Outcome of COVID-19 Patients Receiving 6mg vs 12mg Dexamethasone at a Tertiary Care Hospital in Pakistan

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ABSTRACT

Objective: To compare the outcome in COVID 19 patients on oxygen managed with 6mg and 12 mg Dexamethasone at Pak Emirates Military Hospital Rawalpindi.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Pak Emirates Military Hospital Rawalpindi Pakistan, from Aug 2020 to Aug 2021.

Methodology: Patients diagnosed with COVID-19 on PCR and were oxygen-dependent but not mechanical ventilation dependent were included in the study. They were randomly divided into two groups. Group-I received 6mg Dexamethasone, while Group-II received 12 mg Dexamethasone for ten days. They were followed up for 30 days to look for the outcome (prolonged admission, high dependency unit admission, intensive care admission, death). The difference in outcome in both groups was studied using the Pearson chi-square test.

Results: Out of 600 patients included in the study, 401 (66.8%) were male, while 199 (33.2%) were female. The mean age of the study participants was 47.81 ± 8.716 years. 306 (51%) were given 6mg of Dexamethasone for ten days, while 294 (49%) were given 12mg of Dexamethasone for a similar time. prolonged admission (*p*-value-0.178), high dependency unit admission (*p*-value-0.409), intensive care admission (*p*-value-0.176) and mortality (*p*-value-0.588) were not statistically significantly different in both the groups.

Conclusion: All the outcome variables, including mortality and admission to the critical care unit, were not statistically significant in groups taking 6mg or 12 mg of Dexamethasone, so it could be concluded that a high dose of this medication is not superior in terms of efficacy when compared to the low dose of 6mg.

Keywords: COVID-19, Dose, Dexamethasone, Outcome.

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INTRODUCTION

Human beings long have been facing and fighting different pandemics in different eras.[1] 2019 was the year of COVID 19, which originated in China and spread around the whole world in weeks to months.[2] A very wide clinical spectrum has been observed in these patients ranging from asymptomatic infection to fatal illness. As this hierarchy climbs up from taking precautions to managing complications, the suffering of the patient and the burden on the health system increase manifold.[3]

Various treatment options are in practice for the management of patients with complications of COVID-19. Anti-virals, antibiotics, multivitamins, antipyretics and oxygen supplementation have been commonly used in patients with mild to moderate illness.[4] Patients with a severe form of illness may require critical care support and mechanical ventilation.[5] Immunomodulatory medications and steroids have also been used in a large number of patients on the basis that they have a protective role in managing the immune storm generated by the COVID-19 virus in the human body.[6]

As this pandemic is just two years old, clinicians and researchers are still trying to find suitable management options for COVID 19, especially indications and appropriate doses of steroid medications. Wanger *et al,* 2021 conducted a study regarding the use of systemic corticosteroids to treat COVID-19. They concluded that systemic corticosteroids probably slightly reduce all-cause mortality in people hospitalized because of symptomatic COVID-19. Ventilator-free days were also seen more in patients who used steroids, but the evidence was not convincing.[7] The group published the COVID Steroid 2 Randomized Trial in 2021 regarding using 6 and 12 mg dexamethasone. They revealed no statistically significant difference in patients who received 6 or 12 mg of Dexamethasone.[8] Munch *et al,* in 2021 planned to study the role of high and low dose steroids in patients presenting with severe hypoxemia due to COVID-19. Several clinicians and centres used various steroid regimens for this indication, but the

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evidence was less. The trial conducted by Munch *et al,* is still under process, and results are awaited.[9]

The third wave of COVID-19 struck severely in some parts of Pakistan in April 2021. Many patients have presented with a severe form of illness requiring oxygen supplementation. Clinicians have been using all the available options, but minimal data has been published, mainly regarding various types of steroids.[10] A clear idea regarding the exact dose of Dexamethasone, which may benefit these patients, is still unclear. We, therefore, planned this study with the rationale of comparing the outcome in COVID-19 patients on oxygen managed with 6mg and 12 mg Dexamethasone at Pak Emirates Military Hospital Rawalpindi Pakistan.

