Egyptian Journal of Medical Microbiology Volume 34 / No.3 / July 2025 313-320 Online ISSN: 2537-0979

ORIGINAL ARTICLE

Retrospective Evaluation of the Outcome of Covid-19 Patients Given Pulse Methylprednisolone versus Standard Steroid Therapy

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Key words:
Covid-19 Steroid Therapy
Pulse Methylprednisolone

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ABSTRACT

Background: *Except for corticosteroids, no gold standard therapy globally was approved for COVID-19 pneumonia to the date of this study. Studying the pathophysiology of the disease showed that the deterioration that accompany many of cases of COVID-19 pneumonia is related to hyper-immune response causing what is called Cytokine release syndrome/cytokine storm, so, testing various regimens of steroid therapy to control the disease seemed reasonable idea.* ***Objective:*** *To evaluate the results of using different regimens of steroid therapy as a treatment for moderate to severe cases of COVID-19.* ***Methodology:*** *This Study is a retrospective, observational study done on patients with moderate to severe COVID-19 pneumonia who were admitted to the isolation Hospital of Kasr Alainy Medical School, Cairo University, Egypt, between October 2020 and May 2021.* ***Results:*** *In this study we demonstrated statistical difference and increase incidence (ICU stay, need for & length of MV, The incidence of 2ry bacterial infection & GIT bleeding, in hospital mortality) for COVID-19 moderate to severe pneumonia in group A (received pulse steroid therapy) of patients coming during cytokine release syndrome associated COVID-19 pneumonia.* ***Conclusion:*** *Using pulse methyleprednisolone therapy in combination with standard treatment didn't show additional benefit than that could be achieved using standard regimen alone, it lead to multiple side effects regarding increasing hospital mortality, need for mechanical ventilation (either invasive or non- invasive), duration of ICU stay & increase incidence of 2ry bacterial infection and GIT bleeding in patients with moderate to severe COVID-19 pneumonia. Pulsed dose steroid use was more frequent in patients receiving high respiratory support, so future studies should address patient selection and outcome effects of pulsed steroids in severe and deteriorating patients with COVID-19 pneumonia.*

INTRODUCTION

In the years 2019–2020, a new Cronavirus known as SARS-CoV-2 was discovered to be the causative agent of a number of acute respiratory infections known as COVID-19, which is causing a worldwide pandemic[1].

There are still many unanswered issues about the disease's pathophysiology, particularly the causes for the disease's widely diverse clinical response, which ranges from asymptomatic forms to severe symptoms like Acute Respiratory Distress Syndrome (ARDS)[2].

Evidence points to the so-called "cytokine storm", which can be defined as an uncontrolled overproduction of soluble mediators of inflammation that leads to an abnormal systemic inflammatory response, is a crucial factor in the development of severe forms of the disease and ARDS[3].

There are few treatment options for severe COVID-19. A therapeutic strategy that relies on immuno-modulatory medication to reduce the cytokine storm could provide insight into COVID-19 treatment. The use of an immuno-modulatory drug to attenuate the cytokine storm may allow additional time for patients with COVID-19 to receive supportive care. Using a variety of therapeutic options, several procedures proposed different techniques to control the cytokine release storm [4].

Corticosteroids are one of the most widely prescribed medications for infectious disease immunomodulation. Steroids had a significant favorable effect on SARS-CoV-2 critically ill patients' survival. Corticosteroids are the classical immunosuppressive drugs, which are important to stop or delay the progress of the pneumonia, and have been proved to be effective for the treatment of acute respiratory distress syndrome

(ARDS). But, there is deficient data about using of pulse steroid therapy in treatment of COVID -19 patients [5].

The aim of our work was to evaluate the results of using different regimens of steroid therapy as a treatment for moderate to severe cases of COVID-19. We will compare the efficacy & adverse effects of using Pulse methylprednisolone compared with standard dose of steroid therapy (beside the standard care treatment) in hospital mortality, need for mechanical ventilation and comparing adverse effects of different lines of treatment (incidence of 2ry bacterial infection and GIT bleeding).

METHODOLOGY

This Study is a retrospective, observational study done on patients with moderate to severe COVID-19 pneumonia who were admitted to the isolation hospital of Kasr Alainy Medical School, Cairo University, Egypt, between October 2020 and May 2021.

