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ORIGINAL ARTICLE

Methylprednisolone Vs Dexamethasone in Treating Patients with Covid-19

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ABSTRACT

Aim: To compare the efficacy of intravenous dexamethasone and methylprednisolone on the treatment of hospitalized patients with covid-19.

Methods: Between January 2022 and September 2022, 46 COVID-19 positive patients from the medical ward of ABWA Hospital and Research Centre participated in a randomized controlled trial. Patients in group A were given dexamethasone, whereas those in group B were given methylprednisolone. Hyperglycemia, hypokalemia, duration of oxygen therapy, death, intensive care unit hospitalization, and other outcomes were measured in both groups. For qualitative variables, Chi Square test was used, while for quantitative variables, T-Test was used. A significance level of less than 0.05 was used.

Results: In Group A, the average duration of hospitalization was 7.13±2.26days, but in Group B, it was 9.61±2.33 days (P = 0.0001). Group A had considerably shorter O2 therapy duration than Group B (5.78±1.16 days vs. 8.48±1.90 days; P = 0.0001). Group A had a considerably reduced incidence of hyperglycemia and hypokalemia compared to Group B (34.8% vs 73.9%, P = 0.008) (13% vs 43.5, P = 0.02).

Conclusion: We conclude that 8mg/day dexamethasone is better than 30mg methylprednisolone twice a day in treatment of COVID-19.

Keywords: Efficacy, Covid-19, Dexamethasone, Methylprednisolone

INTRODUCTION

In December of 2019, COVID-19, triggered by a corona virus spread from Wuhan, China, to the rest of the world. About 19% of people with this condition have severe pneumonia, and 5% develop critical pneumonia [1]. Rapid viral replication and a significant inflammatory response during the second week might lead to acute respiratory distress syndrome (ARDS). The viral entry route into human host cells necessitates the presence of the cellular surface protein angiotensin-converting enzyme 2 (ACE2) and the transmembrane protease serine 2. Cleavage allows the virus to penetrate the host cell and merge with its intended host [2].

The antiviral immune response helps clear the virus early on, but the inflammatory reaction causes lung damage. After initial injury at the epithelial, interstitial, and endothelial levels, surfactant is depleted by neutrophil and macrophage exudates, resulting in impaired alveolar capacity and oxygen exchange [3]. When infected cells die, they release inflammatory cytokines such tumour necrosis factor-, interleukin 1, and interleukin 6. This process is known as a cytokine storm. Second, the immunological cycle is triggered by the cytotoxicity induced by the virus's excessive reproduction, which further exacerbates the inflammatory condition [4].

In light of this physiopathology, corticosteroid treatment looks promising. However, because corticosteroids suppress the immune system, there is a greater chance of the infection spreading [5]. In most cases, the risk of developing severe or serious pneumonia is not anticipated to increase with a maintenance dose that is quite modest. Among hypoxic inpatients, methylprednisolone was found to enhance outcomes like length of hospital stay and clinical conditions [6].

The use of corticosteroids in the treatment of COVID-19 has been documented in a number of research papers. These studies, nevertheless, looked at other viruses that cause similar symptoms and not COVID-19 in particular [7, 8]. But other sepsis guidelines in COVID-19 recommend giving corticosteroids to hospitalized patients with ARDS in order to reduce the inflammatory response and treat secondary adrenal insufficiency. All the more so for those experiencing refractory shock. Still, the same guidelines saying that intubated patients without ARDS should not be given corticosteroids have been provided in other articles.[9]

In animal studies, methylprednisolone produced a higher ratio of lung tissue to plasma, suggesting it may be more beneficial than dexamethasone in treating lung injury. Treatment with dexamethasone improved the outcomes of a human study involving patients with severe COVID-19 who required oxygen or artificial breathing [10].

Researchers have found that among corticosteroids, dexamethasone has the longest half-life and greatest anti-inflammatory impact. The prognosis of a condition is also affected by the patient's past medical history [11]. Patients with COVID-19 and DM may have worse clinical outcomes and cardiovascular events due to the higher ACE2 glycation and TMPSS2 expression in cardiomyocytes in individuals with DM compared to patients without DM [11].

This study aims to examine the effectiveness of dexamethasone and methylprednisolone in treating COVID-19 symptoms, ICU admission, mortality, length of hospital stay, and inflammatory markers in inpatients due to the inconsistency of published data on the efficacy of glucocorticoids.

