



Comparison of efficacy of dexamethasone and methylprednisolone in moderate to severe covid 19 disease

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ABSTRACT

Background: The first case of Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were diagnosed in Wuhan, China in 2019. In the first half of 2020 this disease has already converted into a global pandemic. Various treatment options were being tried all over the world. Some studies showed beneficial effects of corticosteroids in covid 19. Hence, we designed this study to compare the effect of two steroids in moderate to severe covid 19 disease.

Objectives: To compare the efficacy and safety of dexamethasone and methylprednisolone in moderate to severe covid 19 disease.

Study Settings: Fatima Memorial Hospital, Lahore and Ganga Ram hospital, Lahore.

Study Design: Quasi experimental, interventional study.

Duration of Study: From 1st June 2020 to 30th June 2020.

Methodology: Sample size and technique: there were total 100 patients; 35 patients received dexamethasone and 65 were kept in methylprednisolone receiving group.

Results: The mean age of patients was 57.91 years in dexamethasone group and 54.86 years in methylprednisolone group. In dexamethasone group, there were 15 (42.8%) critically ill patients who were shifted to Intensive care unit (ICU) and seven (20%) of them needed ventilatory support, whereas in methylprednisolone group 22 (33.8%) had to be admitted in ICU with eight (12.3%) patient needing ventilator. As outcome measure, patients in both the groups showed marked improvement in temperature, oxygen requirement and C-reactive protein (CRP) on day 5. Only six (17.1%) patient died who received dexamethasone while 10 (15.3%) patients died among those receiving methylprednisolone.

Conclusion: Dexamethasone and methylprednisolone both are equally effective in treating moderate to severe covid 19 disease.

1. Introduction

Covid 19 is a disease caused by a virus belonging to SARS Co V2 family of viruses. It primarily affects the lungs resulting in inflammation and pneumonia. On the basis of clinical, biochemical and radiological parameters it is divided into mild, moderate and severe disease. In mild disease there is fever and upper respiratory signs but no documented hypoxia or x-ray infiltrates. In moderate disease, there is tachypnea >30/min, hypoxia (SpO₂ < 94%) and infiltrates > 50% on chest x-ray

and CT scan [1]. Whereas in severe disease patient needs mechanical ventilation and biochemical parameters suggest cytokine storm and patient can develop multi-organ failure.

In mild disease patient can be managed at home with symptomatic treatment. In moderate disease patient is admitted in hospital and given supplemental oxygen along with other treatment modalities. In severe disease patient is shifted to ICU and managed accordingly. Convalescent plasma and IL-6 inhibitors like tocilizumab are given in cytokine release syndrome associated with covid 19.

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Corticosteroids have been used previously in respiratory illnesses like asthma, COPD, severe bacterial pneumonia and acute respiratory distress syndrome. The use of corticosteroids in covid 19 disease is still controversial [1]. Some studies have shown good response to steroids as they reduce inflammation [2,3]. However corticosteroids suppress the patient's immunity making him more prone to superadded infections [2, 4]. A large study in Michigan reports good results of early treatment with short course of steroids [5]. In Michigan study methylprednisolone was used. Studies in china have also reported the use of corticosteroids in covid pneumonia [2,4,6,7]. Recently the recovery trial in UK showed dexamethasone (a corticosteroid), to be the only drug able to reduce mortality in severe covid disease [8].

Hence, we have designed a study to observe the efficacy and safety of corticosteroids in covid 19 disease and to compare the outcome when steroids are given in moderate and severe covid disease in our setup.

2. Objectives

1. To compare the efficacy of dexamethasone and methylprednisolone in covid 19 disease

2. To correlate the effect of corticosteroids on improvement in hypoxia, CRP (C reactive protein) level, and chest x-ray infiltrates in moderate and severe covid 19 disease.

3. Materials and method

It is a Quasi experimental, interventional study involving 100 patients diagnosed with moderate to severe covid 19 disease admitted Covid block and ICU of Fatima memorial hospital Lahore and Ganga Ram hospital Lahore.

Sampling technique: convenience sampling

Duration: 1 month (1st June to June 30, 2020)

3.1. Intervention

Group 1: Intravenous Methylprednisolone 1 mg/kg/day in 2 divided doses per day given for 5 days.

Group 2: Intravenous dexamethasone 8 mg/day given for 5 days

3.2. Inclusion criteria

- 1 Age 18–75 years
- 2 Covid PCR positive
3. Patient having oxygen saturation <94% on room air, regardless of chest x-ray findings
4. Moderate or severe covid 19 disease according to operational definition.
- 5 Patients who sign informed consent

3.3. Exclusion criteria

1. Severe immunosuppression like HIV(Human immunodeficiency Virus) or long term use of immunosuppressant for any other chronic illness
2. Patients who need corticosteroids for any other disease like asthma, rheumatoid arthritis.
- 3 Pregnant or lactating females

3.4. Study

We enrolled first 100 patients admitted in covid unit of Fatima memorial hospital and Ganga Ram hospital who fulfilled the inclusion criteria and signed informed consent. Baseline oxygen saturation and clinical findings were noted. Chest x-ray was done on admission. Baseline labs were sent, initial level of CRP (C-reactive protein) was noted down.

