Original Research Article

Journal of College of Medical Sciences-Nepal, Vol-18, No 3, Jul-Sep 2022
ISSN: 2091-0657 (Print); 2091-0673 (Online) Open Access
DOI: 10.3126/jcmsn.v18i3.47897

Comparative Study of Intravenous Dexamethasone and Methylprednisolone in Severe COVID -19 Patients Requiring Respiratory Support in Intensive Care Unit

Lalit Kumar Rajbanshi,[1] Anuj Jung Rayamajhi,[2] Akriti Bajracharya,[1] Rajat Shah,[1]

[1]Department of Anesthesiology and Critical Care, Birat Medical College and Teaching Hospital, Tankisinuwari, Morang, [2]Civil Service Hospital, Kathmandu, Nepal.

ABSTRACT

Introduction

Numerous steroids have been used to combat the intense cytokine storms in severe COVID pneumonia. The study compares the use methylprednisolone and dexamethasone as an adjuvant steroid therapy in severe COVID-19 pneumonia.

Methods

Prospective comparative study including total of 190 COVID -19 severe pneumonia cases admitted in intensive care unit with 93 patients randomly allocated to receive dexamethasone 6 mg and 97 patients allocated to receive methylprednisolone 1mg/kg in two divided doses both by intravenous route for 7 days. Mortality was compared as primary objective while oxygenation parameters and inflammatory markers, need for invasive mechanical ventilation, duration of ventilation, length of ICU-stay, incidence of multiorgan failure were assessed as secondary variables.

Results

At day zero, the patient in methylprednisolone group had significantly lower PaO2/FIO2 ratio (258.3950.36 vs 285.1868.62, P=0.002). At day seven, methylprednisolone significantly improved PaO2/FIO2 ratio (266.5260.73 vs 244.8175.36, P=0.029) and there was substantial decrease in inflammatory markers CRP, Ferritin (P<0.05). PEEP requirement was significantly less with methylprednisolone (P=0.007). Methylprednisolone significantly reduced the incidence of multiorgan failure, need of invasive mechanical ventilation and duration of mechanical ventilation (P<0.05). However, there was no significant difference in terms of duration of ICU stay and 30 days in hospital mortality between the two groups

Conclusions

Intravenous methylprednisolone significantly improved the oxygenation of COVID -19 pneumonia patients and decreased the inflammatory reactions as compared to similar dose of dexamethasone when given for week duration. However, methylprednisolone did not seem to be superior to dexamethasone in terms of improving mortality.

Keywords: ARDS; COVID-19; COVID pneumonia; cytokine storm syndrome; steroid.

Correspondence: Dr. Lalit Kumar Rajbanshi, Department of Anesthesiology and Critical Care, Birat Medical College and Teaching Hospital, Tankisinuwari, Morang, Nepal. Email: lalitrajbanshi@gmail.com. Phone: +977-9852030496.

INTRODUCTION

COVID-19 is the disease of the respiratory system causing mild to severe form of pneumonia and can lead to severe acute rerspiratory distress syndrome (ARDS) requiring respiratory support. COVID-19 ARDS is characterized by pulmonary hyperinflammation and uncontrolled expression of early response pro-inflammatory cytokines like, C-reactive protein, tumor necrosis factor [TNF], IL-6, and IL-1β and ferritin.[1,2] The release of proinflammatory markers can lead to a condtion called cytokine storm which may lead to increased risk of vascular hyperpermeability, multiorgan failure, and eventually death.[3] Several therapeutic interventions has been proposed to mitigate this cytokine storm in an attempt to improve the outcome of severe COVID-19 pneumonia. Corticosteroids have been studied in critically ill patients with acute respiratory distress syndrome (ARDS) with conflicting results in reduing the inflammatory response and improving the outcome.[4,5] Recently, the RECOVERY Trial, a large multicenter trail on use of steroid in severe covid ARDS has shown to improve the mortality in patients who had received steroid as compared to the usual care patient groups.[6]

Dexamethasone has been used in RECOVERY Trial and has shown a promising result in improving the mortality. Dexamethasone has highest anti-inflammatory action with low mineralocorticoid activity thus having lowest impact on the sodium balance. Dexamethsaone has potential effect in increasy the throbogeneicity in patient with COVID as it increases the clotting factor and fibronigen concentration.[7] Similary, low dose and prolong infusion of methylprednisonle in CO-19 pneumia has shown a lower hazard of death (71%) and increased number of ventilator free days.[8] High doses of Methylprednisolone are actually the preferred agent for anti-inflammation in pulmonary diseases as it achieves a more direct effect on cell membrane associated proteins. However, the use of methylprednisolone in ARDS patient has not been routinely practiced despite improving the cardiopulmonary physiology as it increases the risk of death after two weeks of use.[9]

Hence, the available evidences are insufficient to draw any conclusion of the choice of steroid in the COVID -19 patients. This study hence, has intended to compare the afficacy and safety of dexathesone and methylprednisolone in COVID-19 ARDS patients under mechanical ventilation in ICU. The primary objective of the study was to evaluate and compare the 30 days in hospital mortality of the COVID-19 pneumonia patient receiving dexamethasone or methylprednisolone as an anti-inflammatory agent. The secondary outcomes are to compare the oxygenation parameters, inflammatory markers, incidence of multiorgan failure, duration of mechanical ventilation and length of ICU stay.

