497. Moderate Versus High Dose Corticosteroids in Adult Patients with Severe COVID-19: Less Is More

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Background. The early administration of corticosteroids (CS) in patients with severe COVID-19 (hospitalized with need for supplemental oxygen) has been the only therapy to improve survival. However, the optimal dosing of CS remains unclear. Beginning March 2020 methylprednisolone (MP) in a dose of 40mg twice daily (high dose CS - HDC) was adopted at our institution. Based on emerging trials, this dose of MP was reduced to 16mg twice daily (moderate dose CS – MDC) in November 2020. The study aims to evaluate the outcome difference in patients receiving HDC versus MDC.

Methods. This pre-post quasi-experimental study was done at Henry Ford Hospital, an 877-bed tertiary care hospital in Detroit, Michigan. Consecutive patients in the HDC group from September 1, 2020 to November 15, 2020 were compared to the MDC group from November 30, 2020 to January 20, 2021. Only hospitalized patients with severe COVID-19 were included. The primary outcome was 28-day mortality. Secondary outcomes included progression to mechanical ventilation, length of hospital stay, discharge on supplemental oxygen and CS-associated adverse events. Patient demographics were evaluated using descriptive statistics. Bivariate and multivariable logistic regression analysis was planned to test the association between primary outcome and exposure.

Results. 470 patients were evaluated, 218 and 252 in the HDC and MDC groups respectively. Clinical characteristics and severity of illness on admission were comparable in both groups (Table 1). Among comorbidities - lung disease, cardiovascular disease and hypertension were higher in MDC. Antibiotic and tocilizumab use were lower in MDC. Significantly more patients in MDC group received oral CS. There was no difference in mortality between HDC and MDC through bivariate and multivariate analysis (14.7% and 13.5%, $p < 0.712$, adjusted OR 0.913 [0.514-1.619]) (Table 2,3). Median length of hospital stay was 5 and 6 days in HDC and MDC respectively ($p < 0.001$). There was no difference in CS-associated adverse events.

Table 1. Patient Characteristics and Treatment Administered

Characteristics	Total (n = 470)	HDC (n = 218)	MDC (n = 252)	P value
Demographics				
Median age (IQR), y	64 (53-74)	63 (52-73)	65 (53-75)	0.295
Male sex, no. (%)	245 (52.1%)	110 (50.5%)	135 (53.6%)	
Race, no. (%)				
Black	220 (46.8%)	98 (45.0%)	122 (48.4%)	0.454
White	103 (21.9%)	53 (24.3%)	50 (19.8%)	0.199
Other	147 (31.3%)	67 (30.7%)	80 (31.7%)	0.886
Median BMI (IQR) – kg/m^2	30.7 (26.3-36.2)	30.2 (26.2-35.7)	31 (26.6-37.1)	0.395
Coexisting conditions, no. (%)				
Asthma	47 (10.0%)	23 (10.6%)	24 (9.5%)	0.711
Chronic Obstructive Pulmonary Disease	57 (12.1%)	20 (9.2%)	37 (14.7%)	0.068
Lung Disease	117 (24.9%)	42 (19.3%)	75 (29.8%)	0.009
Immunodeficiency	50 (10.6%)	20 (9.2%)	30 (11.9%)	0.338
Cardiovascular Disease	153 (32.6%)	57 (26.1%)	96 (38.1%)	0.006
Hypertension	320 (68.1%)	135 (61.9%)	185 (73.4%)	0.008
Chronic Kidney Disease	103 (21.9%)	42 (19.3%)	61 (24.2%)	0.197
Malignancy	61 (13/0%)	32 (14.7%)	29 (11.5%)	0.308
Diabetes	195 (41.5%)	81 (37.2%)	114 (45.2%)	0.076
Severity of illness on admission				
Median qSOFA in ED (IQR)	2 (1-3)	2 (1-3)	2 (1-3)	0.870
Direct admission to ICU from ED, no. (%)	77 (16.4%)	41 (18.8%)	36 (14.3%)	0.187
Mechanical ventilation in ED, no. (%)	10 (2.1%)	4 (1.8%)	6 (2.4%)	0.688
Treatment				
Remdesivir, no. (%)	330 (70.2%)	147 (67.4%)	183 (72.6%)	0.220
Antibiotic, no. (%)	193 (41.1%)	120 (55.0%)	73 (29.0%)	<0.001
Tocilizumab, no. (%)	12 (2.6%)	12 (5.5%)	0 (0%)	<0.001
Corticosteroids				
Total corticosteroids PO, no (%)**	342 (72.8%)	133 (61.0%)	209 (82.9%)	<0.001
Total corticosteroids IV, no (%)**	185 (39.4%)	125 (57.3%)	60 (23.8%)	<0.001
Median duration of corticosteroids (IQR), d	5 (3-7)	5 (3-7)	5 (3-6)	0.072
Median time from admission to steroid administration (IQR), d	1 (1-2)	1 (1-2)	1 (1-2)	<0.001

