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RESEARCH ARTICLE

The Effect Of Corticosteroid Therapy on the Frequency of Secondary Bacterial Infections And Mortality in COVID-19 Patients in ICU

Elmas Uysal[1], Işıl Özkoçak Turan[1], Handan Ankaralı[2], Aliye Baştuğ[3]

[1]*Intensive Care Clinic; Ankara City Hospital, Ankara,Turkey*
[2]*Department of Biostatistics and Medical Informatics, İstanbul Medeniyet University; İstanbul,Turkey*
[3]*Department of of Infectious Diseases and Clinical Microbiology, Ankara City Hospital; Ankara, Turkey*

ABSTRACT

Objectives: There are recommendations and studies for the corticosteroid treatment of cytokine storm and ARDS in COVID-19 disease. The aim is to evaluate the rates of secondary infections and mortality in COVID-19 patients receiving various doses of corticosteroid treatment in the ICU.

Methods: In a retrospective approach, 621 patients were analyzed and recorded in terms of age, gender, duration of mechanical ventilation, length of stay in intensive care, CRP, procalcitonin, LDH, IL-6, lymphocyte, D-dimer, ferritin values and corticosteroid doses as well as blood, urine, and tracheal aspiration growths. The patients were examined in 6 groups those who never took corticosteroids and those who took Methylprednisolone (MP) in doses of 250 mg, >250 mg, 80 mg, 40 mg, and 6 mg dexamethasone. The data were evaluated to determine if there have been significant relationships between corticosteroid doses and the rates of secondary infection and mortality.

Results: The mean hospital stay of the patients was 11.2 ± 7.71 days, and the mean of invasive mechanical ventilation was 7.5 days. There was no significant difference between patients who did not use corticosteroids and patients who received 40 mg MP for the length of hospital stay. The length of hospital stay was significantly longer in the corticosteroid groups ($p<0.001$). There was no significant difference between all the groups according to the frequency of secondary infection.

Conclusion: It has been observed that using different corticosteroids in intensive care patients with COVID-19 does not increase the secondary infection rate. *J Microbiol Infect Dis 2022; 12(4):8-16.*

Keywords: *COVID-19 disease, corticosteroids, secondary infection, cytokine storm*

INTRODUCTION

Coronavirus disease (Covid-19), caused by a novel coronavirus (SARS-CoV-2), became a severe pandemic worldwide with high mortality rates. Some patients infected with SARS-CoV-2 infections have exhibited an excessive inflammatory response resulting in severe ARDS and multiple organ failures due to secondary infections. Corticosteroids are recommended to modulate this dysregulated inflammatory response in severe ARDS and multi-organ failure [1]. The Surviving Sepsis Campaign recommends using low-dose corticosteroid (Methylprednisolone at 1–2mg/kg/day) therapy in COVID-19 patients with refractory shock to alleviate the cytokine storm caused by SARS-CoV-2 and reduce peripheral vasodilation [2]. Recently, the RECOVERY study group demonstrated the favorable effect of 6 mg dexamethasone on early mortality rates in Covid 19 patients, and controversies started about using corticosteroids in Covid 19 disease [3]. However, the doubts about the risk of bacterial süper infection have risen concomitantly based on studies with influenza pneumonia and Middle East Respiratory Syndrome (MERS)-CoV [4,5]. Even corticosteroid therapy in COVID-19 patients is claimed to increase the bacterial infection rate without affecting mortality [6].

In this retrospective study, we aimed to evaluate the effects of various doses of corticosteroid treatment in COVID-19 patients

Correspondence: Dr. Elmas Uysal, Ankara City Hospital, Intensive Care Clinic, Ankara, Turkey
E-mail : dr.elmas90@gmail.com
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in terms of secondary bacterial infection frequency and mortality.

METHODS

Patients

We enrolled 621 COVID-19 patients who were PCR test positive and followed up between September 1, 2020, to December 1, 2020, in Ankara City Hospital ICU units.