MATERIAL AND METHODS

We conducted this randomized controlled trial from January 2022 to September 2022 at medical ward of ABWA Hospital and Research Centre hospital. We obtained an ethical clearance certificate from the hospital's ethical committee before commencing the study. The patients were briefed about the study's potential benefits. All the patients were subjected to give their consent in written. Patients were allocated equally in two groups using lottery method. Patients were clinically assessed for COVID-19 virus, swabs were taken from the patients for reverse transcription–PCR (RT-PCR) test, and only those patients were enrolled in the study who had positive PCR. Patients of both genders having age between 40 to 80 years were included. We excluded pregnant women from our study. Those in Group A were given 8 mg of intravenous dexamethasone daily, whereas those in Group B were given 30 mg of methylprednisolone in two divided doses. All of the patients were followed for two weeks after they were released from the hospital. Hospitalization, oxygen support, death, intensive care unit admission, hyperglycemia, and hypokalemia were among the outcomes measured for both sets of

participants. A pre-made pro-forma was used to capture all of the information.

The sample size was calculated using anticipated frequency of hyperglycemia in group A 36.8%[12] and for group B 78.1%[12], keeping the power of test 80%. Sample size was 46.

We used SPSS version 20 for analysis of data. For analysis of qualitative variables, frequency and percentage while Mean ± SDs was used for analysis of quantitative variables. For comparison of qualitative variables between both groups Chi-Square test was used with P value < 0.05 as statistically significant while for quantitative variables T-test was used with P value < 0.05% as statistically significant.

RESULTS

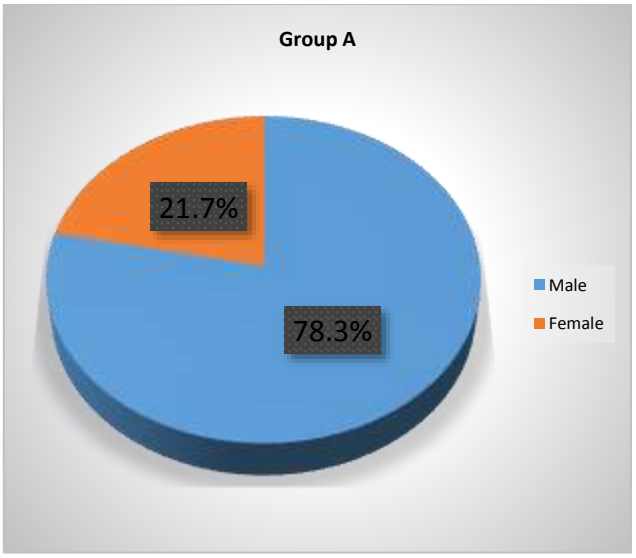
We performed this study on 46 patients divided equally in group A and B. Group A received Dexamethasone therapy and group B received methylprednisolone therapy. In group A mean age calculated was 64.09±11.19 while the mean age calculated in group B was 62.13±10.96 years. The mean duration of symptoms in group A was 7.57±1.70 while the mean duration of symptoms in group B was 7.13±2.26 days. Comparison of the comorbid like diabetes, hypertension, ischemic heart disease and lung disease between both groups can be seen at table no 1.

In group A there were 21.7% female while there were 78.3% male patients. In group there were 34.8% female while 65.2% male patients.

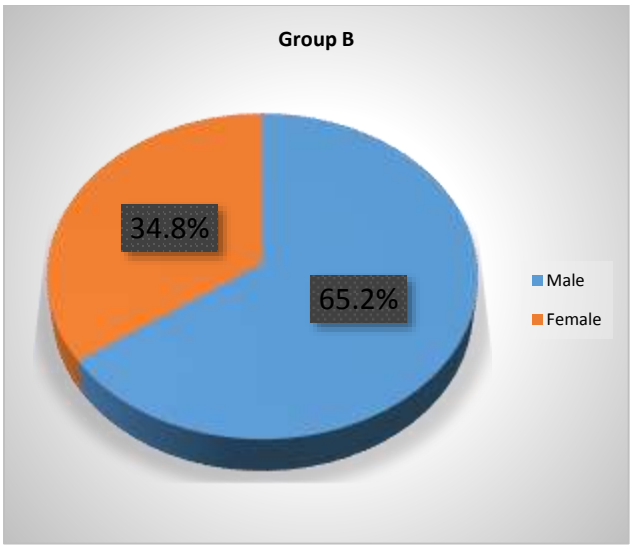
Regarding the comparison between the outcomes between both groups we observed that in group A the mean length of hospital stay was significantly lower than group B (7.13±2.26 days vs 9.61±2.33 days; P = 0.0001). The duration of O2 therapy in group A was significantly lower than group B (5.78±1.16 days vs 8.48±1.90 days; P = 0.0001). Regarding ICU admission and mortality no significant difference was observed between both groups. Hyperglycemia and hypokalemia was significantly lower in group A than group B, (34.8% vs 73.9%; P = 0.008) (13% vs 43.5; P = 0.02)

