with acute respiratory illness due to coronavirus disease-2019 (COVID-19) is unclear. In this study, we describe the clinical course of COVID-19 patients who received early course of corticosteroid treatment in patients with severe respiratory distress secondary to COVID-19.

MATERIALS AND METHODS: The clinical course of 30 COVID-19 patients admitted to King Fahad Military Medical Complex in Dhahran from the period of late March 2020 till June 2020 was assessed and described. All the 30 patients received steroids. Data on demographics, medical history, laboratory findings, chest radiology, medication use, and clinical outcomes were extracted from patients’ records. Data was entered and analyzed with SPSS software.

RESULTS: A total of 30 patients admitted with COVID-19 were included. The mean age 52.53 years (SD=16.31) with a range from 22-98 years; 73.3% were males. About two-thirds of the patients at least had comorbidities; most common were diabetes (46.7%) and hypertension (46.7%), and chronic heart disease (16.7%). About 57% patients had fever, cough, and shortness of breath. The median C-reactive protein (CRP) level was 87.5 mg/dL (IQR 45.0 – 165.65); 46.7% had CRP levels >120 mg/dL. The median white blood cell, lymphocytes, and platelet counts were 4.39, 1.05, and 212 K/μL, respectively. All the patients received corticosteroids; 17 (56.7%) patients were given IV methylprednisolone and 13 (43.3%) received dexamethasone tablets. Of the total patients, 13 (43.3%) patients developed acute respiratory distress syndrome (ARDS); 17 (56.7%) required oxygen, 10 (33.3%) were admitted to Intensive Care Unit (ICU), and 7 (23.3%) required mechanical ventilation. All the patients improved and were discharged home well.

CONCLUSION: Early use of oral corticosteroids in patients with higher CRP levels may lead to better outcomes and may lower risk of transfer to ICU and use of mechanical ventilation.

Keywords: COVID-19, dexamethasone, glucocorticoids, methylprednisolone, Saudi Arabia

Introduction

The outbreak of coronavirus disease-2019 (COVID-19) became a global pandemic of an acute infectious disease, especially with features of possible asymptomatic carriers and high infectivity.[1] It causes acute respiratory distress syndrome and results in a high mortality rate if pneumonia is involved.[2]

There is no specific treatment for COVID-19, a clinical syndrome caused by severe acute respiratory syndrome (SARS)-CoV-2...
infection. Corticosteroids have been widely used for patients with COVID-19, especially those with critical illness, despite its controversial efficacy.[3] However, severely ill COVID-19 patients were found to have lymphopenia, neutrophilia, and higher levels of multiple cytokines, suggesting a role of dysregulated systemic inflammation leading to poor prognosis.[4]

Corticosteroids are not recommended for the treatment of viral pneumonia. The use of corticosteroids in a septic status is beneficial because of the hardening of the host’s insusceptible reaction to bacterial toxin release.[3] Patients with serious COVID-19 can build up a fundamental provocative reaction that can prompt lung injury and multisystem organ damage.[3] It has been recommended that the powerful calming impact of corticosteroids may lessen or relieve the inflammatory impact. Previous valuable clinical results were accounted for when corticosteroids (for the most part prednisone or methylprednisolone) were utilized in patients with other respiratory infections regardless of the causative organisms.[3] In patients with pneumocystis pneumonia and hypoxia, prednisone treatment reduced mortality. Be that as it may, in episodes of other novel coronavirus diseases (i.e., Middle East respiratory condition [MERS] and SARS), corticosteroid treatment was related with postponed infection clearance.[3] In extreme pneumonia brought on by flu, treatment with corticosteroids seems to result in adverse clinical outcome, including bacterial superinfection and mortality.[6]

The Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial showed improved mortality in patients who received dexamethasone; however, it neither examined other corticosteroids nor evaluated their use in patients who were not critically ill.[7] We present here clinical progression and outcome for 30 COVID-19 patients admitted to King Fahad Military Medical Complex (KFMMC) in Dhahran, Saudi Arabia.