Study design

The characteristics of the patients were retrospectively analyzed, and demographic data, comorbidities, all treatments, length of stay in ICU, the number of days between the start of symptoms and admission to ICU (symptom duration), mechanical ventilation days, mortality rates, and secondary infection data were all recorded. In addition, blood, urine, and tracheal aspiration culture result and microorganisms considered infectious according to the Centers for Disease Control and Prevention (CDC) diagnostic criteria were examined. At the same time, C-reactive protein (CRP), interleukin-6 (IL-6), lymphocyte count, AST, ALT, LDH, D-dimer, procalcitonin, ferritin, and fibrinogen values were also recorded as helpful parameters in the diagnosis of macrophage activation syndrome.

The patients in our study were evaluated in 6 groups as follows:

a. Control group: Patients who did not receive any corticosteroids

b. Corticosteroid group: Patients who received Methylprednisolone (MP) in doses of 250 mg, >250 mg, 80 mg, and 40 mg, and those who received 6 mg dexamethasone.

These corticosteroid doses were the initial doses given in the first three days and then continued with 80 mg. After that, steroid administration was continued for 15 days, according to the clinical and laboratory findings of the patients. After that, steroid administration was terminated by reducing the dose.

In our hospital, corticosteroid and anti-cytokine treatments are arranged with the consultation recommendations of the Rheumatology Clinic. Corticosteroid treatment of the patients was arranged according to the COVID-19 guidelines of the Ministry of Health. Treatments were started after secondary infectious probability was eliminated with clinical evaluation and procalcitonin levels (<0,5 µg/L).

In addition, the "cytokine storm score" (CSS) was calculated according to the laboratory values of the patients in our study. Based on IL-6 ≥40 pg/ml and/or two of the following as criteria: CRP ≥100 mg/L, D-dimer ≥1000 ng/ml, ferritin ≥500 ng/ml, and lactate dehydrogenase ≥300 U/L, each criterion was evaluated as 1 point. Patients with a score of 2 or higher were considered to have a cytokine storm [7].

Ethics committee consent

Ankara City Hospital Ethics Committee approval (ethics committee no: E1-20-1364, date: 23/12/2020) was obtained before the study.

Statistical analysis

Descriptive statistics of the obtained data were calculated as mean±SD, median (25th and 75th), count, and percent frequencies. The conformity of numerical variables to the normal distribution was examined using the Shapiro-Wilks test. The Kruskal-Wallis or Mann-Whitney U test was used to compare various groups regarding numerical characteristics. Relationships between categorical features were evaluated with Pearson chi-square analysis. In addition, the relationships between cytokine storm score, length of stay, and intubation time were analyzed by Spearman rank correlation analysis. $P < 0.05$ was accepted as a statistical significance level, and SPSS (version 23) program was used for calculations.

RESULTS

A total of 621 patients were included in the study. The distribution of the categorical characteristics of the patients is given in Table 1.

The mean hospital stay of the patients was 11.2±7.71 days, and the duration of invasive mechanical ventilation was 7.5 days. The shortest hospitalization day was seven days in the group that did not receive corticosteroids. The most prolonged hospitalization period was 11 days in the group that received 250 mg methylprednisolone treatment. There was no significant difference between patients who did not use corticosteroids and patients who received 40 mg methylprednisolone in the length of stay. Patients who did not use corticosteroids and who received 40 mg MP were lenght of stay in ICU shorter than the other groups ($p<0.001$) but there was no significant difference between the other corticosteroid groups (Table 2).

When the cases were evaluated, 342 (55%) of 621 patients were followed up with an invasive mechanical ventilator (IMV). It was observed that the mean IMV day was shorter in the group that did not receive 40 mg MP and

corticosteroids than the other groups. In addition, the number of extubated patients was higher in the >250 mg MP group than in the other groups (Table 2).