Table 1: Baseline characteristics of the patients

Variables	Group A	Group B	P value
Age (Years)	64.09±11.19	62.13±10.96	0.55
Duration of symptoms (days)	7.57±1.70	7.13±2.26	0.46
Diabetes	11 (23.9%)	10 (21.7%)	0.76
Hypertension	7 (15.2%)	6 (13%)	0.74
Ischemic heart disease	3 (6.5%)	2 (4.3%)	0.63
Lung disease	4 (8.7%)	3 (6.5%)	0.68



Graph 1: Gender distribution in group A



Graph 2: Gender distribution in group B

Table 2: Comparison of outcomes between both groups

Outcomes	Group A	Group B	P value
Length of hospital stay	7.13±2.26	9.61±2.33	0.0001
Duration of O2 therapy	5.78±1.16	8.48±1.90	0.0001
Mortality	2 (8.7%)	4 (17.4%)	0.38
ICU admission	4 (17.4%)	6 (26.1%)	0.47
Hyperglycemia	8 (34.8%)	17 (73.9%)	0.008
Hypokalemia	3 (13%)	10 (43.5%)	0.02

DISCUSSION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is discovered to be the primary infectious agent of COVID-19. During the end of December 2019, a strange pneumonia outbreak was noted by multiple symptoms including fever, dry cough, lethargy, and sporadic gastrointestinal manifestations. Critical COVID-19 patients or those with exceptionally high levels of the agitating biomarkers ferritin and C-reactive protein (CRP) may experience inflammatory organ damage. The host's response to pathogens or tissue injury is inflammation. This problem develops when rheumatoid arthritis's persistent inflammation leads to a lasting buildup of inflammatory cells in synovial joints and other conditions such as colitis and chronic bronchitis. A cytokine storm, which is the term used to describe an elevated inflammatory response that occurs from a cytokine storm, may be the main cause of severe COVID-19 disease. In extreme cases of COVID-19 patients, the ensuing cytokine storm results in damage as well as potentially fatal lung inflammation.[13]

Since glucocorticoids suppress the immune system, they increase the risk of secondary infections and make the initial infection harder to treat, which can lead to life-threatening complications like organ failure, septic shock, and sepsis. Glucocorticoids have been documented to treat diseases that are clinically similar to COVID-19, SARS, community-acquired pneumonia, and severe influenza[14]. Until recently, corticosteroids were sufficient to treat respiratory conditions such acute respiratory illness, severe bacterial pneumonia, and chronic obstructive pulmonary disease. While different COVID-19 management procedures stipulated that glucocorticoids would be either contradicted or not given until the research was completed, glucocorticoids have also been chosen in China in severe situations[15]. Adrenocortical insufficiency illnesses often require replacement therapy with natural glucocorticoids such as cortisone and hydrocortisone, which also have sodium-retaining characteristics. Dexamethasone is one of many synthetic hormone derivatives widely used for their anti-inflammatory effects. At comparable anti-inflammatory doses, dexamethasone does not

have the sodium-retention feature of hydrocortisone and its derivatives. Methylprednisolone is an intermediate-acting corticosteroid, but while the Food and Drug Administration [FDA1] approved its use on October 30, 1958, no such trials have been conducted on dexamethasone[16].

In the current study, we examined the efficacy of intravenous dexamethasone 8mg and methylprednisolone 30 mg in the management of COVID-19 in hospitalized patients.. The results showed that dexamethasone was more effective in addressing COVID-19 problems than placebo, while also posing a lower hazard for hyperglycemia and hypokalemia.

No statistically significant variation in patient age or gender was found between Groups A and B. Considering the underlying comorbid (diabetes, hypertension, ischemic heart disease and lung disease) between both groups we did not find any significant difference either. Our findings are in line with a study[12] which also reported no difference between the above mentioned baseline characteristics of the COVID-19 patients in their trail.

In our study we observed that there was no significant variance between both groups with regards to ICU admission (17.4% vs 26.1%) and mortality (8.7% vs 17.4%). Our results are comparable with a study[12] which also reported the same findings. A study[17] conducted in Pakistan also reported that there was not difference in ICU admissions and mortality between Dexamethasone group and methylprednisolone group.

We found in our study that the duration of hospital stay was lower in the Dexamethasone group as compared to the methylprednisolone group (7.17±1.26 days vs 9.61±2.33 days), these findings are similar to study[12] which also reported significantly lower hospital stay in dexamethasone group. In our study the duration of oxygen therapy was 5.78±1.66 while in the methylprednisolone group it was 8.48±1.90 days, the difference was statistically significant, our findings are backed by a study[18] conducted in Pakistan which reported that Dexamethasone group in their study had significantly lower duration of oxygen therapy. In our study the frequency of hyperglycemia and hypokalemia was significantly lower in the dexamethasone group as compared to methylprednisolone group. The aforementioned study[12] also reported significantly lower frequency of hyperglycemia and hypokalemia.