The study population was adults (between 18-80 years) with COVID-19, confirmed by PCR on nasopharyngeal swab, who were admitted to ICU of isolation hospital of Kasr Alainy Medical School. Eligible patients had moderate to severe pneumonia, defined by at least one of the followings: Respiratory rate at least 30 per minute or more, oxygen saturation in the periphery decreased to a level less than 93 percent on ordinary room air, Hypoxic index of less than 300 mm Hg on ordinary room air, and the presence of infiltrations in both lungs not less than of 50 percent in radiological imaging, based on the 6th version of guidelines of management of COVID-19 from China. [6,7]

Exclusion criteria

- Patients under the age of 18 or above the age of 80
- Patients presented by acute respiratory failure or known heart failure patients
- Patients who need Long-term oxygen treatment or home ventilation equipment.
- Patients with history of lung fibrosis, progressive neuromuscular problems (e.g., Duchenne, Amyotrophic lateral sclerosis, ALS), dementia or decompensated mental conditions
- prolonged use of immunosuppressive therapies and chronic use of corticosteroids
- pregnancy

The Ethical Committee of Cairo University's Faculty of Medicine gave its approval to the project (MD-423-2021) 6 June 2023. All of the patients signed a written, informed consent form.

Patients were divided into two groups, group (A): Patients got pulse dose of methylprednisolone in addition to standard of care treatment. Patients were considered to be eligible for pulse steroid treatment if they had a SaO_2 of less than 93 percent and a PaO_2/FiO_2 ratio of less than 300 mm Hg in room air or a more than 30 percent decrease in their PaO_2/FiO_2 ratio in the previous 24 hours during hospitalization, bilateral infiltrates in CT chest, and elevated inflammatory markers (CRP, Ferritin, LDH, IL-6 Levels). Pulse steroid was given intravenously in doses of 500mg to 1 GM given for 3 days. Group (B): got just standard steroid therapy (Methylprednisolone 1-2mg/kg/day or dexamethasone 6mg intravenous for 10 days) with standard treatment according to local recommendations issued by the Egyptian Ministry of Health and Population at the time of the epidemic .[8]

Standard of care treatment included oxygen therapy with a target SaO_2 of at least 92 percent, broad spectrum antibiotics at the decision of the physician if a bacterial respiratory superinfection occurred, low molecular weight heparin prophylactic doses based on bodyweight and renal function, proton pump inhibitor, and poly-vitamins. It should be noted that the guidelines were amended subsequently in response to new scientific papers and WHO recommendations. At hospital admission, all patients were subjected to complete medical history, chronic comorbidities, demographic and epidemiological data, and baseline oxygen saturation was recorded. Other therapies were documented as well. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score was used to determine the risk of multi-organ failure and death, while the Pneumonia Severity Index was used to measure the severity of respiratory symptoms (PSI) [9,10]

Clinical informations such as clinical pictures, complete blood count, coagulation, inflammatory and biochemical indicators were routinely recorded in patients' files in accordance with the hospital's local regulations.

The primary outcome of the study was to evaluate effect of both regimens on ICU stay, overall hospital stay, in hospital mortality, need for mechanical ventilation (either invasive or non-invasive), and the incidence of complications related to the drugs as secondary bacterial infection and GIT bleeding.

Statistical analysis:

Data were coded and entered using the statistical Package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Then comparisons were done using appropriate statistical analyses. The confidence interval was set to 95% and the margin of error accepted was set to 5%.

RESULTS

Fifty patients (50%) received pulse dose of methylprednisolone therapy in addition to standard

therapy group A with median age 60 years, 50 patients (50%) received standard steroid therapy group B with median age 60 years, with no significant difference between two groups Table 1.

Overall 73 out of 100 (73%) of the patients were males, 27 (27%) were females, in Group (A) 36 out of 50 (72%) were males, 14 (28%) were females, in Group (B) 37 (74%) out of 50 were males, 13 (26%) were females, p-value 0.822. with no significant difference between two groups Table 2.

Data for comorbidities among patients showed that Group B had a higher burden of diabetes, 20 (40%) out of 50 patients compared to 17 (34%) out of 50 in Group A however no significant statistical difference between two groups, p-value 0.53.Also Group B had higher percent of patients suffering cardiac conditions (ischemia) (22%) compared to 16% in Group A however no significant statistical difference was noted, P-value 0.05, to be mentioned that ischemic heart disease is identified as a risk factor for mortality in Covid pneumonia [4,7,6].

