

COMPARATIVE EFFICACY OF METHYLPREDNISOLONE AND DEXAMETHASONE IN INTENSIVE CARE PATIENTS WITH SEVERE COVID-19: A PROSPECTIVE STUDY FROM PAKISTAN

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Abstract: The study aimed to determine the comparative efficacy of dexamethasone and methylprednisolone in treating severely ill COVID-19 patients in terms of mortality. Using a quasi-experimental design, the study was conducted at Mayo Hospital, Lahore, from May 2021 to October 2021. A total of 148 patients, divided into two groups of 74 each (groups A and B), were included in the study. Group A was given 6mg of dexamethasone, while group B was given methylprednisolone 40mg twice daily for 10 days. All the collected data was analyzed using SPSS 26.0, and Chi-square was used to find the mortality association between the two groups. A p-value of less than 0.05 was considered significant. The results showed that the age and gender distribution for the methylprednisolone and dexamethasone groups were 56.89±13.3 (M=36, F=38) and 57.69±12.6 (M=38, F=36), respectively. In terms of mortality, 45 patients died in the methylprednisolone group, while 54 people died in the dexamethasone group. There was statistical significance regarding mortality in both groups (p=0.003). In conclusion, the study found that administering 40mg of methylprednisolone twice daily produced better outcomes than 6mg of dexamethasone once daily in treating severe COVID-19 patients in the hospital.

Keywords: Severe COVID-19, Dexamethasone, Methylprednisolone, Mortality.

Introduction

A trailblazing contagion of some unknown etiology broke into Wuhan, China, in December 2019. A new sort of coronavirus was identified as the main culprit and was later known as Coronavirus Disease-19 (COVID-19) by the World Health Organization (WHO). It was declared a pandemic by WHO in March 2020 (Budhathoki et al., 2020). It is atypical pneumonia with a pathological range extending from mild to severe symptoms depending upon co-morbidities and risk factors (Singhal, 2020). The mild to moderate clinical features in a patient suffering from COVID-19 include fever, non-productive cough, malaise, sore throat, anosmia, breathlessness, and other less common features. Sometimes, very few patients suffer from ARDS, cytokine storm, or multi-organ failure due to this deadly virus (Farooqi et al., 2022).

With time and a better understanding of the virus, different antiviral therapies came forward to cope with this deadly pandemic, including chloroquine and hydroxychloroquine, azithromycin, remdesivir, lopinavir/ritonavir, and ivermectin. These all showed results in vitro against Severe Acquired Respiratory Syndrome- Coronavirus 2 (Costanzo et al., 2020). However, in RCTs, there were no favorable results of chloroquine and hydroxychloroquine alone or with azithromycin.

Corticosteroids are released from the adrenal medulla, and their mode of action, unlike other drugs, is not to attack the virus; instead, they behave as anti-inflammatory and immunosuppressive agents. Corticosteroids decline the

nuclear transcription factor signaling and hamper the transcription and translation of inflammatory agents (Cruz-Topete and Cidlowski, 2014). This property of corticosteroids is the basis for treating different medical conditions, including viral and bacterial pneumonia (Stern et al., 2017). Corticosteroids are used for treating COVID-19 because of the similarity in genetic setup with MERS and SARS. However, they are not identical, so there is a need to find the effectivity of different corticosteroids on COVID-19.

In some studies, the use of 6 mg dexamethasone for up to 10 days was proved to be very effective than those who didn't get dexamethasone (Añón and Villar, 2021; Fadel et al., 2020). Early systemic corticosteroids proved to help decrease ventilation time and the mortality rate in moderate to severe ARDS (Villar et al., 2020). However, there is significantly less evidence about the efficacy of intermediately acting corticosteroids, methylprednisone (Williams, 2018). A Michigan study reported promising results regarding the early use of methylprednisolone in COVID-19 pneumonia (Fadel et al., 2020).

There are very few studies regarding the comparison of dexamethasone and methylprednisolone in treating COVID-19 pneumonia, so this study aims to dig up the comparison between these two drugs. We are standing on the verge of a time when thousands of people will need these drugs to save their lives. So, as healthcare professionals, we must find what is best for our patients. It is a dire need of the hour to see the difference in all aspects of these drugs

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regarding COVID-19. So, our study aimed to determine the comparative efficacy of dexamethasone and methylprednisolone in severely ill patients of COVID-19 in terms of mortality.