METHODS

This is a prospective comparative study in patients with COVID -19 admitted in intensive care unit of Birat Medical College Teaching Hospital (BMCTH) for a duration of 6 months during the peak second wave of COVID -19 pandemic in Nepal (July to December 2021). Ethical approval was obtained from the Institutional Review Committee, BMCTH (IRC-PA-142/2077-78). COVID -19 was confirmed with rt-PCR and supported by the radiological changes in the CT chest . Equivalent doses of intravenous dexamethasone and methylprednisolone were compared in terms of efficacy and safety in eligible COVID-19 patients

Inclusion criteria:

- Age >18 years
- COVID -19 confirmed by rt-PCR

- ARDS Patients with Pa02/FI02 <300 mmHg (according to Berlin definition of ARDS) requiring noninvasive or invasive ventilation within 24 hours of admission in intensive care unit.

Exclusion criteria

- Patients <18 years,
- Pregnancy
- Established end organ failure ; heart failure , chronic liver disease, COPD with cor pulmonale, CKD, previous history of neuromuscular disease
- Patients on chronic steroid or immunomodulator therapy
- Quadriplegia/Hemiplegia or quadriparesis/ hemiparesis
- Do Not Resuscitate or Do Not Intubate

Using these mortality rate of 37.5% and 18.6% with the use of dexamethasone and methylprednisolone respectively, from study by Keivan Ranbar et al,[10] the sample size was calculated to be 90 in each group considering 80% as power of study and 5% as an type I error. With 10% expected dropout the sample size was calculated to be 200 which were divided into two equal groups by a computer-generated randomization system.

1. Group D: Intravenous dexamethasone 6 mg/ day single dose for 7 day
2. Group M: intravenous methyl prednisone 1/ mg/kg in two divided doses for 7 days

The base line demographic characteristics, comorbid clinical conditions were observed and compared between the groups on the first day of intervention (Day 0). Similarly, inititial inflammatory markers (CRP, Ferritin, D-dimr, Procalcitonin) and oxygenation parameter (SPO2, Pa02, FIO2 and Sa02), ventilation parameter (proportion of invasive ventilation required, PEEP) was observed and compared at day zero and seven of the intervention respectively. Outcome of the patients were assessed in terms of 30 days in-hospital mortality, duration of mechanical ventilation, development of multiorgan failure, duration of mechanical ventilation, length of ICU stay. Finally any adverse effect associated solely with the use of steroids was also assessed.

In addition to the intervention, the usual care for the management of severe COVID-19 patients were continued in the following forms

- Prone ventilation was done regularly if Pa02/FI02 <150 mmHg for 16 hours after optimization of PEEP and FIO2
- Sedation and muscle relaxants were used accordighly whenever needed
- Nasogastric feeding started immediately after intubation
- DVT prophyalxis was continued with low molecular heparin single subcutaneous dose and with TED stocking
- Remdisivir was used if indicated
- Convalescent plasma was not used in any patients in the study

The observed values were entered in Microsoft excel and statistical analysis was done with IBM SPSS version 21. The categorical data were interpreted as percentage by Chi-Square formula while continuous data were presented as mean, median and standard deviation and were analyzed by using Mann Whitney U test. P value less than 0.05 was considered statistically significant.

RESULTS

Total of 1260 COVID-19 cases were admitted in six-month duration from July - December 2021 in Birat Medical College Teaching Hospital. A total of 190 COVID positive cases were finally enrolled for data analysis. COVID diagnosis was made with RT-PCR in 150 while CT chest radiography confirmed COVID in 40 cases.