In our study, infection was found in 51.0% of the patients; sites of infection and microorganisms are presented in Table 3. The most common bloodstream infection was followed by pneumonia and urinary tract infection, 24.9%, 22.2%, and 23.8%, respectively. When the foci were examined one by one, it was seen that the most reproducing factor in blood culture and tracheal aspiration culture was acinetobacter species (27.7% and 59.4%, respectively) and E.coli (41.3%) in urine culture (Table-3).

Although the highest culture growth rate was seen in the group that received 6 mg dexamethasone with 96 (30.2%) patients out of 317 patients, there was no significant difference in corticosteroid doses and additional growth frequency compared to those who did not use corticosteroids (p=0.169). When the individual foci were examined, it was seen that the growing frequency in the blood culture did not show a significant change according to the corticosteroid dose groups (p=0.433). The most common Acinetobacter growth in blood culture was seen in 43 patients. Although 13 of these patients received>250 mg methylprednisolone, no statistical significance was found regarding steroid dose and Acinetobacter growth (Table 3).

It was observed that the frequency of growth in urine and DTA did not show a significant change according to the corticosteroid dose groups (Respectively; p=0.287, p=0.286) (Table 3).

When the inotropic needs of the patients were evaluated in detail, it was seen that 367 (59%) of 621 patients did not need inotropes. There was no significant relationship between corticosteroids and inotropic use (p=0.375).

When tocilizumab (TCZ) use and corticosteroid use are considered together;

a. Those who did not use TCZ and did not use corticosteroids (n=64)

b. Those who do not use TCZ but use corticosteroids (n=519)

c. Those using TCZ but not using corticosteroids (n=2)

d.TCZ users and corticosteroid users (n=37) were evaluated. Since there were two individuals in the group in which only TCZ was used, the values of this group were not used in the statistical comparison. The length of hospital stay and intubation time were significantly shorter in individuals who did not use TCZ or corticosteroids compared to other groups (p=0.002, p=0.05, respectively). In addition, it was observed that there was no significant increase in the frequency of infection and the mortality rate in patients who used TCZ and corticosteroids together (respectively; p=0.173, p=0.79).

When anakinra use and corticosteroid use are considered together;

a. Those who do not use anakinra and do not use corticosteroids (n=66)

b. Those who do not use anakinra but use corticosteroids (n=532)

c. Using anakinra but not using corticosteroids (n=0)

d. Anakinra users and corticosteroid users (24).

No patient who was given only Anakinra was detected. It was observed that the hospital stay and mechanical ventilation time were significantly longer when anakinra and corticosteroid were used together (respectively; p=0.001, p=0.009). It was observed that there was no significant increase in the frequency of infection and mortality in patients who used anakinra and corticosteroids together (respectively; p=0.906, p=0.63).

When the patients included in the study were divided into three groups those who did not receive steroids, those who received ≤250 mg MP, and those who received >250 mg MP, the mortality rate was lower in patients who received >250 mg MP (p=0.02) (Table-4).

Afterward, patients were reevaluated according to CSS. The number of patients with CSS 5 was 122 (19%), 4 were 164 (26%), 3 were 176 (28%), and 2 were 123 (19%). The number of patients with a cytokine storm score below two was 37 (5%). When the results were evaluated, mortality rates were found to be significantly lower in the CSS≥2 groups given >250 mg of Methylprednisolone compared to other doses (p=0.046) (Table 5). Regarding the frequency of secondary infections, no significant difference was observed between the groups (Table 3).

DISCUSSION

This study examined the relationship between corticosteroid doses, secondary infection rates, and mortality in COVID-19 disease. No significant relationship was found between corticosteroid use and secondary infections, but the mortality rate was lower in patients who used corticosteroids in doses >250 mg.

Table 1. Comparison of patients according to comorbidities and corticosteroid doses.