Other comorbidities (Hypertension and Chronic kidney disease) showed no significant difference in both groups Table 2.

Vital signs and biochemical markers, total leukocytic count, inflammatory markers were compared between the two groups upon admission and after one week of steroid therapy, they didn't show significant difference Table 3, except for oxygenation on admission, temperature and CRP level

Oxygenation on admission which was significant lower in Group A (P-Value 0.019). Also temperature degree which was significant higher in Group A (P-Value 0.002).

Analysis of the results showed significant laboratory decrease of inflammatory markers (CRP) in both groups within 1 week from starting treatment, group A, Mean on admission was 89, Median 85, SD 48, Compared to mean 65, median 57, SD 53 after 1 week of treatment with p-value 0.002. In group B**,** on admission CRP Mean was 102, Median 90, SD 82, compared to Mean 43, median 35, SD 44 after 1 week of treatment, p-value <0.001 Table 4.

But by Comparing the two groups showed no significant difference in delta change of CRP level after one week Table 5, 6.

Table 1: Age of patients in each group

	Pulse group					Standard group					P value
	Mean	SD	Median	Mini	Maxi.	Mean	SD	Median	Mini.	Maxi.	
AGE	60.42	14.59	63.50	27.00	79.00	59.58	16.10	60.50	25.00	78.00	0.730

Table 2: Characteristics and comorbidities of patients in each group

		Pulse group		Standard group		P value
		Count	%	Count	%	
Gender	**Male**	36	72.0%	37	74.0%	0.822
	Female	14	28.0%	13	26.0%	
HTN	**Yes**	34	68.0%	29	58.0%	0.300
	No	16	32.0%	21	42.0%	
DM	**Yes**	17	34.0%	20	40.0%	0.534
	No	33	66.0%	30	60.0%	
Cardiac history	**Yes**	8	16.0%	11	22.0%	0.444
	No	42	84.0%	39	78.0%	
Chronic respiratory proplem	**Yes**	7	14.0%	3	6.0%	0.182
	No	43	86.0%	47	94.0%	
CKD	**Yes**	2	4.0%	5	10.0%	0.436
	No	48	96.0%	45	90.0%	
CLD	**Yes**	2	4.0%	0	0.0%	0.495
	No	48	96.0%	50	100.0%	

Table 3: Clinical and laboratory findings on admission and after steroid therapy in both groups

	Pulse group					Standard group					P value
	Mean	SD	Median	Mini.	Maxi.	Mean	SD	Median	Mini.	Maxi.	
AGE	60.42	14.59	63.50	27.00	83.00	59.58	16.10	60.50	25.00	95.00	0.730
Oxygenation on admission	78.94	11.85	83.00	40.00	98.00	83.12	10.54	86.00	50.00	93.00	0.019
Temperature O/A	38.85	0.53	39.00	38.00	40.00	38.50	0.54	38.50	37.50	40.00	0.002
FERRETIN on admission	733.22	351.55	668.00	162.00	1896.00	675.12	395.66	630.00	98.00	2200.00	0.401
FERRETIN after steroid therapy	620.31	320.22	620.00	110.00	1700.00	612.32	340.54	610.00	90.00	2110.00	0.521
D-DIMER on admission	507.32	456.38	335.00	118.00	2360.00	727.43	899.66	390.00	200.00	3970.00	0.443
D-DIMER after steroid therapy	490.72	433.67	320.00	109.00	2180	709.56	839.56	340.00	180.00	3460.00	0.431
TLC before steroid therapy	9.42	5.55	7.80	2.80	34.00	9.39	3.97	8.90	2.50	20.00	0.511
TLC after steroid therapy	14.49	10.58	12.35	4.00	67.00	11.33	3.94	11.00	4.90	19.80	0.199
Procalcitonin on admission	1.02	3.18	0.24	0.10	20.00	1.26	3.77	0.16	0.10	20.00	0.192
PCT after steroid therapy	1.20	2.25	0.33	0.10	11.70	0.35	0.50	0.13	0.10	2.90	0.062
IL -6	131.87	113.20	99.00	3.00	414.00	114.60	111.20	82.00	4.00	340.00	0.672

Table 4: CRP level in Group A before and after one week of steroid therapy

	pulse group					P value
	Mean	SD	Median	Mini.	Maxi.	
CRP on admission	89.61	48.51	85.00	5.00	251.00	0.002
CRP after steroid therapy	65.79	53.31	57.50	1.80	199.00	