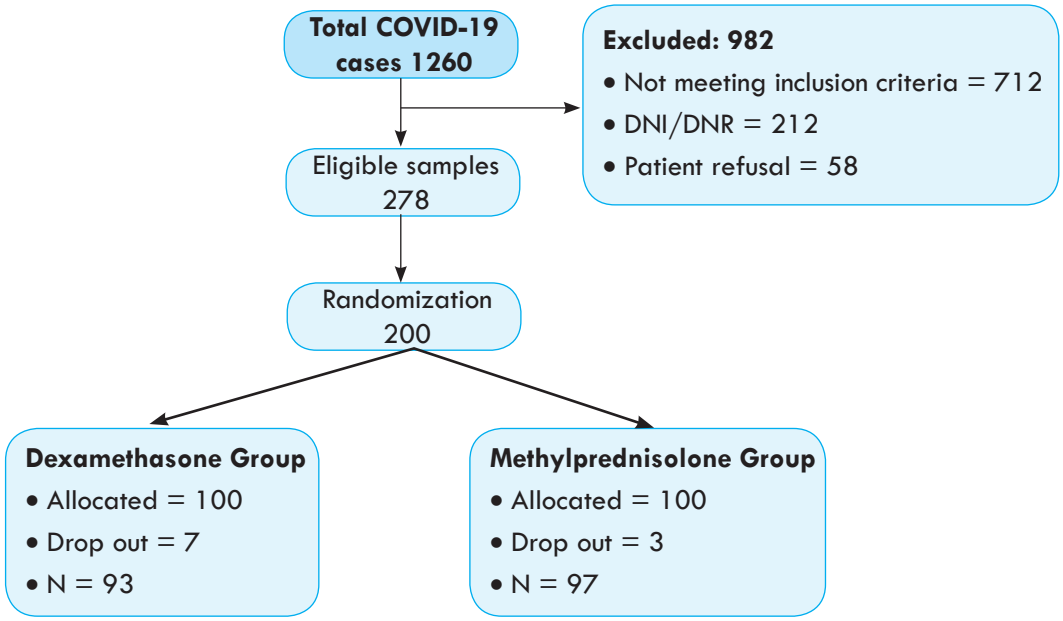


Figure 1. Flow diagram of the participants in the study.

A total of 93 patients were randomized in dexamethasone group while 97 patients were grouped in methylprednisolone group. The mean age of the cases was 53.88±12.36 with male predominance (63.6%). The most common clinical presentation was fever (70.5%) followed by malaise (63.6%) and dry cough (53.6%) subsequently. The demographic profiles (age and sex) and clinical profiles of the patients (Table1) in both the groups were statistically non-significant (P>0.05).

Hypertension was the most common (38.8%) comorbidities associated in the study population followed by diabetes mellitus (22.7 %) and previous history of ischaemic heart disease but not in heart failure (11.1%). 35.35% of th patient

Table 1. Demographic and clinical profile of COVID -19 patients involved in the study.

Variables		Dexamethasone (n=93)	Methylprednisolone (n=97)	p value	Total (n=190)
Age (Years)		52.15 11.08	55.6114.25	0.143	53.8812.66
Sex	Male	58 (62.3%)	63(64.9%)	0.711	63.6
	Female	35 (37.7%)	34 (35.1%)		
Fever		63 (67.7%)	71(73.1%)	0.731	(70.5%)
Cough		52(55.9%)	50(51.5%)	0.740	(53.6%)
Sore throat		31(33.3%)	28(28.8%)	0.629	(31.0%)
Loss of smell/taste		40 (43.0%)	33(34.0%)	0.3950	38.4%
Malaise		58(62.3%)	63(64.9)	0.861	63.6%

Note: Chi-Square Test for categorical data and Mann Whitney U test for continuous data. P value < 0.05 is statistically significant

had current or past smoking history (Table 2). These comrobidities were comparable inbetween the two groups (P>0.05).

Table 2. Co-morbidities of the COVID-19 patients involved in the study.				
Variables	**Dexamethasone (N = 93)**	**Methylprednisolone (N = 97)**	**P Value P = 0.05**	**Total (N = 190)**
HTN	31 (33.3%)	43 (44.3%)	0.302	38.8%
DM	28(30.1%)	15(15.4%)	0.055	22.7%
IHD	14((15.0%)	7(7.2%)	0.123	11.1%
Smoking	39(41.9%)	28(28.8%)	0.192	35.35%

Note: HTN- hypertension, DM-diabetes mellitus, IHD-ischemic heart disease . Chi-Square test was applied. P value < 0.05 is statistically significant *

The table 3 shows the clinical characteristics of severity of respiratory failure due to the COVID infection, oxygenation parameters and inflammatory markers compared at the time of enrollment in the study (day 0).The median GCS in dexamethasone was 14 (IQR 8-15) while it was 13 (IQR 9-15) with methylprednisolone. Similarly, majority of the patients in both the group had tachypnoea at the time of presentation. Patients in methylprednisolone group significantly higher temperature (p=0.046) as compared to dexamethasone. In terms of respiratory failure, patients in methylprednisolone had statistically significant lower Pa02/FI02 ratio and the pulse oximeter showed relatively lower oxygen saturation as compared to patients in dexamethasone group. 53.6% and 22.6% of patients in in methylprednisolone group required non-invasive and invasive mechanical ventilation respectively as compared to 51.6% and 16.1% respectively in dexamethasone group

Table 3. Day zero clinical characteristics, oxygen parameters, ventilation status and inflammatory markers.			
Variables	**Dexamethasone (n=93)**	**Methylprednisolone (n=97)**	**p value**
GCS	14 (8-15)	13 (9-15)	
RR (breaths/min)	22 (16-40)	26 (18-44)	
Temp (°F)	99.372.24	100.25 3.62	**0.046***
MAP (mmHg)	74.187.63	72.0910.22	0.113
P/F	285.1868.62	258.3950.36	**0.002***
SP02 (%)	91.216.25	90.137.32	0.276
NIV	48 (51.6%)	52(53.6%)	0.878
Invasive Ventilation	15(16.1%)	22(22.6%)	0.373
D-dimer (ng/ml)	243.12 72.12	264.8290.23	0.069
Ferritin(ng/ml)	258.4398.65	283.7287.34	0.062
Procalcitonin(ng/ml)	0.280.11	0.320.17	0.056
CRP (mg/L)	45.3410.22	42.2316.63	0.124