Methodology

This was a prospective Quasi-Experimental study conducted at King Edward Medical University, Mayo Hospital, Lahore, after having permission from the ethical board of the institution for 6 months. A sample size of 148 (74 in each Group) was calculated, assuming the mortality percentage was 18% and 38% in methylprednisolone and dexamethasone groups, respectively (Ranjbar et al., 2021). All the patients of both genders of age greater than 17 years having SARS CoV-2 infection confirmed by PCR and hospitalized having Oxygen saturation less than 93% at room air and required supplemental oxygen defined as severe disease were included in the study. All those patients of age less than 17 years and having oxygen saturation above 92% at room air were excluded from the study. Patients with uncontrolled diabetes and hypertension, cancer patients, patients on immune suppressants, or with any immune-deficient state were also excluded from the study.

Trained data collector who collected data using a structured questionnaire was provided with all required personnel protection tools (PEPs). Data on socio-demographic factors, including age, gender, etc, was collected. Information including disease severity, comorbidities like diabetes, hypertension, chronic obstructive pulmonary disease (COPD), Ischemic heart disease(IHD), chronic Kidney disease (CKD), cerebrovascular accident (CVA), including both ischemic and hemorrhagic events, etc, and type of

ventilation being given was also noted. All social and ethical considerations were taken into account. All participants or close relatives signed valid informed consent.

All the patients were randomly allocated to either Group A or Group B. Group A will be given 6mg of dexamethasone, and Group B will be given methylprednisolone 40mg intravenously twice daily with standard care for COVID-19. Any patient with elevated blood pressure and glucose during the study was excluded. The primary endpoint was mortality during a hospital stay, with secondary endpoints being the length of hospital stay and the need for a ventilator.

Data was analyzed using SPSS version 26.0. Qualitative statistics were determined as frequency and percentages. The application of the chi-square test determined quantitative correlations among variables. P-value ≤ 0.05 was considered significant. Whereas clinical indices were compared using paired sample t-tests before and after drug use.

Results

A total of 148 patients were included in this study, in which half (74) of the patients took methylprednisolone along with other standard treatments. In contrast, the rest of the critically ill patients were given dexamethasone besides their usual management plan. And there was no significant difference in underlying conditions among both groups.

The age and gender of the methylprednisolone and dexamethasone group were 56.89±13.3 (M=36, F=38) and 57.69±12.6 (M=38, F=36). There is no significant difference between age and gender between both groups. Age, gender, and underlying conditions are mentioned in Table 1.

Table 1: Demographic status of subjects in Methylprednisolone group and Dexamethasone group (n=148)

Characteristics		Methylprednisolone group (n=74)	Dexamethasone group (n=74)	p-value
Age (mean ± Std Dev.)		56.89±13.3	57.69±12.6	0.50
Sex	Male	36(48.6%)	38(48.6%)	1.00
	Female	38(51.4%)	36(51.4)	
Comorbidities	COPD	11(14.9%)	7(9.5%)	0.04
	Diabetes mellitus	23(31.1%)	24(32.4%)	0.72
	Hypertension	22(29.7%)	31(41.9%)	0.04
	Tuberculosis	10(13.5%)	9(12.2%)	0.60
	HIV	9(12.2%)	11(14.9%)	0.33
	Malignancy	6(8.1%)	8(10.8%)	0.29
	Obesity	4(5.4%)	2(2.7%)	0.09
	IHD	7(9.5%)	9(12.2%)	0.29
	CVA	5(6.8%)	5(6.8%)	1.00
	CKD	8(10.8%)	8(10.8%)	1.00
Asthma	4(5.4%)	2(2.7%)	0.09	

*COPD = Chronic Obstructive Pulmonary Disease *HIV= Human Immunodeficiency Virus

*IHD= Ischemic Heart Disease

*CVA= Cerebrovascular Accident

*CKD= Chronic Kidney Disease

In terms of symptoms on presentation, 48(64.9%) patients had a fever, 40 (54.1%) patients had a cough, and 13(17.6%) had dyspnea in the methylprednisolone group, whereas 40(54.1%) patients had a fever, 40(54.1%) had cough whereas 1(1.4%) patient had shortness of breath on presentation in the dexamethasone group. For the mode of ventilation, the most intensive therapy needed by the patient was documented. It was NRBM for 59(79.7%) patients,

CPAP for 3(4.1%), and 12(16.2%) patients were on a ventilator in the methylprednisolone group; however, for dexamethasone group 55(74.3%) patients were having NRBM, 7(9.5%) patients had CPAP and ventilator was attached to 12(16.2%) patients. Meanwhile, patients' oxygen saturation on the 1st, 5th, and 10th day is documented in Table 2.

