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Are high dose steroids are preferable than low dose steroids in COVID 19 pneumonia?

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Abstract

Background: In COVID 19 there is systemic inflammatory response that can lead to lung injury and multisystem organ dysfunction. It has been proposed that the potent anti-inflammatory effects of corticosteroids might prevent or mitigate these deleterious effects. Conversly at the other end of the dose range high levels of corticosteroids are immunosuppressive and can increase risk of fatal infection including sepsis. Giving optimal level of corticosteroids at the right time is vital to control infections and restore homeostasis.

Aim: The aim of the study is to compare benefits and side effects of high dose corticosteroids and low dose corticosteroids in treatment of covid 19 pneumonia.

Materials and Methods: This study is retrospective, observational study of 80 patients diagnosed with covid 19 pneumonia. They were divided into two groups, one group of patients received low dose of steroids (0.5-1mg/kg/day for 7-10days) and other group of patients received high dose of steroids(>250mg/day for 7-10days). In these two groups of patients we compared duration of hospital stay, duration of oxygen support, mortality rate of the patients. These group of patients are followed up for development of side effects of corticosteroids, here we look into three side effects-recurrent infections, poorly controlled diabetes and skin manifestations. Data was analysed.

Results: Out of 80 patients (40 in high dose group and 40 in low dose group) mean duration of hospital stay and mean number of days of oxygen support were more in high dose group compared to low dose group. However, the difference was not found to be statistically significant (P value >0.05). In low dose group 22.5% died as compared to 40% in high dose group. However, on performing chi square test, this difference was not found to be statistically significant (P value >0.05). In low dose group 3.2% had complications as compared to 25% in high dose group. On performing chi square test, this difference was found to be statistically significant (P value <0.05). In low dose group 9 patients were expired and in out of remaining 31 patients, 1 patient developed acne. In high dose group 16 patients were expired and in out of remaining 24 patients, 1 patient developed mucormycosis, 1 patient developed lung abscess,2 patients had acne,1patient had poorly controlled diabetes mellitus, 1 patient had recurrent UTI with poorly controlled diabetes mellitus.

Interpretation: Our study showed there are equal benefits with both high dose and low dose of steroids in covid 19 pneumonia but high dose steroids have more side effects than low dose of steroids. So low dose steroids are more preferable than high dose steroids in covid 19 pneumonia. However our sample being small, a study with a large number of samples required to predict the outcome.

Keywords: Covid-19, mucormycosis, UTI, corticosteroids, mortality, uncontrolled diabetes

Introduction

Covid 19 is a global pandemic. Its clinical spectrum ranges from asymptomatic to severe covid pneumonia. Recently some studies showed use of high dose of steroids in covid pneumonia results in early recovery and decreased mortality rate but no trial done comparing the benefits and side effects of high dose of steroids and low dose of steroids. This study is done to know whether high dose steroids are preferred over low dose steroids.

Material and Methods Study design and participants

This study is retrospective, observational study of 80 patients diagnosed with covid 19 pneumonia in april and May 2021 in Hyderabad. Here we have included

Patients with microbiologically confirmed covid 19 with radiological evidence of covid pneumonia

b) Patients who are coming under category of moderate to severe covid 19 with either Respiratory rate >24cpm or saturation <94% on room air

Patients coming under mild category that is who are asymptomatic and with Respiratory rate <24cpm or saturation 94% on room air are excluded. Data is collected from the medical records.

Procedure

Total 80 patients were divided into two groups, one group of patients receiving low dose of steroids(0.5-1mg/kg/day for 7-10days) and other group of patients receiving high dose of steroids (>250mg/day for 7-10days). Both groups received other standard treatment.

Statistical analysis

In these two groups of patients we compared duration of hospital stay, duration of oxygen support, mortality rate of the patients. These group of patients are followed up for development of side effects of corticosteroids, here we look into three side effects-recurrent infections, poorly controlled diabetes and skin manifestations. Data was analysed using SPSS v21.Categorical data was presented as frequencies and percentages. Continuous data was presented as mean and standard deviation. Chi square test was used as test of significance for categorical data. Mann Whitney test was used as test of significance for continuous data (two groups) (skewed data/abnormal data).p value less than 0.05 was considered as statistically significant.

Results

Among two groups mean duration of hospital stay and mean number of days of oxygen support were more in high dose group compared to low dose group. However, the difference was not found to be statistically significant (P value >0.05).

Table 1: Duration of Hospital stay

	Steroid	N	Mean	Std. deviation	P Value	
Duration of hospital stay	Low dose	40	7.88	3.568	550 (NC)	
	High dose	40	8.48	4.432	.552 (NS)	
N £	Low dose	40	5.25	4.425	160 (NC)	
Number of days of oxygen support	High dose	40	6.45	4.557	.169 (NS)	

^{*}Mann Whitney test

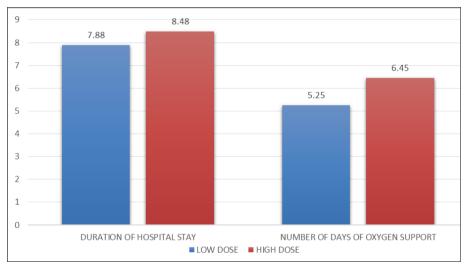


Fig 1: Duration of Hospital stay

In low dose group 22.5% died as compared to 40% in high dose group. However, on performing chi square test, this

difference was not found to be statistically significant (P value >0.05).