CONCLUSION

From our study we conclude that dexamethasone has better efficacy in treatment of COVID-19 patients. We observed significantly lower duration of oxygen therapy and hospital stay in the group receiving dexamethasone. We also found that in the dexamethasone group, the incidence of hypokalemia and hyperglycemia was significantly reduced.

REFERENCES

1. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239-42.
2. Matarese A, Gambardella J, Sardu C, Santulli G. miR-98 regulates TMPRSS2 expression in human endothelial cells: key implications for COVID-19. Biomedicines. 2020;8(11):462-71.
3. Mac Sweeney R, McAuley DF. Acute respiratory distress syndrome. Lancet. 2016;388(10058):2416-30.
4. Jafarzadeh A, Chauhan P, Saha B, Jafarzadeh S, Nemati M. Contribution of monocytes and macrophages to the local tissue inflammation and cytokine storm in COVID-19: Lessons from SARS and MERS, and potential therapeutic interventions. Life Sci. 2020;257:118102.
5. Singh AK, Majumdar S, Singh R, Misra A. Role of corticosteroid in the management of COVID-19: A systemic review and a Clinician's perspective. Diabetes & Metabolic Syndrome: Clin Res Rev. 2020;14(5):971-78.
6. Ranjbar K, Moghadami M, Mirahmadizadeh A, Fallahi MJ, Khaloo V, Shahriarirad R, et al. Methylprednisolone or dexamethasone, which one is superior corticosteroid in the treatment of hospitalized COVID-19 patients: a triple-blinded randomized controlled trial. BMC Infect Dis. 2021;21(1):1-8.
7. Chaudhuri D, Sasaki K, Karkar A, Sharif S, Lewis K, Mammen MJ, Alexander P, Ye Z, Lozano LE, Munch MW, Perner A. Corticosteroids in COVID-19 and non-COVID-19 ARDS: a systematic review and meta-analysis. Intensive Care Med. 2021;47(5):521-37.
8. Prescott HC, Rice TW. Corticosteroids in COVID-19 ARDS: evidence and hope during the pandemic. JAMA. 2020;324(13):1292-95.
9. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). Intensive Care Med. 2020;46(5):854-87.
10. Annane D, Pastores SM, Rochwerg B, Arlt W, Balk RA, Beishuizen A, Briegel J, Carcillo J, Christ-Crain M, Cooper MS, Marik PE. Guidelines for the diagnosis and management of critical illness-related corticosteroid insufficiency (CIRCI) in critically ill patients (Part I): Society of Critical Care Medicine (SCCM) and European Society of Intensive Care Medicine 2017. Intensive Care Med. 2017;43(12):1751-63.
11. D'Onofrio N, Scisciola L, Sardu C, Trotta MC, De Feo M, Maiello C, et al. Glycated ACE2 receptor in diabetes: open door for SARS-COV-2 entry in cardiomyocyte. Cardiovasc. Diabetol. 2021;20(1):1-6.
12. Dastenae ZH, Bahadori A, Dehghani M, Asadi-Samani M, Izadi I, Shahraki HR. Comparison of the effect of intravenous dexamethasone and methylprednisolone on the treatment of hospitalized patients with COVID-19: a randomized clinical trial. Int J Infect Dis. 2022;122:659-664.
13. Zhu, L., Xu, X., Ma, K., Yang, J., Guan, H., Chen, S., et al. Successful recovery of COVID-19 pneumonia in a renal transplant recipient with long-term immunosuppression. Am. J. Transplant. 2020, 1859–1863.
14. Siemieniuk, R. A., Meade, M. O., and Alonso-Coello, P. Corticosteroid therapy for patients hospitalized with community-acquired pneumonia: a systematic review and meta-analysis. Ann. Intern Med. 2015;163, 519–528.
15. Williams, D. M. Clinical pharmacology of corticosteroids. Respir Care. 2018;63, 655–670.
16. Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., et al. A novel coronavirus from patients with pneumonia in China. N. Engl. J. Med. 2020;382, 727–733.
17. Fatima SA, Asif M, Khan KA, Siddique N, Khan AZ. Comparison of efficacy of dexamethasone and methylprednisolone in moderate to severe covid 19 disease. Ann Med Surg (Lond). 2020 Dec;60:413-416.
18. Rana MA, Hashmi M, Qayyum A, Pervaiz R, Saleem M, Munir MF, et al. Comparison of efficacy of dexamethasone and methylprednisolone in improving PaO2/FiO2 ratio among COVID-19 patients. Cureus. 2020;12:e10918.