Note: GCS- Glascow coma scale, RR-respiratory scale, MAP-mean arterial pressure, P/F- Pa02 to FIO2 ratio, NIV-non-invasive ventilation, CRP- C reactive protein. Chi-Square Test was applied for categorical data and Mann Whitney U test for continuous data. P value < 0.05 is statistically significant *

and comparison between the two groups were statistically non-significant (P>0.05). Day Seven comparison (Table 4)

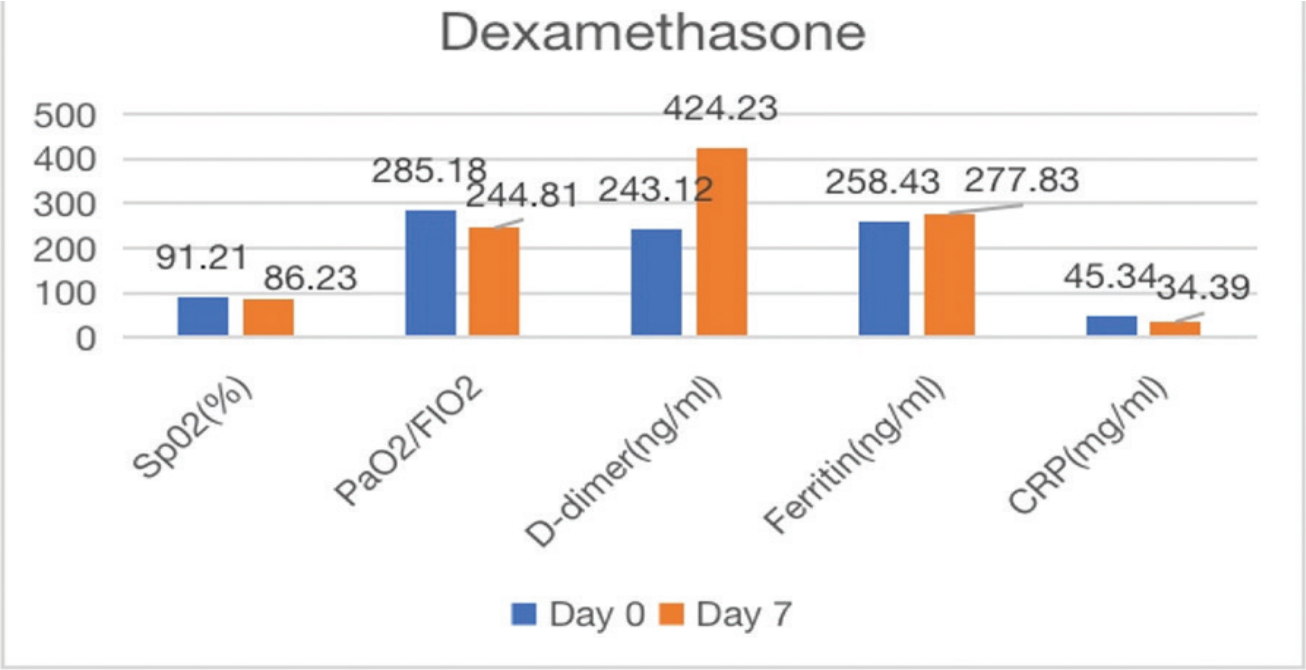
with the patient receiving methylprednisolone as compared to dexamethasone group.D-dimer, C-reactive protein, ferritin and procalcitonin were considered as inflammatory markers of COVID and were also compared between the groups at day seven. D-Dimer, CRP and ferritin values were significantly lower with the patients receiving methylprednisolone (P<0.05) as compared to the patient receiving dexamethasone while procalcitonin was statistically comparable between the two groups.

Table 4. Day 7 comparison of oxygenation parameters and inflammatory markers of COVID-19 patients involved in the study.

Variables	Dexamethasone (n=93)	Methylprednisolone (n=97)	p value
SP02	86.238.23	90.129.01	**0.002***
P/F	244.8175.36	266.5260.73	**0.029***
PEEP	13.344.13	11.833.62	**0.007***
D-Dimer (ng/ml)	424.2370.23	398.6286.30	**0.026***
CRP (mg/L)	34.3911.17	22.258.20	**0.040***
Ferritin (ng/ml)	277.8377.32	250.4682.64	**0.019***
Procalcitonin (ng/ml)	1.241.02	1.350.74	0.394

Note: P/F-PaO2 to FIO2 ratio, PEEP- positive end expiratory pressure, CRP- C reactive protein. Mann Whitney U test. P value < 0.05 is statistically significant *

At the end of day seven, oxygenation parameters were compared between the patients enrolled in two groups. The patients receiving methylprednisolone had significantly better oxygenation in terms of improved SPO2 and Pa02 /FIO2 ratio as compared to patients receiving dexamethasone (P<0.05). Similarly, PEEP requirement was significantly lower (p=0.007)