Materials and Methods

A total of 30 patients were included, all of them had corticosteroid treatment. Administration of corticosteroid was defined as systemic use (oral, or intravenous) of corticosteroids. These patients were admitted on the basis of the severity of the symptoms. Data on demographics, medical history, laboratory findings, chest radiology, medication use, and clinical outcomes were extracted from patients’ records.

Ethical approval was obtained from the Institutional Review Board of the Armed Forces Hospital of the Eastern Region vide Letter No. AFHER-IRB-2020-031, dated 08/10/2020. The data was entered and analyzed using Statistical Package for the Social Sciences (SPSS), version 22.0 (SPSS Inc., Chicago, IL, USA). Descriptive analysis were performed; we described continuous variables as median and interquartile range (IQR) and categorical variables as frequencies and percentages.

Results

A total of 30 patients admitted with COVID-19 were included. The mean age 52.53 years (SD=16.31) with a range from 22-98 years; 73.3% were males (Table 1). Eleven patients (36.7%) had no comorbidities, whereas 63.35 had at least comorbid condition. Most common comorbidities were diabetes (46.7%) and hypertension (46.7%) followed by chronic heart disease (CHD) (16.7%), asthma and end-stage renal disease (ESRD) (3.3%); 14 patients (46.7%) were obese (Table 1). The most common symptoms were fever (96.7%), cough (73.4%), and shortness of breath (56.7%) followed by sore throat (36.7%), and myalgia (23.3%); about 57% patients had fever, cough, and shortness of breath. The median C-reactive protein (CRP) level was 87.5 mg/dL (IQR 45.0 – 165.65). Seven patients (23.3%) had CRP level from 10.0 – 44.99, 30% had CRP between 45 – 120, and 46.7% had CRP levels >120 mg/dL (Table 1).

Table 2 presents laboratory findings at the time of admission. The median white blood cell, lymphocytes, and platelet counts were 4.39, 1.05, and 212 K/μL, respectively. The median lactate dehydrogenase (LDH) was 336.14 μg/L; the median ferritin and procalcitonin levels were 459.75 and 0.12 ng/L, respectively. The median lactate dehydrogenase at admission was 95.0% (IQR 89.75 – 97.0); 23% patients had oxygen saturation <90%.

All the patients received corticosteroids; 17 (56.7%) patients were given IV methylprednisolone and 13 (43.3%) received dexamethasone tablets. Oral steroid were started on an average 4 days after admission, whereas IV steroid were started on an average 4 days after admission. The median duration of steroids use was 5 days (IQR = 5-11.25 days).

Of the total patients, 13 (43.7%) patients developed acute respiratory distress syndrome (ARDS); 17 (56.7%) patients required oxygen, 10 (33.3%) patients were admitted to Intensive Care Unit (ICU), and 7 (23.3%) patients required mechanical ventilation. The average length of hospital stay was 9.3 days (Range = 3-22 days) and median was 8.5 days (IQR = 5-11.25 days). However, all the 30 patients included in this study improved and were discharged home in good health.

Discussion

Owing to the spread of the SARS-CoV as a global pandemic, more affordable and widely available medications such as
Glucocorticoids had to be used. Our study reaffirms the finding of the RECOVERY trial that glucocorticoids were of benefit in a subset of patients with COVID-19.\[5\] The result of this study showed that early glucocorticoid use and an initial CRP of 45 mg/dL or higher were associated with a significantly reduced risk of mechanical ventilation use and admission to ICU. However, in our study, CRP values were found to be higher in those patients owing to multiple risk factors as many of them had medical comorbidities and presented with the hyperinflammatory status of COVID-19. These findings were consistent with a previous study that indicated the early use of glucocorticoids is not associated with morality nor the need for mechanical ventilation in unselected COVID-19 patients with markedly elevated CRP levels.\[8\]