		>250 mg MP (N=120)	250 mg MP (N=90)	80 mg MP (N=101)	6 mg DX (N=190)	40 mg MP (N=54)	No steroid (N=66)
Age (y)	<65	69 (%57.5)	29 (%32.2)	26 (%25.7)	50 (%26.3)	17 (%31.4)	14 (%21.2)
	>65	51 (%42.5)	61 (%67.8)	75 (%64.3)	140 (%73.7)	37 (%68.6)	52 (%78.7)
Gender(Male)		90 (%75)	60 (%66,6)	61 (%60,3)	107 (%56,3)	31 (%57,4)	35 (%53)
APACHE-2 score		8 (2-28)	10.3 (2-26)	12.1 (2-37)	13.0 (4-38)	12.7 (4-29)	15 (2-35)
SOFA score		3.8 (2-15)	4.6 (3-14)	5.6 (3-16)	5.9 (3-15)	5.7 (3-15)	6.3 (3-14)
DM (n=200)		36 (%30)	33 (%36.6)	31 (%30.6)	61 (%32.1)	21 (%38.8)	18 (%27.2)
HT (n=334)		49 (%40.8)	53 (58.8)	56 (%55.4)	109 (%57.3)	32 (%59.2)	35 (%53)
CAD (n=191)		18 (%15)	28 (%31.1)	34 (%33.6)	67 (%35.2)	21 (%38.8)	23 (%34.8)
COPD (n=83)		14 (%11.6)	10 (%11.1)	14 (%13.8)	32 (%16.8)	9 (%16.6)	4 (%6.0)
CRF (n=59)		7 (%5.8)	5 (%5.5)	12 (%11.8)	20 (%10.5)	8 (%14.8)	7 (%10.6)
Malignancy (n=63)		4 (%3.3)	9 (%10)	8 (%7.9)	27 (%14.2)	6 (%11.1)	9 (%13.6)
Neurological disease (n=136)		7 (%5.8)	9 (%10)	24 (%23.7)	55 (%28.9)	12 (%22.2)	29 (%43,9)

APACHE-2=Acute Physiology and Chronic Health Evaluation, SOFA=Sequential Organ Failure Assessment Score, DM=Diabetes mellitus, HT=Hypertension, CAD=Coronary Artery Disease, COPD=Chronic Obstructive Pulmonary Disease, CRF=Chronic Renal Failure

Table-2. The number of patients in need of IMV according to corticosteroid doses and the extubation rate in these patients, and the average days of hospitalization and mechanical ventilation in the intensive care unit.

Corticosteroid Doses	Intubation n=341(%)	No. of extubations n=25 (%)	Length of stay in intensive care	Average MV day
>250 mg MP (n=120)	58 (17.0)	9 (15.5)	12.2 ± 6.5 (8-15)	8.0 (1-22)
250 mg MP (n=90)	47 (13.7)	2 (4.2)	11.6 ± 7.1 (7-15)	8.2 (1-26)
80 mg MP (n=101)	62 (18.1)	4 (6.45)	10.5 ± 6.6 (6-14)	7.0 (1-25)
40 mg MP (n=54)	30 (8.7)	1 (3.3)	10.3 ± 8.1 (4.7-13)*	5.4 (1-16)
6 mg Deksametazon (n=190)	107 (31.3)	8 (7.47)	11.5 ± 8.2 (6-15)	8.8 (1-45)
No steroid (n=66)	37 (10.8)	1 (2.7)	9.3 ± 9.7 (2.75-12)*	3.5 (1-24)

*P<0,001

Table 3. The distribution of microbial agents responsible for secondary infections in COVID-19 patients treated with different steroid doses