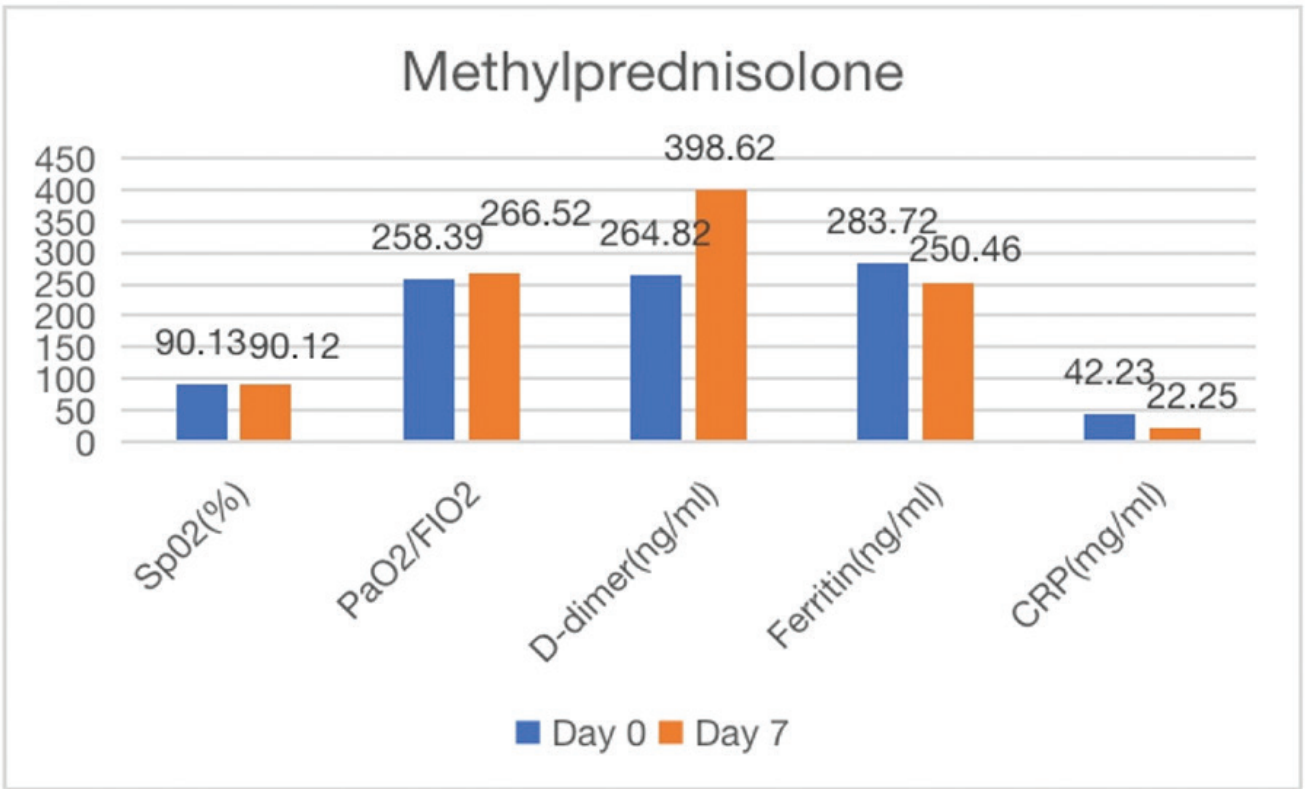


Graph 1. Comparison of oxygenation parameters and inflammatory markers at day 0 and 7 in patient receiving dexamethasone.

Graph 1 and 2 shows the comparison of oxygenation parameters and inflammatory markers at day zero and seven in the patients receiving individual drug. Oxygen saturation and Pa02/FIO2 ratio has decreased while D-dimer and Ferritin has substantially increased in patient receiving dexamethasone coming to day seven (Graph1). The patient receiving methylprednisolone showed an improved Pa02/FIO2 ratio and decreased inflammatory markers (Ferritin and CRP, Graph 2) at the end of day seven.

new organ failure developed by the patient after the enrollment apart from the respiratory failure.

The patients in methylprednisolone group had significantly lower proportion of organ failure (29.8% vs 51.6% and P=0.047) as compared to dexamethasone groups. Similarly need for vasoactive drugs for cardiac support and renal replacement therapy were comparable between the groups (P>0.05). Methylprednisolone produced significant hyperglycemia (198.6126.45 vs189.2320.41, P=0.010) as compared to the



Graph 2. Comparison of oxygenation parameters and inflammatory markers at day 0 and 7 in patient receiving methylprednisolone.

Outcome: The outcome variables (Table 5) in terms of multiorgan failure, need for organ support treatment, need for invasive ventilation, duration of mechanical ventilation length of stay in ICU were compared between the two groups till the end of ICU stay while mortality was compared for 30 days stay in ICU or hospital. Multiorgan failure (MOF) was considered the

patient receiving dexamethasone. The need for invasive ventilation during ICU-stay and duration of invasive ventilation were statistically less and shorter respectively (P<0.05) for the patients receiving methylprednisolone. However, the total length of ICU-stay and 30 days mortality both were comparable between the groups (P.0.05).