Patients with oxygen saturation <94% on room air with normal chest x-ray and CRP between 30 and 50, were labelled as having moderate covid 19 disease. Patients with CRP > 50 and having infiltrates on chest x-ray at the time of admission were considered having severe covid 19 disease. Intravenous methylprednisolone in a dose of 1 mg/kg/day in 2 divided doses or dexamethasone 8 mg/day IV was given to alternate patients for 5 days. After 5 days, we again recorded the oxygen saturation, CRP level and repeat chest x-ray findings.

Patients were given tocilizumab and convalescent plasma as and when indicated. Oxygen was given by nasal cannula and face mask. Patient was shifted to ICU if clinical condition deteriorated and/or mechanical ventilation is needed.

We noted the improvement in clinical, radiological and biochemical parameters of the patient on day 0 that is admission day and later on day 5 after giving steroids (methylprednisolone or dexamethasone) for 5 days. We also correlated the effect of steroids with level of CRP at time of admission, and presence of infiltrates on initial chest x-ray in our patients and noted the improvement in CRP and x-ray after giving corticosteroids. In this way we compared the difference in outcome in patients receiving methylprednisolone or dexamethasone.

Data was analyzed using SPSS version 25.0. Mean and standard deviation was computed for quantitative variables whereas frequency and percentage were calculated for categorical variables. Paired sample *t*-test was applied for comparison of the two groups.

4. Results

We studied 100 patients admitted in covid unit of Fatima memorial and Ganga Ram hospital in Lahore, who were recruited in our study after fulfilling inclusion criteria, 35 patients received dexamethasone and 65 received methylprednisolone. The mean age of patients was 57.91 years in dexamethasone group and 54.86 years in methylprednisolone group. In dexamethasone group, there were 15 (42.8%) critically ill patients who were shifted to ICU and seven (20%) of them needed ventilatory support, whereas in methylprednisolone group 22 (33.8%) had to be admitted in ICU with eight (12.3%) patient needing ventilator.

Both groups were matched for comorbid conditions like pre-existing lung disease, diabetes, hypertension and ischemic heart disease (Table 1).

In patients receiving dexamethasone, there was a significant reduction in mean temperature on day 5, from 100.77 F on day 0–98.9 F on day 5 ($p < 0.0001$). Mean oxygen requirement was reduced from 12.5 L on day 0–10.3 litres on day 5. There was significant reduction in CRP from 139.5 to 73.9 ($p = 0.0001$).

In methylprednisolone group, the mean reduction in temperature was from 100.66 F on day 0–98.7 F on day 5. Mean oxygen requirement reduced from 11.8 L to 7.8 L. Mean CRP reduced from 129.8 to 59.07 in 5 days which is quite significant improvement ($p < 0.0001$).

Only six (17.1%) patient died among those who received dexamethasone while 10 (15.3%) patients died among those receiving methylprednisolone.

Table 1
Basic characteristics.

Basic characteristics	Dexamethasone	Methylprednisolone	p-value
Age	57.91 ± 16.4	54.86 ± 14.3	0.338
PCR(+)	33 (94%)	60 (92%)	1.0
Tocilizumab	12 (34%)	27 (41.5%)	0.525
Plasma therapy	6 (17%)	8 (12.3%)	0.553
Antibiotics	35 (100%)	65 (100%)	0.446
Smoker	7 (20%)	19 (29%)	0.350
Pre-existing lung disease	6 (17%)	10 (15%)	0.515
Diabetes mellitus	24 (68.5%)	30 (46%)	0.037
hypertension	19 (54%)	35 (53.8%)	1.000
IHD	12 (42.8%)	13 (20%)	0.148
CKD	2 (5.7%)	4 (6.1%)	1.000

5. Discussion

It is a very relevant study in the time of covid pandemic. We have compared two different corticosteroids in the treatment of moderate to severe covid disease. There have been number of studies on dexamethasone and methylprednisolone alone in treatment of covid but this is first head to head comparison between dexamethasone and methylprednisolone. In our study we selected 100 patients with moderate to severe covid disease, they were assigned to two groups by convenience sampling technique depending on availability of the drugs as dexamethasone was not freely available in the market during the period of our study. So, we were able to give dexamethasone to 35 patients and methylprednisolone to 65 patients. We couldn't enroll more patients as the declining peak of covid 19 in Pakistan resulted in no further admissions with severe covid 19 in our hospital. The groups were age and gender matched. However, the patients in dexamethasone group were sicker as they have co-morbid conditions like diabetes heart disease, kidney failure. And these were the patients who needed ICU care more frequently and also required invasive ventilation apart from oxygen inhalation (Table 2). Similar standard of care was given to both groups including the use of antibiotics, plasma therapy and tocilizumab for cytokine storm where indicated by biochemical parameters. We noted that both groups had similar primary and secondary outcomes despite the fact that patients in dexamethasone group were more critical (see Table 3).