Table 2: Oxygen saturation of subjects in both group

		Methylprednisolone group (n=74)	Dexamethasone group (n=74)	p-value
Oxygen saturation	At 1 st day	92.2±3.6 (n=65)	91.4±7.5 (n=66)	0.08
	At 5 th day	93.1±3.9 (n=31)	92.2±5.8 (n=39)	0.159
	At 10 th day	90.6±7.7 (n=3)	94.0±1 (n=3)	0.053

In terms of mortality, 45 mortalities were reported in the methylprednisolone group, while 54 people died in the

dexamethasone group. There is a statistical significance regarding mortality in both groups (p=0.003). (figure 1)

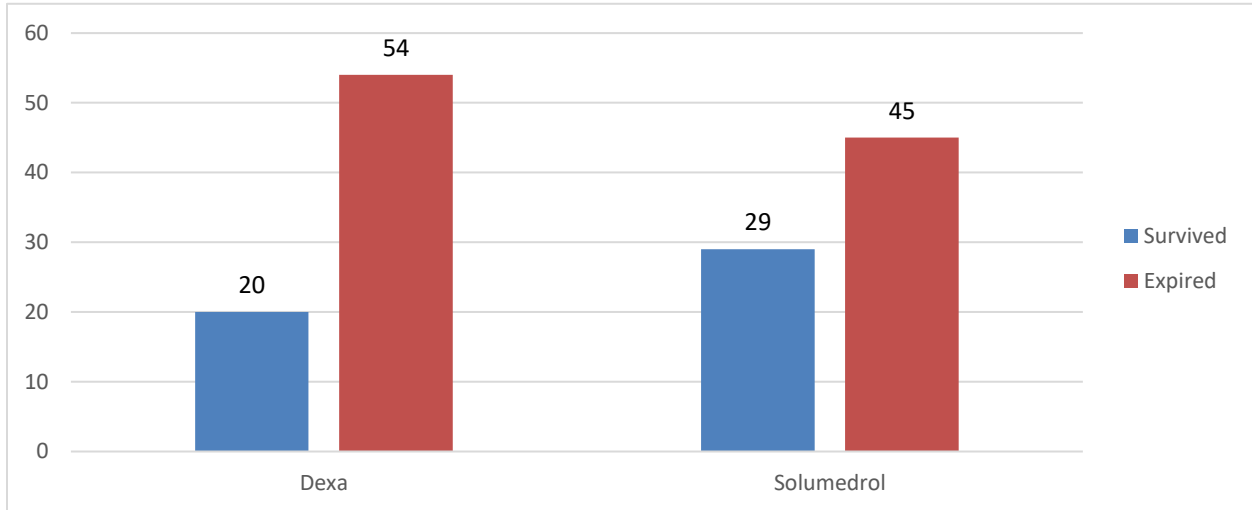


Figure 1: Comparison of mortality between the groups

Antibiotic coverage was also given to all patients in both groups, depending on culture reports and clinical experience. Piperacillin/tazobactam was given to 37(50%) and 49(66%), Azithromycin to 17(23%) and 49(66%) patients, rivaroxiban to 64(86%) and 71(95.9%) patients, levofloxacin to 18(24.3%) and 11(14.9) patients, moxifloxacin was given to 22(29.7%) and 31(41.9%) patients while 48(64.9%)and 25(33.8%) patients got meropenam in methylprednisolone and dexamethasone group respectively.

Discussion

Since the commencement of the COVID-19 pandemic, the whole world has been facing financial and mental stress. It has been more than a year since the beginning of this deadly contagion, and vaccines are showing promising results now. But the vaccine is used as a prevention tool; once this deadly virus enters the body and starts multiplying in the body, then the vaccine's injection would be useless. We needed some wonder drugs that could save this ailing humanity from this disease. In the beginning, physicians didn't know about the pathophysiology of this disease and had to make decisions without solid evidence. But with the passage of time and progress in the field of research, some life-saving drugs are coming into account.