Type of infections	>250 mg MP (N=120)	250 mg MP (N=90)	80 mg MP (N=101)	6 mg DX (N=190)	40 mg MP (N=54)	No steroid (N=66)	p value
Blood Culture (N=155)							
Acinetobacter spp. (n=43)	13 (%10,8)	11(%12,2)	6(%5,9)	9 (%4,7)	3 (%5,6)	1 (%1,5)	
S. aureus (n=37)	5 (%4,1)	5 (%5,6)	7(%6,9)	15(%7,8)	3 (%5,6)	2 (%3,0)	
CNS (n=21)	5(%4,1)	2(%2,2)	4(%4,0)	4(%2,1)	2 (%3,7)	4(%6,0)	
Enterococcus spp. (n=20)	2 (%1,7)	2 (%2,2)	7 (%6,9)	6 (%3,2)	3 (%5,6)	0 (%0)	0,433
Other infections (n=30)	6 (%5,0)	2(%2,2)	5 (%4,9)	8(%4,2)	3 (%5,6)	6 (%9)	
Candida spp. (n=4)	1 (%0,8)	1 (%1,1)	0 (%0)	1 (%0,5)	1 (%1,9)	0 (%0)	
Urine Culture (N=138)							
E. coli (n=57)	9 (%7,5)	7 (%7,7)	9 (%8,9)	16 (%8,4)	8(%14,8)	8 (%12,1)	
Enterococcus spp. (n=30)	6 (%5,0)	5 (%5,6)	3 (%3,0)	10 (%5,3)	4 (%7,4)	2 (%3,0)	
Klebsiella spp. (n=27)	6 (%5,0)	2 (%2,2)	6 (%5,9)	10 (%5,3)	2 (%3,7)	1 (%1,5)	0,287
Other infections (n=24)	3(%2,5)	4 (%4,4)	4 (%4)	7(%3,6)	3(%5,6)	3 (%4,5)	
Tracheal aspiration Culture (N=148)							
Acinetobacter spp. (n=88)	19 (%15,8)	12 (%13,3)	23 (%22,8)	23 (%12,1)	6 (%11,1)	5 (%7,6)	
Methicillin-resistant Staphylococcus aureus (n=20)	1 (%0,8)	2 (%2,2)	6 (%5,9)	5 (%2,6)	3 (%5,6)	3 (%4,5)	
Klebsiella spp.(n=13)	3 (%2,5)	0 (%0)	0 (%0)	7 (%3,7)	1 (%1,9)	2 (%3,0)	0,286
S. Maltophilia (n=7)	1(%0,8)	2(%2,2)	1(%0,99)	2 (%1,05)	0 (%0)	1(%1,5)	
Other infections (n=20)	1 (%0,8)	2(%2,2)	4(%4,0)	10(%5,3)	1 (%1,9)	2 (%3,0)	

Table-4: Mortality rates when patients were divided into 3 groups according to corticosteroid doses

Result	No steroid (N=66)	≤250 mg MP (N=435)	>250 mg MP (N=120)
Exıtus (n=324)	37 (%56)	238 (%52,2)	49 (%40,8)
Dicharged (n=297)	29 (%43,9)	197 (%47,8)	71 (%59,2)*

(*p=0.02)

Table-5. Mortality rates according to corticosteroid doses when 2 and above are separated according to cytokine storm score.

Patient Groups		>250 mg MP (N=120)	250 mg MP (N=90)	80 mg MP (N=101)	6 mg DX (N=190)	40 mg MP (N=54)	No steroid (N=66)
CSS<2 (n=37)	Exitus (n=8)	0 (%0)	4 (%80)	0 (%0)	3 (%20)	0 (%0)	1 (%14,3)
	Discharged (n=29)	3 (%100)	1 (%20)	4 (%100)	12 (%80)	3 (%100)	6 (%85,7)
CSS≥2 (N=584)	Exitus (n=316)	49 (%41,9)	43 (%50,6)	59 (%60,8)	99 (%56,6)	30(%58,8)	36 (%61)
	Discharged (n=268)	68* (%58,1)	42 (%49,4)	38 (%39,2)	76 (%43,4)	21 (%41,2)	23 (%39)

*P=0.046

In a study conducted in non-COVID patients, in early severe ARDS (<72 hours), it was observed that there was a significant improvement in pulmonary and extrapulmonary organ dysfunction and a decrease in mechanical ventilation time and ICU length of stay in patients treated with low-dose (1 mg/kg) methylprednisolone [8]. In addition, it was reported that the infection rates of the treated patients were lower [8]. Another study reported that using corticosteroids in ARDS patients reduced the length of stay in the hospital and intensive care unit and did not have a significant relationship with infection rates [9]. A study conducted with COVID-19 patients reported that bacterial and fungal infection rates were higher in the corticosteroid group than in the group not used. However, there was no significant difference in the mortality rate (6). Annane D. stated in her review that corticosteroids do not cause an increase in bacterial infections; therefore, their use in the treatment of COVID-19 should be encouraged [10].