METHODOLOGY

This comparative cross-sectional study was planned and conducted at Pak Emirates Military Hospital Rawalpindi Pakistan between August 2020 and August 2021. The sample size was calculated using the WHO sample size calculation by using the population prevalence of response to steroids in COVID-19 patients as 73.5.5%.[11] Non probability consecutive sampling was used to gather the sample.

Inclusion criteria: All the COVID-19 polymerase chain reaction positive patients between the age of 18 and 70 years diagnosed with severe illness (on HRCT scan) and required oxygen supplementation were included in the study.

Exclusion criteria: Patients with evidence of bacterial or fungal sepsis before administering Dexamethasone or those who were on any immunosuppressant agents before the diagnosis of COVID- 19 were excluded from the study. The study did not include those with any contraindication for Dexamethasone or who refused to take steroid therapy. Pregnant or lactating women were excluded as well. Those who required mechanical ventilation or critical care support at the time of inclusion were not included in the study.

Ethical approval was taken from the Ethical Committee of the hospital via letter no A/28. Patients were randomly divided into two groups via the lottery method. Group-I received 6 mg dexamethasone, while Group-II received 12mg dexamethasone for ten days as per protocol.[12,13] Patients were followed up for 30 days to see the outcome in both the groups. Outcome variables included prolonged hospital ward admission (>2 weeks), High dependency unit admission, critical care admission and death. Patients were shifted to the critical care unit as per set criteria.[14]

Statistical analysis was carried out by using Statistical Package For Social Sciences (SPSS 24). Frequency and percentage were calculated for the qualitative variables like gender and all outcome variables. In contrast, the mean and standard deviation was calculated for the quantitative variables like the age of the patients included in the study. The Chi-square test was used to compare the outcome variables in patients with COVID-19 who were given 6mg and 12mg of Dexamethasone. The *p*-value ≤0.05 was sued to establish a statistically significant difference.

RESULTS

A total of 600 patients with severe COVID-19 illnesses were included in the final analysis. Out of these 600, 401 (66.8%) were male, while 199 (33.2%) were female. The mean age of the study participants was 47.81 ± 8.716 years. Table-I summarized the general characteristics of patients with COVID-19 included in the study. 306 (51%) were given 6mg dexamethasone for ten days, while 294 (41%) were given 12mg dexamethasone for a similar duration. 577 (82%) patients were alive at the end of one month, while 23 (18%) patients died within one month after the diagnosis of COVID-19. In addition, 535 (74%) patients were admitted to the critical care unit, while 65 (26%) patients did not require transfer to the critical care unit.

Table-I: Characteristics of study participants.

Study Parameters	n (%)
Age (years)	
Mean ± SD	47.81 ± 8.716 years
Range (min-max)	20-63 years
Gender	
Male	401 (57.4%)
Female	199 (42.6%)
Treatment Received	
6mg dexamethasone	306 (57.4%)
12mg dexamethasone	294 (42.6%)
Mortality	
Alive at 30 days	577 (82%)
Dead within 30 days	23 (18%)
Shifted to Critical Care Unit	
No	535 (74%)
Yes	65 (26%)

Table-II showed the results of the statistical analysis. It was revealed that prolonged admission (*p*-value 0.178), high dependency unit admission (*p*-value 0.409), intensive care admission (*p*-value-0.176) and mortality (*p*-value-0.588) were not statistically significantly different in both the groups.

Table-II: Comparison of various variables among patients of severe COVID 19 receiving 6 and 12 mg of dexamethasone.