*Abbreviations: IQR = interquartile range, BMI = body mass index, ICU = intensive care unit, ED = emergency department, qSOFA = quick Sequential Organ Failure Assessment

*Definitions: Lung disease = obstructive sleep apnea, interstitial lung disease, pulmonary hypertension

*Admission to ICU = use of high flow nasal cannula, noninvasive positive pressure ventilation, mechanical ventilation

**Some patients may have received both PO and IV CS during admission

Table 2. Bivariate Analysis of Patient Outcomes

Outcomes	HDC (n = 218)	MDC (n = 252)	P value
Primary outcome			
28d mortality, no. (%)	32 (14.7%)	29 (13.5%)	0.712
Secondary outcomes			
Progression to mechanical ventilation, no. (%)	28 (12.8%)	19 (7.5%)	0.056
Median total hospital admission length of stay (IQR), d	6 (4-11)	5 (3-7)	<0.001
Discharged on supplemental oxygen, no. (%)	36 (16.5%)	51 (20.2%)	0.300
Corticosteroid-associated adverse events			
Bacteremia, no. (%)	7 (3.2%)	10 (4.0%)	0.661
HAP/VAP, no. (%)	18 (8.3%)	18 (7.1%)	0.651
Fungemia, no. (%)	4 (1.8%)	1 (0.4%)	0.130
Hyperglycemia, no. (%)	93 (42.7%)	112 (44.4%)	0.697

Table 3. Multivariable Regression Model for Associations with Mortality

Variable	Expired (n = 66)	Survived (n = 404)	Adjusted OR (95% CI)
Age ≥ 60 years	59 (89.4%)	232 (57.4%)	6.1 (2.636-14.118)
Baseline ICU	29 (43.9%)	48 (11.9%)	6.576 (3.537-12.227)
High dose Moderate dose	32 (48.5%) 34 (51.5%)	186 (46%) 218 (54%)	0.913 (0.514-1.619)

Conclusion. The survival in severe COVID-19 patients treated with MDC is comparable to HDC. Oral corticosteroids are an equally effective option.

Disclosures. **Rachel Kenney, PharmD**, **Medtronic, Inc.** (Other Financial or Material Support, spouse is an employee and shareholder)

498. Baricitinib in Patients with Severe Pneumonia due to COVID-19 in Veracruz, Mexico

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Background. Patients affected by COVID-19 pneumonia who present severe symptoms with manifest hypoxemia and cytokine storm have a high mortality rate, which is why therapies focused on reducing inflammation and improving lung function have been used, one of them being jakinibs through of the blocking of the JAK tracks.

Methods. Patients who presented data of severe pneumonia due to COVID-19 with data of severe hypoxemia and cytokine storm were selected, from June to August 2020, to whom the SaO_2/FiO_2 ratio is measured at the beginning, intermediate and end of treatment, as well as D dimer and serum ferritin. Comorbidity and drugs taken previously are analyzed. The patients being cared for at home.

Results. We included data from 30 patients, 8 (27%) women and 22 (73%) men, with a median age of 58.5 (46.5 - 68.0) years. 23 patients (77%) had comorbidities, the most frequent being arterial hypertension (43%), followed by obesity (30%), type 2 diabetes mellitus (27%), among others. In the laboratory, the medians of D-Dimer 982 ng/mL, Ferritin 1,375 ng/mL and C-Reactive Protein 10.0 mg/dL. Regarding the use of previous medications, we found that 29 (97%) patients had treatment with some medication, the most frequent: azithromycin (77%), ivermectin (53%) and dexamethasone (47%). The median number of medications received was 3. The initial pulse oximetry ($SaO_{2)}$ measurement with room air had a median of 80.5% and the median SaO_2/FiO_2 (SAFI) was 134; Regarding the type of SIRA, 90% had moderate SIRA and 10% had severe SIRA.

The median day of evolution on which baricitinib was started was 10 days, all received 4 mg/day, and the median days of treatment with baricitinib was 14.0 days. At follow-up, SaO_2 at 7 days had a median of 93.0% and the median SAFI at 7 days was 310.0; the median SaO_2 at 14 days was 95.0% and the median SAFI at 14 days was 452.0. In comparative analysis, baseline SaO_2/SAFI was significantly lower compared to 7 and 14 days ($p = 0.001$ for both comparisons). The outcomes, 27 (90%) patients improved and there were 3 (10%) who died.

Demographic Variables