Table 5. Comparison of outcome variables of COVID -19 patients involved in the study.

Variables	Dexamethasone (n=93)	Methylprednisolone (n=97)	p value
MOF	48 (51.6%)	29(29.8)	**0.047***
Vasoactive drugs	25 (26.8%)	17(17.5%)	0.214
RRT	7(7.5%)	4(4.1%)	0.343
Invasive ventilation	52(55,9%)	30(30.9%)	**0.028***
Blood glucose (mg/dl)	189.2320.41	198.6126.45	**0.010***
Duration of Mechanical ventilation	14.244.72	12.546.72	**0.045***
Length of ICU stay	18.475.22	17.407.29	0.248
Mortality (30 days)	16 (17.20%)	13(13.40%)	0.532

Note: MOF-multiorgan failure, RRT- renal replacement therapy. Chi-Square Test for categorical data and Mann Whitney U test for continuous data. P value < 0.05 is statistically significant

DISCUSSION

Since the emergence of the disease, the world population has faced a tremendous challenge in the management of the disease as few are known about the definitive management. The natural course of the disease might vary from mild to severe form of pneumonia leading to ARDS and multiorgan failure and death.[11,12] 17,18 It is well known fact that COVID-19 is associated with remarkable increase in the inflammatory markers and various cytokines leading to the severe form of acute respiratory distress The current focus has been directed towards the complications associated with COVID-19; ARDS and Cytokine Release Syndrome, both characterized by an increase in tumor necrosis factor-alpha (TNF alpha), interleukin (IL) 1B, IL-2 IL- 6, IL-8, IL-10, and interferon y (IFN y).[13] Corticosteroids have been used widely for the suppression of inflammatory reactions with the few evidences of reducing the severity of the disease and mortality as well. A placebo-controlled randomized multicenter study by Viller et al. has demonstrated that patients receiving dexamethasone had lower mortality (21% vs 36 %, P value <0.0047).[14] Similarly Wu et al showed a lower risk of death (HR, 0.38; 95% CI, 0.20–0.72) in COVID patients receiving methylprednisolone.[15] The RECOVERY trail is the large multicentered trail that has shown improved morality with the use of steroid.[6] The current study has intended to compare the outcome of the COVID-19 patients with acute respiratory distress with the use of dexamethasone and methylprednisolone separately.

In our study, the mean age of the COVID infected patients was 53.88 years and there was male predominance while fever being the commonest clinical presentation followed by body ache/ malaise and cough. Hypertension (38.8%) was the most common comorbid clinical condition associated with the patient cohort in the study. These findings in the current study were supported by a systematic review of 5 retrospective clinical studies for a total of 1556 patients where fever was present in 85.6% population followed by dry cough. Similarly, hypertension was present in 17.4% of population.[16]

The study showed that majority of the COVID infected patients were conscious tachypneic and febrile at the time of enrollment in the study.

The patients with the Pa02 /FIO2 ratio less than 300 were included in the study. The cohort in methylprednisolone group had significantly lower Pa02/FIO2 ratio as compared to that of dexamethasone group (P=0.002). Oxygen saturation was relatively also lower in the patients receiving methylprednisolone group. Low Pa02/FIO2 ratio and low oxygen saturation both suggested that the patient in methylprednisolone group relatively had a more severe form of pneumonia. The clinical severity of the COVID-19 infection in methylprednisolone group patients was also supported by relatively high level of inflammatory markers like D-dimer, ferritin, CRP and procalcitonin in methylprednisolone group at the time of enrollment. A higher proportion of the patients allocated in to receive methylprednisolone received non-invasive and invasive mechanical ventilation at the time of enrollment (53.6% vs 51.6% and 22.6% vs 16.1% respectively). The need of respiratory support in the form of noninvasive and invasive ventilation can be explained by the fact that as all the patients included in the study had mild to severe form of ARDS and were in respiratory distress at the time of enrollment.

We used intravenous dexamethasone 6mg/day and methylprednisolone 1mg/kg in two divided doses for 7 days in the study population. At day seven the patient receiving methylprednisolone had improved Pa02/FIO2 ratio (266.5260.73 vs 244.8175.36, P=0.029) and better oxygen saturation (90.129.01 vs 86.238.23) as compared to patient cohort in dexamethasone group. Similarly, the study showed a significant reduction in PEEP requirement in patient receiving methylprednisolone (13.344.13 vs 11.833.62, P=0.007). The inflammatory markers (D-dimer, ferritin and CRP) were significantly lower in methylprednisolone cohort. In addition to this CRP and ferritin were significantly reduced in patient receiving methylprednisolone as compared to the values at the time of enrollment in the same cohort. Our finding in terms of improved oxygenation and suppressed inflammatory markers were supported by a retrospective clinical trial by Edalatifard et al where they found improved oxygenation and lesser clinical findings such as myalgia, chest pain, cough, and gastrointestinal symptoms in those who were treated with methylprednisolone compared to those who received standard care.[17]

Methylprednisolone has a better lung penetration and thus its immunosuppressive effect is more prominent in COVID-19 pneumonia leading to improvement of oxygenation and other respiratory complications.[18,19] The use of methylprednisolone leads to a dose dependent suppression of inflammatory reactions; higher the dose more is the immunosuppression.[10] Thus, due to the dose dependent anti-inflammatory action of methylprednisolone, the present study observed a significant decrease in CRP and ferritin in same cohort.