Table 5: CRP level in Group B on admission and after one week of steroid therapy

	Standard group					.
	Mean	SD	Median	Mini.	Maximum	
CRP on admission	102.33	82.11	90.00	17.00	432.00	<0.001
CRP after steroid therapy	43.48	44.99	35.50	0.40	253.00	

Table 6: CRP changes in both groups (on admission and after 1 week)

	Pulse group					Standard group					P value
	Mean	SD	Median	Mini.	Maxi.	Mean	SD	Median	Mini.	Maxi.	
CRP on admission	89.61	48.51	85.00	5.00	251.00	102.33	82.11	90.00	17.00	432.00	0.837
CRP after steroid therapy	65.79	53.31	57.50	1.80	199.00	43.48	44.99	35.50	0.40	253.00	0.034
CRP (Delta change)	57.39	564.16	-43.10	-96.35	3880.00	-40.80	74.38	-64.75	-98.26	211.76	0.066

Severity of symptoms and expected mortality in both groups were assessed and compared using APACHE II & pneumonia severity index (PSI) which showed no significant difference among both groups.

APACHE II score in group A, was mean 16.64, median 15, SD 5.15, while in group B, was mean 15.7, median 15, SD 3.97, p-value 0.576. Mean expected mortality in group A 23.9%, Median 25%, SD 7.4, mean expected mortality in group B 22.64%, Median 25%, SD 6.79, p-value 0.350 Table 4.

PSI in group A, Mean 131, Median 132, SD 22.5, In group B, Mean 126, Median 122, SD 21.9, P-value 0.135.

Expected mortality in group A, Mean 21%, Median 29%, SD 9.6, In group B, expected mortality, mean 19.20%, median 15%, SD 9.59%, P-value 0.301 Table 7**.**

One week after steroid therapy, there was significant difference in oxygen requirement and the need for mechanical ventilation (either invasive or non-invasive).

Among 50 patients in group A, 42 (84%) needed high oxegen requirement 34 of them needed non-invasive Mechanical Ventilation in later stage, compared to 30 (60%) out of 50 in group B, 12 0f them needed NON invasive MV later (p-value 0.001) Table 8**.**

On the other side... 26(52%) in Group A needed for invasive MV while 14 (28%) patients in Group B needed invasive MV (p-value 0.014). There was no significant difference as regards duration of oxygen therapy in both groups. In Group A, Mean duration of oxygen support was 7.6 days, Median 7 days, SD 4.7, compared to Mean 7.6 days, Median 7.5 days, SD 4.2 in Group B, P-value 0.93. The two groups didn't show significant differences as regards duration of mechanical ventilation (either invasive or non- invasive)

Table 7: Evaluation of severity and expected mortality in both groups

	Pulse group					Standard group					P value
	Mean	SD	Median	Mini.	Maxi.	Mean	SD	Median	Mini.	Maxi.	
Apache II	16.64	5.15	15.00	10.00	29.00	15.76	3.97	15.00	10.00	25.00	0.576
Apache II Expected Mortality	23.98	7.47	25.00	15.00	37.00	22.64	6.79	25.00	13.00	35.00	0.350
PSI	131.78	22.57	132.00	64.00	166.00	126.52	21.95	122.00	64.00	166.00	0.135
PSI Expected Mortality	21.26	9.61	29.00	9.00	30.00	19.20	9.59	15.00	9.00	30.00	0.301

Table 8: Need for oxygen requirement and MV after one week of steroid therapy

		Pulse group		Standard group		P value
		Count	%	Count	%	
Non rebreather mask	**Yes**	42	84.0%	30	60.0%	0.008
	No	8	16.0%	20	40.0%	
NIV	**Yes**	34	68.0%	12	24.0%	< 0.001
	No	16	32.0%	38	76.0%	
Intubation and MV	**Yes**	26	52.0%	14	28.0%	0.014
	No	24	48.0%	36	72.0%	