In light of these studies, there are still ongoing controversies about corticosteroid use and its side effects on COVID-19 disease.

It is known that dexamethasone treatment suppresses proinflammatory cytokines such as IL-1, IL-2, IL-6, IL-8, TNF, and IFN-γ and increases IL-10 gene expression, which has anti-inflammatory activity [11]. It also inhibits macrophage activation together with neutrophil adhesion in endothelial cells. Due to its effects on all these pathways, it was thought it could be used in COVID-19 disease, and studies related to this were emphasized [11]. In the RECOVERY study, mortality rates were 8-26% lower in patients treated with 6 mg/day dexamethasone [5]. However, in the current study, it was stated that it should be kept in mind that relatively young patients (mean age: 59 years) would not give an idea about the efficacy of dexamethasone treatment in elderly patients due to the need for ventilation support [5]. In our study, when the patients were examined in 2 groups under 65 years old and over, it was seen that there was no difference between corticosteroid doses and mortality rates. In another single-center, retrospective study, no significant difference was observed in the mortality rate between the patients who received pulse corticosteroid (≥250 mg MP) and 1 mg/kg/day corticosteroid dose. However, it was seen that mortality decreased compared to the group that did not receive corticosteroids [12]. In a study comparing Methylprednisolone (2 mg/kg/day; intervention group) or dexamethasone (6 mg/day; control group), no significant difference was found in the mortality rate, but the need for mechanical ventilators was found to be significantly lower in those receiving methylprednisolone treatment [13]. In the REMAP study, which included 903 patients, it was found that the number of days without organ support for 21 days was significantly higher in severe COVID-19 patients who used hydrocortisone therapy (50-100 mg every 6 hours) [14]. On the other hand, in line with all these experiences, the Chinese Thoracic Society stated that corticosteroid therapy should be used cautiously and appropriately in COVID-19 disease, and the dose applied should be low to medium (≤0.5−1 mg/kg/day

methylprednisolone or equivalent) doses and its duration should be short (≤7 days) [15,16].

It has been stated that there are two types, hyper-inflammatory and hypo-inflammatory in COVID-19 disease, and the hyper-inflammatory type of corticosteroid therapy, which is defined by high proinflammatory cytokine levels, high SOFA level, and high complication rates, may be beneficial [17]. In this study, the initial and maximum dose of Methylprednisolone was used as 40 mg for an average of 6.5 days. Although complications such as ARDS, coagulopathy disorders, acute renal failure, septic shock, and acute cardiac damage were seen more frequently in patients using corticosteroids compared to those not using corticosteroids, no difference was found in 28-day mortality [17]. However, when compared, it was found that the 28-day mortality rates were significantly lower in hyperinflammatory type patients using corticosteroids compared to the hypoinflammatory type [17]. In our study, when our patients were evaluated in 3 groups according to corticosteroid use and as patients with CSS≥2, mortality rates were found to be significantly lower in those given >250 mg methylprednisolone compared to other groups. Regarding the mean age of the patients in the current group, it was seen that they were younger than the other corticosteroid groups (mean age: 61). This result made us think that pulse corticosteroid therapy may play a role in reducing mortality in young patients. However, it is stated that corticosteroid treatment causes inhibition of proinflammatory cytokines with its genomic effects and suppresses inflammation by binding to membrane-dependent glucocorticoid receptors of T cells with its non-genomic effects [18]. From this point of view, MP treatment >250 mg reduces mortality may also be due to its non-genomic effects.