So far, the largest trial on various treatment modalities of covid 19 is the Recovery trial conducted in UK which proves efficacy of dexamethasone. It shows significantly less mortality in dexamethasone group as compared to standard care group however this difference was more significant in patients requiring oxygen and/or ventilatory support. Overall, 482 (22.9%) patients in dexamethasone group while 1110 (25.7%) in standard care group expired within 28 days of the intervention [8]. Recovery trial had a large database of more than 4000 patients whereas our study had only 100 patients. Recovery trial did not study the effects of methylprednisolone as per the investigators own choice. However, we considered some other trials which showed good results of methylprednisolone so we used the opportunity to compare both corticosteroids and find out the better of the two. Both methylprednisolone and dexamethasone have a role in management of severe respiratory illness. So far, our results didn't show any significant difference in outcome in both the groups.

A study in Wuhan China, conducted on 46 patients compared the effect of IV methylprednisolone in patients with severe covid pneumonia to those patients who did not receive methylprednisolone [2]. There was significant reduction in morbidity and mortality with methylprednisolone.

A study in Michigan compared the effect of early short course of methylprednisolone with the standard care regime in 213 covid patients [5]. They observed significant improvement in outcome and shorter length of stay in hospital in the methylprednisolone group. Unlike our study they did not compare methylprednisolone with dexamethasone.

Corticosteroids have been used previously for various respiratory illnesses other than covid 19. Steroids have a proven role in reducing inflammation in asthma and sometimes acute exacerbation of COPD [9]. There is also a significant role of steroids in septic shock [10]. Steroids are frequently given to ICU patients in shock and have shown clinical improvement in hypotension and shock. So, it is difficult to state whether the effect of steroids observed in our study was due to its

Table 2
Outcome comparison.

Outcome measures	dexamethasone	Methylprednisolone	P value
ICU transfer	15 (42.8%)	22 (33.8%)	0.393
Ventilator needed	7 (20%)	8 (12.3%)	0.381
Mortality	6 (17.1%)	10 (15.3%)	1.00

Table 3
Between intervention comparison.

Medicine or treatment	Variables	Mean \pm SD		P-value
		Dexamethasone	methylprednisolone	
Day zero (pre)	Temperature	100.77 \pm 1.43	100.66 \pm 1.20	0.687
	Oxygen	12.5 \pm 4.28	11.8 \pm 4.9	0.463
	CRP	139.57 \pm 69.6	129.89 \pm 71.39	0.516
Day 5 (post)	Temperature	98.9 \pm 1.09	98.7 \pm 1.03	0.429
	Oxygen	10.34 \pm 7.48	7.84 \pm 6.44	0.10
	CRP	73.9 \pm 56.0	59.07 \pm 50.88	0.181

Independent sample *t*-test.

anti-inflammatory properties or due to its effect on septicemia. Although none of our patients developed super added bacterial pneumonia by the use of corticosteroids which we monitored by checking their pro-calcitonin levels [11] and serial chest x-ray to look for new opacities. The rise in procalcitonin indicates underlying bacterial infection [11]. This was probably because we used corticosteroids for a short period of 5 days. If we had used steroids for longer duration there could have been significant risk of bacterial pneumonias.

Another common side effect of steroids was hyperglycemia observed in almost all of our diabetic patients in both groups. The hyperglycemia was managed effectively with insulin. There were no serious complications of hyperglycemia like hyperosmolar coma or ketoacidosis. (Table 4). In another study it was noted that almost half of hospitalized patients develop hyperglycemia when given high dose corticosteroids [12].

The patients who expired in our study were critically sick. Two of them were chronic kidney failure patients on hemodialysis and they developed multi-organ failure. One patient developed pneumothorax while on invasive ventilator for two weeks. One of our patients developed subcutaneous and mediastinal emphysema from which he recovered but later developed a subdural hematoma due to which he expired.

5.1. Limitations

The major limitation of our study was that we did not have a control group and the patient number in both groups was not equal. The number of patients could not be increased further as the covid 19 began settling in Pakistan and there were no further admissions with severe covid 19 in our hospital.

Our patients were not followed up after discharge from hospital.