Table 9: Oxygen support and ICU days with timing of starting steroid therapy

	Pulse group					Standard group					P value
	Mean	SD	Median	Mini.	Maxi.	Mean	SD	Median	Mini.	Maxi.	
Daysof oxgen support	7.65	4.76	7.00	1.00	30.00	7.69	4.27	7.50	1.00	25.00	0.935
Days of MV	8.73	3.56	8.00	4.00	17.00	8.07	3.15	7.00	5.00	15.00	0.644
Days of NIV	4.94	2.35	5.00	1.00	13.00	6.33	3.98	5.00	1.00	15.00	0.301
ICU days	12.98	5.43	12.00	5.00	35.00	11.13	5.20	9.50	6.00	30.00	0.017
Timing of Steroid Therapy from Onset of Symptoms (Days)	8.50	4.10	7.50	3.00	25.00	7.37	4.07	7.00	1.00	21.00	0.165

There is no significant difference in timing of starting of steroid therapy between two groups as mean 8.5sd 7.5 with average 8 days in Group A while mean 7.3sd 4 with average 7 days in Group B p-value 0.16. Analysis of ICU days between two groups showed significant difference decrease in ICU days in GROUP B as in Group A mean 12.9sd 12, median 5.4 with average days 13, while in Group B average ICU days was 10 with mean 11sd 5.2 median 9.5 P-value (0.017). Regarding mortality, there was significant increase of mortality rate in group A, as 28 patients (56%) out of 50 in group A died compared by 14 patients (28%) out of 50 died in group B. (P-value 0.005) Table 10.

Also there was significant increase in rate of 2ry bacterial infection after steroid therapy in group A. Twenty six patients (52%) in group A had 2ry bacterial infection defined by radiological data with positive cultures (mostly bacterial pneumonia & urinary tract infection) compared to 12 patients (24%) in group B, (P-value 0.004) Table 11.

Analysis of results showed significant increase in GIT bleeding in Group A. As thirteen patient (26%) had GIT bleeding after pulse steroid therapy in Group A compared 4 patients (8%) in Group B with P-value 0.017 Table 12.

Table 10: Mortality in both groups

Outcome	**Died**	28	56.0%	14	28.0%	0.005
	Alive	22	44.0%	36	72.0%	

Table 11: Secondary bacterial infection in both groups

		Pulse group		**Standard group**		**P value**
		Count	**%**	**Count**	**%**	
2ry bacterial infection	**Yes**	26	52.0%	12	24.0%	0.004
	No	24	48.0%	38	76.0%	

Table 12: GIT bleeding in both groups

		Pulse group		**Standard group**		**P value**
		Count	**%**	**Count**	**%**	
GIT Bleeding	**Yes**	13	26.0%	4	8.0%	0.017
	No	37	74.0%	46	92.0%	

DISCUSSION

The aim of this study was to determine the effect of pulse steroid therapy administered to patients hospitalized in an intensive care unit (ICU) with moderate to severe COVID-19 pneumonia.

Our results showed no significant difference in epidemiological data and comorbidities among both groups matched with result of study done by Salvarani etal.[11] which showed no significant difference according to comorbidities among both groups.

Regarding the clinical data on admission, Group A had lower significant decrease in oxygen saturation and higher grades of fever matched with the studies done by Christopher et al., and Gundogdu et al.,) [12,13]. There was no statistically significant difference in APACHE II and PSI scores on admission between the two groups, denoting uniform selection of patients included in this study and nullify the risk of selection bias.

Regarding to timing of starting of steroid therapy from onset of symptoms, there is no significant difference among both groups.

After one week of steroid therapy: Regarding to inflammatory parameters. The results showed significant decrease in CRP level in both groups. As in Group A, the mean CRP level on admission was 89ml (±48), Compared to mean 65, (±53) after 1 week of treatment... Also in Group B, on admission CRP Mean was 102, (±82), compared to Mean 43 (±44) after 1 week of treatment. These results matched with the study done by Gundogdu etal.[13] which showed significant decrease in CRP level among both groups but disagreed with the study done by Christopher etal.[12] which showed no significant changes in CRP Level... This conflict may be explained by the type of patients in this study was more sick (ECHMO and invasive MV).

There was no significant difference in delta change of CRP level among both groups after one week from starting treatment. However to be noted that change in CRP wasn't associated with clinical improvement of symptoms or severity of inflammatory response in all cases.

In spite of Procalcitonine results after one week of steroid therapy showed no significant difference among both groups, But PCT had higher tendency to decrease

after steroid therapy in Group B than Group A (Group A mean 1.2 to 1.02vs Group B mean 1.26 to 0.35).