Our study observed that the use of methylprednisolone had significantly decreased the proportion of multiorgan failure during ICU stay. Relatively a smaller number of patients in methylprednisolone group required organ support therapy in terms of use of vasoactive drugs and renal replacement therapy. Similarly, the need for invasive ventilation was significantly less in patients receiving methylprednisolone. We observed that those patients who were mechanically ventilated in methylprednisolone group had significantly shorter days in ventilation. Saeed et al compared dexamethasone 6 mg and methylprednisolone 2mg/kg for 10 days in COVID-19 pneumonia patients and observed better outcome ,improved lung conditions, decreased inflammatory reactions and rapid

weaning from ventilator.[20] This is mostly due to the better penetration of methylprednisolone in the lung tissue in comparison to dexamethasone. Similarly, Ranjbar et al demonstrated that the use of high dose methylprednisolone in COVID pneumonia patients had improved the clinical outcome as well as decreased the dependency on mechanical ventilation.[10]

However, the use of methylprednisolone did not show any benefit over dexamethasone on the duration of ICU stay of the patients. The patients in both the cohort were managed in intensive care unit for non-respiratory supportive care as well as psychological support thus the benefit in terms of length of ICU stay was not observed. Similarly, there was no significant difference in the 30 days mortality in either of the group. Even though there was significant improvement in the oxygenation and reduction in the inflammatory reaction, mortality was not reduced with methylprednisolone in our study as majority of the patient in methylprednisolone group were associated with comorbid condition like hypertension and diabetes. Moreover, the severity of pneumonia or ARDS was more with the methylprednisolone cohort as observed by significantly lower Pa02/FI02 ratio at the time of enrollment. Saeed et.al demonstrated highly significant beneficial effects of the methylprednisolone infusion on the patients' ICU stay and mortality rates in comparison to the patients who received dexamethasone 6 mg as they included a large sample size in their study.[20] Saeed et al used a large dose of methylprednisolone (2mg/kg) for 10 days as compared to our study where we used only 1mg/kg for 7 days only. As there is a dose dependent reduction in the inflammatory reactions and improvement in the clinical outcome, the lower dose selected in our study might have contributed for non-significant benefit of methylprednisolone on mortality.

Corticosteroid can cause hyperglycemia and in our study the patients receiving methylprednisolone had higher blood sugar level as compared to dexamethasone group but however the high blood sugar level was successfully managed by glycemic control protocol in ICU and there was no any adverse effect of hyperglycemia observed.

Limitations

One of the limitations of our study was the patient recruited in methylprednisolone group were sicker in terms of oxygenation and inflammatory markers. This might have masked the potential benefit of the strong anti-inflammatory action of methylprednisolone. There was no control group in the study where steroid was not used as during COVID -19 pandemic steroid was considered as one of the integral parts of management of severe cases. Similarly, the duration of the steroid treatment was very short in our study that would have not been sufficient to demonstrate over all benefit in terms of mortality.

CONCLUSIONS

The study aimed to evaluate whether the use of methylprednisolone in severe COVID-19 pneumonia has better outcomes in terms of mortality as compared to use of dexamethasone in equivalent doses. There was no mortality benefit of using methylprednisolone over dexamethasone in severe COVID-19 ARDS patients. However, The use of methylprednisolone has significantly improved the oxygenation, reduced the inflammatory markers, reduced the need of invasive ventilation and reduced the days on ventilator as compared to use of dexamethasone.