At the beginning of the pandemic, the role of steroids was controversial. Only some of the medications, like Redeliver, were approved by the Food and Drug Administration (FDA) as antiviral drugs for COVID-19 (Wang et al., 2020b). Now,

all of the focus of COVID-19 management is directed towards the management of complications which are ARDS and Cytokine release syndrome., inflammatory markers are increased in both of these complications and this causes deregulated inflammatory reactions and eventually death of the patients, so the management of this type of situation could be handled with those drugs that can decrease the levels of inflammatory markers so that cytokine storm can be taken down (Ragab et al., 2020).

In our study, we compared the effect of methylprednisolone and dexamethasone on the outcomes of the patients. We compared our data with previous steroid management. According to them, methylprednisolone has better lung penetration than dexamethasone, so it will be a better drug for immunosuppression and treatment of COVID-19 (Cherkes et al., 2020; Meduri et al., 2018). Out of a total of 148 patients; overall mortality was lesser in the methylprednisolone group, which was 60.8%(45 patients) than dexamethasone group in which death was reported in 54 patients (73%). An RCT in Iran enrolled 86 patients; 44 were in the methylprednisolone group, while 42 belonged to the dexamethasone group. They compared both of these drugs, and there were significant results regarding improved oxygen saturation levels and decreased mortality and morbidity. The methylprednisolone group also reported a decrease in the requirement for a ventilator (Ranjbar et al., 2021). Our study has the same outcome as this RCT; there was decreased mortality in the methylprednisolone group compared to another group, and there was no significant association between underlying conditions in both studies.

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There are not many studies regarding the comparison of both of these drugs. These drugs are discussed independently or collectively, but comparison studies are rare. One of the most prominent trials has been done in the UK, the RECOVERY trial, which opened new horizons for more evidence in the management of COVID-19; in this trial, there was significant decrease in the mortality in dexamethasone group to the other group who was on standard care. However, this decrease in oxygen requirement and mortality was more significant in moderate and severe COVID-19 patients. There were 482(22.9%) patients in the dexamethasone group, while 1110(25.7%) patients were in the standard care group. However, the RECOVERY trial had an extensive database of more than 4000 patients (Wilkinson, 2020). Whereas, they didn't study the effects of methylprednisolone, which our study did. Some studies did show promising results regarding the therapeutic effects of methylprednisolone, and they are much more promising than dexamethasone.

A study in China studied patients who got IV methylprednisolone with the patients who didn't get methylprednisolone. The outcome was exciting, and there was a significant decrease in mortality and morbidity in patients who got this wonder drug compared to the other group (Wang et al., 2020a). A study in Michigan compared the early usage of methylprednisolone with the other group on standard care, with a sample size of 213 COVID-19 patients. They reported a significant decrease in mortality and a promising decrease in hospital stays (Fadel et al., 2020). They didn't compare dexamethasone, unlike our study, which compared both types of steroids.

It is well-known that corticosteroids would benefit when used appropriately during the disease (Darwish et al., 2011). For example, some studies showed an elevation in mortality morbidity and also increased the duration of viral clearance, using steroids for MERS and influenza (Arabi et al., 2018; Lansbury et al., 2020). Managing patients with COVID-19 do come with some complication like superadded infection, immunosuppression, and hyperglycemia (Edalatfard et al., 2020). our study didn't report any side effect other than hyperglycemia in diabetic patients, and this hyperglycemia was slightly more in the methylprednisolone group. Therefore, total doses of antibiotics and immunomodulators should also be administered as prophylactic medication to prevent superinfections and improve immunity, respectively (Corral-Gudino et al., 2020; Wang et al., 2020a). We gave prophylactic medication to all our patients to prevent this super-added infection.

This study has limitations like small sample size and limited data regarding compilations, laboratory parameters, and radiological investigations. Larger RCTs should be done to achieve further, more accurate evidence. There is a need for patient follow-ups so that the long-term effects of methylprednisolone can be evaluated.

Conclusion

In severe COVID-19 patients in hospital, the administration of 40mg twice daily of methylprednisolone resulted in better outcomes than 6mg once daily of dexamethasone. The Methylprednisolone group had lesser morbidity and lower mortality.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate.

Approved by the department Concerned.

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

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