6. Conclusion

The results of our study show that both drugs dexamethasone and methylprednisolone are effective in improving clinical and biochemical parameters of moderate to severe covid 19 disease. The patients in dexamethasone group were slightly older age group and had more pre-existing comorbidities and more of these patients required ICU care as compared to the patients in methylprednisolone group. However, the difference in outcome between the two groups, in terms of mortality is not statistically significant. Hence, we can conclude that both dexamethasone and low dose methylprednisolone are equally effective in management of moderate to severe covid 19 disease.

Table 4
Comparison between adverse effects.

Adverse effects	Dexamethasone	Methylprednisolone
Hyperglycemia (>180 mg/dl)	32 (91%)	58 (89.2%)
Hyperglycemic coma/DKA	0	0
Super added bacterial infection	0	0

Provenance and peer review

Not commissioned, externally peer reviewed.

Ethical Approval

The study was approved by institutional review board of Fatima memorial hospital.

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Certificate can be provided on request.

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None.

Author contribution

1. Syeda Arzinda Fatima, study concept, design, methodology and writing the paper

2. Mohsin Asif: Data analysis

3. Khurshid Khan: study concept, supervision, review of final results

4. Nasir Siddique: Data collection

5. Aijaz Zeeshan Khan: review of final paper and editing

Research registration number

1. Name of the registry: clinicaltrials.gov

2. Unique Identifying number or registration ID: [Clinicaltrials.gov](https://clinicaltrials.gov)

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Hyperlink to your specific registration (must be publicly accessible and will be checked): <https://clinicaltrials.gov/show/NCT04603729>

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Declaration of competing interest

None

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References

- [1] M. Cascella, M. Rajnik, A. Cuomo, S.C. Dulebohn, R. Di Napoli, Features, evaluation, and treatment of coronavirus (COVID-19), in: *StatPearls. Treasure Island (FL), StatPearls Publishing, 2020. August 10.*
- [2] Y. Wang, W. Jiang, Q. He, et al., A retrospective cohort study of methylprednisolone therapy in severe patients with COVID-19 pneumonia, *Sig Transduct Target Ther* 5 (2020) 57, <https://doi.org/10.1038/s41392-020-0158-2>.
- [3] Z. Ye, Y. Wang, L.E. Colunga-Lozano, et al., Efficacy and safety of corticosteroids in COVID-19 based on evidence for COVID-19, other coronavirus infections, influenza, community-acquired pneumonia and acute respiratory distress syndrome: a systematic review and meta-analysis, *CMAJ (Can. Med. Assoc. J.)* 192 (27) (2020) E756–E767, <https://doi.org/10.1503/cmaj.200645>.
- [4] W. Zhang, Y. Zhao, F. Zhang, et al., The use of anti-inflammatory drugs in the treatment of people with severe coronavirus disease 2019 (COVID-19): the Perspectives of clinical immunologists from China, *Clin. Immunol.* 214 (2020) 108393, <https://doi.org/10.1016/j.clim.2020.108393>.
- [5] R. Fadel, A. Morrison, A. Vahia, Z. Smith, Z. Chaudhry, P. Bhargava, et al., Early Short-Course Corticosteroids in Hospitalized Patients with COVID-19, *Clinical Infectious Diseases*, 2020.
- [6] Coronavirus Disease 2019 (COVID-19), Centers for Disease Control and Prevention, 2020 [cited 29 August 2020]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/index.html>.
- [7] G. Wang, C. Wu, Q. Zhang, et al., C-reactive protein level may predict the risk of COVID-19 aggravation, *Open Forum Infect Dis* 7 (5) (2020), <https://doi.org/10.1093/ofid/ofaa153> ofaa153. Published 2020 Apr 29.
- [8] E. Wilkinson, RECOVERY trial: the UK covid-19 study resetting expectations for clinical trials, *BMJ* (2020) m1626.
- [9] G.R. Sethi, K.K. Singhal, Pulmonary diseases and corticosteroids, *Indian J. Pediatr.* 75 (10) (2008) 1045–1056, <https://doi.org/10.1007/s12098-008-0209-0>.
- [10] P.E. Marik, Steroids for sepsis: yes, no or maybe, *J. Thorac. Dis.* 10 (Suppl 9) (2018) S1070–S1073, <https://doi.org/10.21037/jtd.2018.04.35>.
- [11] M. Meisner, Update on procalcitonin measurements, *Ann Lab Med* 34 (4) (2014) 263–273, <https://doi.org/10.3343/alm.2014.34.4.263>.
- [12] H.E. Tamez-Pérez, D.L. Quintanilla-Flores, R. Rodríguez-Gutiérrez, J.G. González-González, A.L. Tamez-Peña, Steroid hyperglycemia: prevalence, early detection and therapeutic recommendations: a narrative review, *World J. Diabetes* 6 (8) (2015) 1073–1081, <https://doi.org/10.4239/wjd.v6.i8.1073>.