We identified patient groups on the basis of widely available laboratory tests with high CRP, where we could give the glucocorticosteroid in early illness. Our results are also consistent with previous studies of patients with SARS-CoV and MERS-CoV, in which no associations between glucocorticoid treatment and mortality were found.\[8\] However, the results of studies examining the effect of glucocorticoids in patients with COVID-19 are less consistent.\[9]-[11\] It is known that elevated CRP level is associated with pro-inflammatory cytokines, namely interleukin-6, which results in a hyperinflammatory condition known as cytokine storm syndrome (CSS) leading to multi-organ dysfunction that occurs in a subset of COVID-19 patients.\[12\] Therefore, patients with higher CRP levels benefit more from glucocorticoid therapy though more harm is caused in patients with lower CRP without oxygen requirements. In our subset of patients with a lower CRP value of <45 mg/dl, approximately 10 patients with severe illness requiring oxygen had very good outcomes with steroid use. Therefore, our study suggests that CRP levels could be used as a guide to the early start of steroid.

The decision to use either oral or intravenous glucocorticoids was based on the clinical presentation of the patients. However, we found in our study that patients who were put on oral steroids had sequential organ failure assessment (SOFA) score of 0, while the patients who were given intravenous steroids had a median SOFA score of 6. This was an incidental finding, but we believe this could be used as a guidance tool for possible routes of administration of glucocorticoid.

All our selected cases presented for admission 7 days after manifestation of symptoms though per treatment guidelines the viremia phase would have elapsed when most likely, the use of antivirals would be of little benefit and anti-inflammatory agents, either glucocorticoid or anti-interleukin-6 agents might be better since our patients would be considered in the inflammatory stage at presentation.\[12-14\]

As this is a single center study, the results may not be generalized. The limitations include sample size and lack of comparison group. Therefore, larger studies are...
required with a comparison group comprising patients not receiving steroids.

**Conclusion**

Early use of Corticosteroids resulted in better outcome, and reduced intensive care unit transfer and use of mechanical ventilations. Moreover, it was of greater benefit when used in patients with higher CRP. Further larger studies are needed to validate and understand the underlying mechanisms.

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**Conflicts of interest**
There are no conflicts of interest.

**References**

1. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu S, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020;382:1708-20.
2. Zhou F, Yu T, Du R, Fan G, Liu Y, Li Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet 2020;395:1054-62.
3. Shang L, Zhan J, Hu Y, Du R, Cao B. On the use of corticosteroids for 2019-nCoV pneumonia. Lancet 2020;395:683-4.
4. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020;323:1061-9.
5. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Lancet 2020;395:473-5.
6. WHO. Who Director General Remarks on Covid 19; 2020. Available from: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-mediacrieng-on-covid-19—11-march-2020. [Last accessed on 2020 Aug 14].
7. Horby P, Lim WS, Emberson J, Faid M, Bell J, Linsell L, et al. Dexamethasone in hospitalized patients with COVID-19. N Engl J Medicine 2020;384:693-704. [DOI: 10.1056/NEJMoa2021436].
8. Keller MJ, Kitis EA, Arora S, Chen JT, Agarwal S, Ross M, et al. Effect of Systemic Glucocorticoids on Mortality or Mechanical Ventilation in Patients With COVID-19. J Hospital Med 2020;15:489-93.
9. Wu C, Chen X, Cai Y, Xia J, Zhou X, Zu X, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020;180:934-43. [doi: 10.1001/jamainternalmed.2020.0994].
10. Cao J, Tu WJ, Cheng W, Yu L, Liu YK, Hu Y, et al. Clinical features and short-term outcomes of 102 patients with coronavirus disease 2019 in Wuhan, China. Clin Infect Dis 2020;71:748-55.
11. Wang Y, Jiang W, He Q, Wang C, Wang B, Zhou P, et al. A retrospective cohort study of methylprednisolone therapy in severe patients with COVID-19 pneumonia. Signal Transduct Target Ther 2020;5:57.
12. Chen G, Wu D, Guo W, Cao Y, Xiang D, Wang H, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest 2020;130:2620-9.
13. McConaghy D, Sharif K, O’Regan A, Bridgewood C. The role of cytokines including interleukin-6 in COVID-19 induced pneumonia and macrophage activation syndrome-like disease. Autoimmun Rev 2020;19:102537.
14. Manjili RH, Zarei M, Habibi M, Manjili MH. COVID-19 as an acute inflammatory disease. J Immunol 2020;205:12-9.