Also total leucocytic count had higher tendency to increase in Group A after steroid therapy than Group B but no significant difference presence (Group A mean 9.4to 14vs Group B mean 8.9 to 11).

Other inflammatory parameters as the D-dimer and ferritin showed no significant decrease either among each group or in comparing with the other group after one week from starting therapy however our results disagreed with study done by Gundogdu et al. [13] which showed significant decrease in both D-dimer and ferretin more in standard group

Regarding oxygen requirement and the need for mechanical ventilation, Group A had higher need for oxygen requirement, non-invasive mechanical ventilation after one week of steroid therapy than Group B. As among 50 patients in Group A, 42 (84%) needed high oxygen requirement 34 of them needed non invasive MV in later stage, compared to 30 (60%) out of 50 in group B needed high o2 requirement, 12 0f them needed non- invasive MV later.

Also group A had higher need for invasive MV, in comparison to Group B (26 patients (52%) in Group A vs 14 patients (28%) in Group B.

Our results match with the study done by Gundogdu et al.[13] which showed same results in pulse group. There was no significant difference as regards duration of oxygen therapy and duration of mechanical ventilation (either invasive or non- invasive) in both groups.

According to length of ICU stay, Group A had significant longer duration in ICU than Group B**...** As in Group A the mean was 12.9(±12) with average 13 days while in Group B average ICU days was 10 days with mean 11(±5.2). This result matches with the study done by Christopher et al.[12] which showed the same result in pulse group. But disagreed with the Salvarani et al. study[11] which showed no significant difference according to length ICU stay.

Regarding to outcomes**,** Group A had higher mortality rate than Group B. As 28 patients (56%) out of 50 in Group A died compared by 14 patients (28%) out of 50 died in Group B. P-value 0.005. These results matches with similar results from studies done by Christopher et al., Gundogdu et al., and Monreal et al**.,**[12,13,14] which showed increase in the mortality rate in pulse steroid group.

Also, in the Recovery Trial the study done by Peter Horby etal.[15] showed decrease in mortality rate by using standard dexamethasone dose only.

Another study done by Salvarani et al.[11] showed no benefit from adding of pulse steroid therapy in decrease of mortality rate compared by using standard treatment alone

On the other hand, our results disagreed with the study done by Edalatifard et al.[16] which showed higher survival rate with using of pulse steroid therapy…. may be due to that study was prospective randomized controlled study included small number of patients (n 68), and lower dose of pulse steroid was given (250mg for 3 days).

Even the incidence of complications associated with use of steroids (2ry bacterial infection & GIT bleeding) showed significant increase after pulse steroid therapy. As in Group A twenty six patients (52%) had 2ry bacterial infection based on positive cultures and inflammatory markers for bacterial infection) compared to twelve patients (24%) in Group B.

Also, Group A had higher rate in GIT bleeding. As thirteen patients (26%) had GIT bleeding after pulse steroid therapy in group A compared 4 patients (8%) in Group B.

Some studies showed no benefits from adding pulse steroid therapy to standard treatment of Covid 19 pneumonia like the study done by Salvarani et al.[11]

This study had limitations. First of all, this was a single-Centre analysis with no standardised protocol for the use of pulsed steroids. Also, the limited number of patients included in this study .Being a retrospective study not being a prospective randomised trial, therefore unmeasured confounding cannot excluded (as seen in heterogenicity between both groups regarding severity of disease. At last, the data on corticosteroids received after discharge from our ICU was not available for analysis.

There are a lot of questions still in need for answer. These data should be looked to in relation to various epidemiological circumstances. Pulse steroid therapy use in COVID-19 with severe form of the disease still under studying and the best further more randomized trials are needed to establish clear treatment strategies.

CONCLUSION

Despite strong evidence in support of corticosteroids for patients with COVID-19 pneumonia, the optimal dose of corticosteroidsis still unclear. Using pulse methylprednisolone therapy in combination with standard treatment didn't show additional benefit than that could be achieved using standard regimen alone, In addition that leads to multiple side effects regarding increasing hospital mortality, need for mechanical ventilation (either invasive or non- invasive), duration of ICU stay and increase incidence of 2ry bacterial infection and GIT bleeding in patients with moderate to severe COVID-19 pneumonia. Pulsed dose steroid use was more frequent in patients receiving high respiratory support, so future studies should address patient selection and outcome effects of pulsed steroids in severe and deteriorating patients with COVID-19 pneumonia.

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