Conflict of Interest: None

REFERENCES

1. Mehta, P., McAuley, D. F., Brown, M., et al. (2020). COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet,395(10229), 1033–1034. https://doi.org/10.1016/S0140-6736(20)30628-0
2. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med 2020;46:846-848. PMID: 32125452; PMCID: PMC7080116. https://doi.org/10.1007/s00134-020-05991-x
3. Meduri GU, Kohler G, Headley S, Tolley E, Stentz F, Postlethwaite A. Inflammatory cytokines in the BAL of patients with ARDS. Persistent elevation over time predicts poor outcome. Chest 1995; 108: 1303–14. PMID: 7587434. DOI: 10.1378/chest.108.5.1303
4. 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):829-840. PMID: 26508525.DOI: 10.1007/s00134-015-4095-4
5. Meduri GU, Golden E, Freire AX, et al. Methylprednisolone infusion in early severe ARDS: results of a randomized controlled trial. Chest. 2007;131(4):954-963. PMID: 17426195.DOI: 10.1378/chest.06-2100
6. The RECOVERY Collaborative Group Dexamethasone in Hospitalized Patients with Covid-19—Preliminary Report. N. Engl. J. Med. 2021, 384, 693–704. PMID: 32678530. PMCID: PMC7383595, DOI: 10.1056/NEJMoa2021436
7. Brotman DJ, Girod JP, Posch A, Jani JT, Patel JV, Gupta M, Lip GY, Reddy S, Kickler TS. Effects of short-term glucocorticoids on hemostatic factors in healthy volunteers. Thromb Res. 2006;118(2):247-52. doi: 10.1016/j.thromres.2005.06.006. Epub 2005 Jul 11. PMID: 16005496. https://doi.org/10.1016/j.thromres.2005.06.006
8. Salton F, Confalonieri P, et.al.Prolonged Low-Dose Methylprednisolone in Patients With Severe COVID-19 Pneumonia. Open Forum Infect Dis. 2020 Sep 12;7(10):ofaa421. doi: 10.1093/ofid/ofaa421. eCollection 2020 Oct.
9. Steinberg KP Hudson LD Goodman RB et alEfficacy and safety of corticosteroids for persistent acute respiratory distress syndrome.N Engl J Med. 2006; 354: 1671-1684 PMID: 16625008,DOI: 10.1056/NEJMoa051693
10. Ranjbar, K., Moghadami, M., Mirahmadizadeh, A. 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 21, 337 (2021). https://doi.org/10.1186/s12879-021-06045-32
11. Grant MC, Geoghegan L, Arbyn M, Mohammed Z, McGuinness L, Clarke EL, Wade RG. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries. PLoS One. 2020 Jun 23;15(6):e0234765. doi: 10.1371/journal.pone.0234765. PMID: 32574165; PMCID: PMC7310678.

12. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, Xie C, Ma K, Shang K, Wang W, Tian DS. Dysregulation of Immune Response in Patients With Coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis. 2020 Jul 28;71(15):762-768. doi: 10.1093/cid/ciaa248. PMID: 32161940; PMCID: PMC7108125.

13. Ragab D, Salah Eldin H, Taeimah M, Khattab R, Salem R. The COVID-19 Cytokine Storm; What We Know So Far. Front Immunol. 2020 Jun 16;11:1446. doi: 10.3389/fimmu.2020.01446. PMID: 32612617; PMCID: PMC7308649.

14. Villar J, Ferrando C, Martínez D, Ambrós A, Muñoz T, Soler JA, Aguilar G, Alba F, González-Higueras E, Conesa LA, Martín-Rodríguez C, Díaz-Domínguez FJ, Serna-Grande P, Rivas R, Ferreres J, Belda J, Capilla L, Tallet A, Añón JM, Fernández RL, González-Martín JM; dexamethasone in ARDS network. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. Lancet Respir Med. 2020 Mar;8(3):267-276. doi: 10.1016/S2213-2600(19)30417-5. Epub 2020 Feb 7. PMID: 32043986.

15. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, Huang H, Zhang L, Zhou X, Du C, Zhang Y, Song J, Wang S, Chao Y, Yang Z, Xu J, Zhou X, Chen D, Xiong W, Xu L, Zhou F, Jiang J, Bai C, Zheng J, Song Y. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med. 2020 Jul 1;180(7):934-943. doi: 10.1001/jamainternmed.2020.0994. Erratum in: JAMA Intern Med. 2020 Jul 1;180(7):1031. PMID: 32167524; PMCID: PMC7070509.

16. Lovato A, de Filippis C. Clinical Presentation of COVID-19: A Systematic Review Focusing on Upper Airway Symptoms. Ear Nose Throat J. 2020 Nov;99(9):569-576. doi: 10.1177/0145561320920762. Epub 2020 Apr 13. PMID: 32283980

17. Edalatifard M, Akhtari M, Salehi M, Naderi Z, Jamshidi A, Mostafaei S, et al. Intravenous methylprednisolone pulse as a treatment for hospitalised severe COVID-19 patients: results from a randomised controlled clinical trial. Eur Respir J. 2020;56(6):2002808. https://doi.org/10.1183/13993003.02808-2020

18. Braude A, Rebuck AJTL. Prednisone and methylprednisolone disposition in the lung. Lancet. 1983;2(8357):995–7. https://doi.org/10.1016/s0140-6736(83)90981-9

19. Hirano T, Homma M, Oka K, Tsushima H, Niitsuma T, Hayashi TJI. Individual variations in lymphocyte-responses to glucocorticoids in patients with bronchial asthma: comparison of potencies for five glucocorticoids. Immunopharmacology. 1998;40(1):57–66. https://doi.org/10.1016/s0162-3109(98)00025-3

20. Saeed, M., Mohamed, A. H., & Owaynat, A. H. (2022). Comparison between methylprednisolone infusion and dexamethasone in COVID-19 ARDS mechanically ventilated patients. The Egyptian journal of internal medicine, 34(1), 19. https://doi.org/10.1186/s43162-022-00113-z

Citation: Rajbanshi L, Rayamajhi A, Bajracharya A, Shah R. Comparative Study of Intravenous Dexamethasone and Methyl-prednisolone in Severe COVID -19 Patients Requiring Respiratory Support in Intensive Care Unit. JCMS Nepal. 2022; 18(3); 194-205.