Table 2: Outcome compared with low and high doses

			Steroid		Total
			Low dose	High dose	Total
Outcome	Death	Count	9	16	25
		%	22.5%	40.0%	31.3%
	Discharged	Count	31	24	55
		%	77.5%	60.0%	68.8%
Total		Count	40	40	80
		%	100.0%	100.0%	100.0%

Chi Square = 2.851, P value = 0.091 (NS)

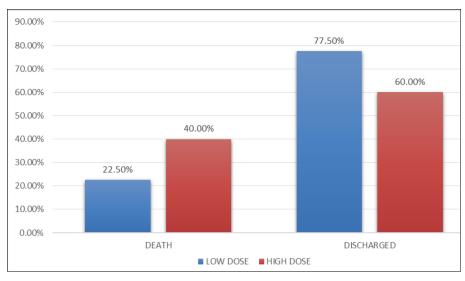


Fig 2: Outcome compared with low and high doses

In low dose group 9 patients were expired and in out of remaining 31 patients, 1 patient developed acne. In high dose group 16 patients were expired and in out of remaining 24 patients,1 patient developed mucormycosis,1 patient developed lung abscess,2 patients had acne,1patient had poorly controlled diabetes mellitus,1 patient had recurrent UTI with poorly controlled diabetes mellitus. In low dose group 3.2% had complications as compared to 25% in high dose group. On performing chi square test, this difference was found to be statistically significant (P value <0.05).

Table 3: Complications

		Ste	Total		
			Low dose	High dose	Total
Complications	No	Count	30	18	48
		%	96.8%	75.0%	87.3%
	Yes	Count	1	6	7
		%	3.2%	25.0%	12.7%
Total		Count	31	24	55
		%	100.0%	100.0%	100.0%

Chi square = 5.774, P value = 0.016 (S)

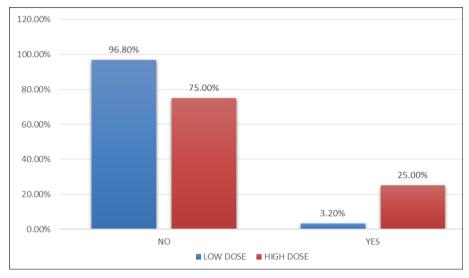


Fig 3: Complications

Discussion

The ongoing pandemic of Corona virus Disease 2019 (COVID-19), caused by the novel Severe Acute Respiratory Syndrome-Coronavirus (CoV)-2 (SARS-CoV-2), was declared a Public Health Emergency of International concern on January 30, 2020 by the World Health Organization (WHO) [1]. Its first case reported in December 2019 in Wuhan, China. SARS-CoV-2 has a zoonotic source closely related to bat-origin SARS-like coronavirus [3]. Most patients with COVID-19 predominantly have a respiratory tract infection associated with SARS-CoV-2 infection. However, in a small proportion of cases, they can progress to a more severe and systemic disease characterized by the Acute Respiratory Distress Syndrome (ARDS), sepsis and

septic shock, multi organ failure, including acute kidney injury and cardiac injury [3].

Several pharmacological agents have been proposed as a potential treatment based on theoretical considerations, *in vitro* studies, or clinical trials conducted in conditions by other related viruses. However, current evidence has not confirmed the presence or absence of benefit of these treatments and even warns of their probable risks or adverse effects associated with their use ^[4]. The anti-inflammatory properties of corticosteroids reduce systemic inflammation, exudative fluid in the lung tissue and also prevents the further diffuse alveolar damage, thereby improving the hypoxia and minimizes the risk of respiratory failure ^[5].

Glucocorticoids are essential during infection or following trauma. Conversely at the other end of the dose range high levels of glucocorticoids are immunosuppressive and can increase risk of fatal infection including sepsis. Hitting the optimal level of glucocorticoids at the right time is vital to control infections and restore homeostasis [2]. Therefore what is lacking is knowledge on the optimal start of corticosteroid of illness, administration after the start subpopulations and dose and duration type, corticosteroids [8]. Given the diversity in the mechanism of action of glucocorticoids, they can cause a wide array of adverse effects ranging from mild to severe, some of which are unavoidable. Of all the factors influencing the adverse effects of glucocorticoids, dose and duration of therapy are the most important independent and well-documented risk factors [6] several other factors may influence the adverse effects of glucocorticoids. Older age, comorbid conditions (such as diabetes mellitus), concomitant use of other immunosuppressive agents, severity and nature of the underlying disease, and poor nutritional status can all influence the occurrence and magnitude of side effects^[6]. Short-term corticosteroid use is associated with generally mild side effects, including cutaneous effects, electrolyte abnormalities, hypertension, hyperglycemia, pancreatitis, hematologic, immunologic, and neuropsychological effects, although occasionally, clinically significant side effects may occur [9].

Here this study is retrospective, observational study in covid 19 patients. This study is done to avoid confusion among physicians in choosing the steroid dosage in covid pneumonia patients. After analysis of both study groups, it showed both groups have equal benefits but more side effects are seen in high dose group.

Conclusion

Our study showed there is no significant difference in duration of hospital stay, duration of oxygen support and mortality rate of patients who received high dose of steroids than low dose of steroids in covid pneumonia but there are more side effects with high dose group compared to low dose group. High dose steroids are to be used with caution. Low dose steroids are more preferable than high dose steroids. However our sample being small, a study with a large number of samples required to predict the outcome.

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Conflict of Interest

None

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