Outcome Parameters	6mg Dexamethasone	12mg Dexamethasone	*p*-value
Hospital Ward Stay			
<2 weeks	251 (41.5%)	253 (25.4%)	0.178
>2 weeks	55 (58.5%)	41 (74.6)	
High Dependency Unit Admission			
No	266 (58.5%)	262 (52.4%)	0.409
Yes	40 (41.5%)	32 (47.6%)	
Critical Care Unit Admission			
No	278 (36.5%)	257 (69.8%)	0.176
Yes	28 (63.5%)	37 (30.2%)	
Death within 30 days			
No	293 (78.4%)	284 (53.9%)	0.588
Yes	13 (21.6%)	10 (46.1%)	

DISCUSSION

The dose of Dexamethasone had no relationship with outcome variables in our data set. COVID-19, initially considered similar to viral flu, has caused significant mortality and morbidity among individuals of all age groups across the globe.[2] Various supportive and curative management options have been tried in the last few months for these patients, especially those with severe forms of illness. The use of steroids has been controversial from the beginning of this pandemic. The effect of steroids seems beneficial with available data, but still, there is no consensus on the dose of Dexamethasone used for this purpose. Therefore, we planned and conducted this study to compare the outcome in COVID-19 patients on oxygen managed with 6mg and 12 mg dexamethasone at Pak Emirates Military Hospital Rawalpindi Pakistan.

Granholm *et al,* in 2019 compared dexamethasone 12 versus 6mg daily for up to 10 days in patients with COVID-19 and severe hypoxaemia. Then, they followed up with all the patients for 90 days. They concluded that there are high probabilities of benefit and low probabilities of clinically significant harm with Dexa-+methasone 12mg versus 6mg daily in patients with COVID-19 and severe hypoxaemia on all outcomes up to 90 days.[15] Our results were slightly different as patients receiving 6mg or 12mg had no statistically significant difference in outcome para-meters within 30 days of follow up after ten days' use.

A study by Vecchié *et al,* in 2021 regarding high dose use of steroids in acute respiratory syndrome caused by COVID-19.[16] They concluded that in hospitalized patients with COVID-19 related acute respiratory distress syndrome, high-dose Dexamethasone rapidly improved the clinical status and decreased the inflammatory biomarkers. Unfortuna-tely, they did not conduct a study with a randomized controlled design, so findings remain raw. Our target population was not ARDS patients, but patients dependent on oxygen only, and findings suggested that no significant difference existed in 6mg and 12 mg dexamethasone.

Munch *et al,* in 2021, studied the use of low-dose Hydrocortisone in patients with COVID-19 and severe hypoxia.[17] They had to terminate the trial early because of external evidence indicating benefit from corticosteroids and clear benefit in patients in our study as well. Our results were not significantly different, but our objective was not to look for the benefit of steroids but instead look for the best dose for these patients. We found that 6mg is equally effective as 12mg of Dexamethasone.

Kumar *et al*, in 2021, conducted a study to look at the findings that do high dose corticosteroids have any added advantage over low dose steroids in patients suffering from COVID-19 complications. They revealed that unadjusted in-hospital mortality was higher in patients who received high-dose corticosteroids.[18]

It was also associated with higher odds of death but not with the development of hospital-acquired infections, readmissions, or requirement of invasive mechanical ventilation. In addition, high-dose corticosteroids were associated with lower rates of acute kidney injury requiring hemodialysis. Our results showed that low or high doses did not cause much difference in outcome variables.

LIMITATIONS OF STUDY

The cause and effect relationship with outcome variables and dose of Dexamethasone is complicated to establish with this design, and that was one of the main limitations of this study. In addition, though we tried to control the confounders by strict inclusion/exclusion criteria, multiple factors in patients with secure COVID admitted to the hospital may contribute to the outcome parameters studied in our analysis.

CONCLUSION

All the outcome variables, including mortality and admission to the critical care unit, were not statistically significant in groups taking 6mg or 12 mg of Dexamethasone, so it could be concluded that a high dose of this medication is not superior in terms of efficacy when compared to the low dose of 6mg.

Conflict of Interest: None.

Author's Contribution

SB: Main Author, AN: Guided in study protocols, AZK:, KS: Guided in article writing, MA:, FS: Assited in data collection.

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