In the multicenter REACT study in which has conducted with COVID-19 patients who received 678 corticosteroid treatments and 1025 received placebo or standard treatment were compared, it was observed that 28-day mortality rates were lower in those receiving corticosteroid treatment [19]. In the same study, no significant difference was found in all-cause mortality rates between patients given dexamethasone treatment and patients given a placebo (p=0.13). In addition, no significant difference was found between dexamethasone and hydrocortisone treatments and all-cause mortality rates. The same study found no evidence that higher-dose corticosteroid therapy is more beneficial than low-dose corticosteroid therapy [19]. In our study, when mortality rates were compared, the mortality rate of those given >250 mg methylprednisolone was significantly lower than that of patients who received other corticosteroid doses. In addition, when the combination of TCZ and Anakinra treatments and corticosteroids were examined, it was observed that the length of hospital stay and mechanical ventilation time were significantly shorter in individuals who did not use both TCZ and corticosteroids. The length of hospitalization and intubation time were significantly longer when Anakinra and corticosteroids were used together. This result was thought to be due to the use of Anakinra or TCZ in patients with a more severe course. In addition, it was determined that there was no significant increase in secondary reproduction frequency and mortality rate in both groups compared with the other groups.

In another study, it was reported that patients treated with Methylprednisolone (1-2 mg/kg/day for 5-7 days) had a faster improvement in their saturation, a shorter duration of oxygen therapy, and a decrease in mechanical ventilation needs [20]. While no significant difference was observed in the mortality rate in those receiving methylprednisolone treatment, a significant decrease was observed in the length of stay in the intensive care unit. This study emphasized that early, low-dose, and short-term administration of Methylprednisolone is associated with better clinical outcomes in severe patients with COVID-19 pneumonia and should be given before ARDS occurs [20]. In our study, when the frequency of IMV and the association of corticosteroid treatment were evaluated, it was seen that the need for IMV did not change according to the corticosteroid dose groups. However, it was determined that the mean IMV day and mean hospital stay were shorter in the group that did not receive 40 mg MP and steroids than in the other groups. As a result, it was observed that these patients died in a shorter time. There was no significant relationship between the duration of symptoms and the mortality rate according to corticosteroid doses, which shows that the time of initiation of corticosteroid therapy does not affect mortality.

Our study determined that the frequency of additional bacterial growth did not differ significantly between corticosteroid dose groups and those who did not use corticosteroids. Furthermore, when evaluated separately according to the foci of infection, it was found that the incidence of bloodstream infection, urinary tract infection, and pneumonia was similar between the groups, and there was no difference according to steroid dose. Accordingly, the use of different doses of corticosteroids does not cause an increase in the frequency of infection in COVID-19 patients.

Cytokine storm findings in a study conducted in Spain (IL-6 ≥40 pg/ml and/or two of the following: CRP ≥100 mg/L, D-dimer ≥1000 ng/ml, ferritin ≥500 ng/ml and lactate dehydrogenase It was reported that there was a 14% decrease in mortality when 30 mg dexamethasone or 125 mg methylprednisolone was given for 2-5 days to 64 patients with ≥300 U/L [12]. In our study, mortality rates in patients given >250 mg Methylprednisolone was significantly lower than in other doses.

The limitations of this study were that the patients were heterogeneous. Second, the duration of steroid treatments given could be more optimal.

Conclusion

In conclusion, we found no significant correlation between using different corticosteroid doses and the increased frequency of infection in COVID-19. However, when the patients were evaluated according to the corticosteroid doses and CSS scores, it was found that the mortality rate was reduced with the use of a pulse dose (over 250 mg) of Methylprednisolone. In addition, there was no correlation between corticosteroid onset time and mortality rate according to symptom onset. Therefore, further studies are needed on the treatment initiation time, dose, duration, and efficacy of corticosteroid and anti-cytokine treatments in COVID-19 disease to find evidence about the likely fatal side effects of corticosteroid treatment as secondary bacterial infection.

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