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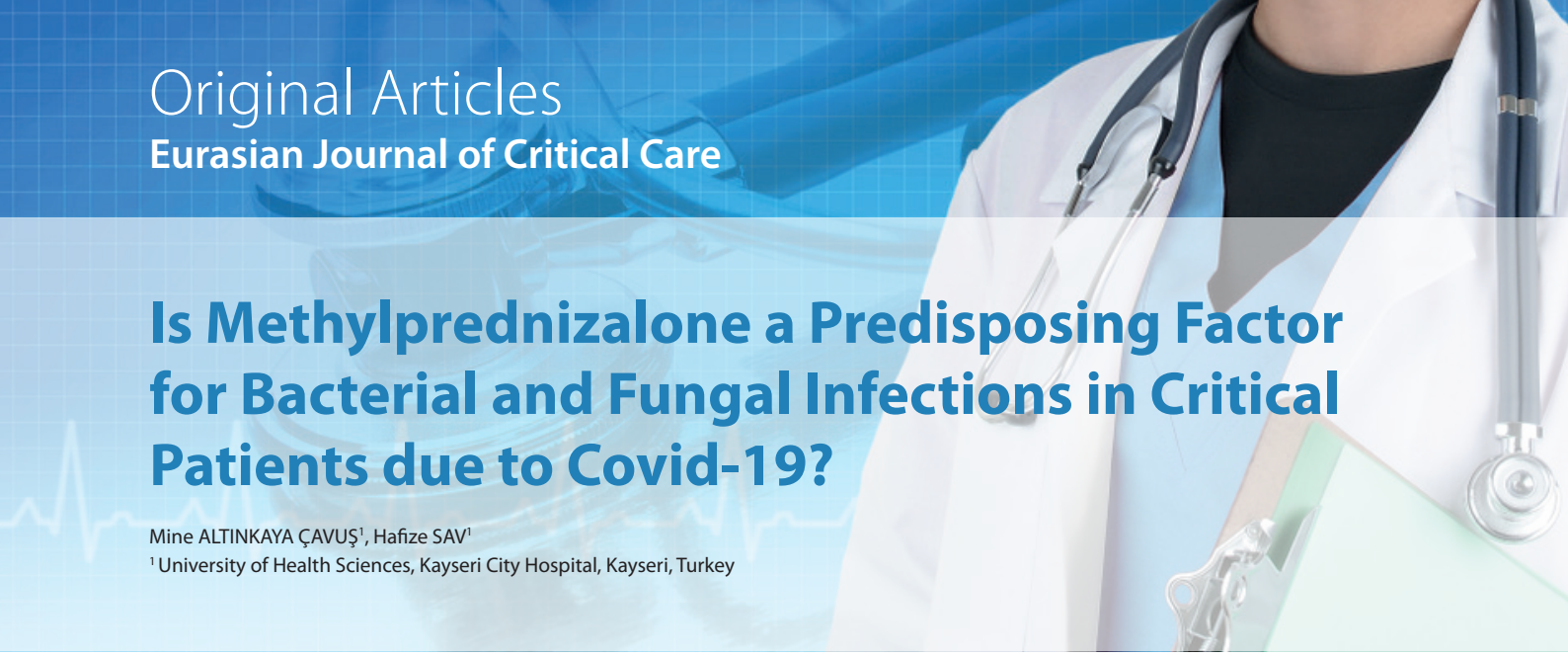

Is Methylprednizalone a Predisposing Factor for Bacterial and Fungal Infections in Critical Patients due to Covid-19?

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Abstract

Aim: The COVID -19 outbreak was first seen in Wuhan, China\'s Hubei province. Lung infections caused by COVID-19; It can progress to severe ARDS (acute respiratory distress syndrome) with a high mortality.For ARDS patients, methylprednisolone (1-2 mg / kg per day) is recommended to be as short as possible

Methods: All patients with a diagnosis of covid-19 over the age of 18 who were hospitalized in the pandemic intensive care unit between March 2020 and September 2020 were retrospectively screened.Patients; demographic data, hospitalization APACHE II scores, length of stay in hospital and intensive care, laboratory values (d-dimer, creatinine, CRP (C reactive protein)), culture results, mortality and morbidity, mechanical ventilator needs. On the first day of intensive care admissions, methylprednizalone was added to the treatment intravenously at 0.5 mg/kg/day for 5 days.

Results: A total of 201 patients hospitalized in adult level 3 intensive care were included in the study. All patients were PCR positive. 44.8% of the patients were female (n: 90), 55.2% were male (n: 111). Blood, urine and ETA cultures; there was no statistically significant relationship between gender, IMV need, mortality and prednol use.

Conclusion: COVID-19 is a viral infectious disease that manifests mainly as fever and pneumonia. Corticosteroid therapy; in addition, it includes the following risks: hyperglycemia, poor wound healing, psychosis, pancreatitis, and prolonged muscle weakness in impaired functional status in a meta-analysis published in 2012, nine randomized controlled trials, 1001 patients were included. Consequently, the use of corticosteroids did not decrease mortality.

Keywords: Methylprednisolone, bacterial and fungal infections, COVID-19

Introduction

Coronavirus disease 2019 (COVID-19) severe acute respiratory syndrome coronavirus 2 (SARS-CO-V-2) is a member of the betacoronavirus. The COVID -19 outbreak was first seen in Wuhan, China's Hubei province. It quickly spread to over 50 cities in December 2019[1]. It quickly spread to more than 100 countries around the world. The disease is primarily spread by inhalation with droplets, but the possibility of other transmission routes (feces and urine) cannot be excluded[2]. The course of the disease can range from mild self-limiting flu-like illness to fulminant pneumonia and death. Report of the World Health Organization dated March 5, 2020; 3.4% of 95,333 confirmed COVID-19 cases result in death[3]. However, a lower mortality rate of 1.4%; Analysis of data from 1099 patients with laboratory-confirmed COVID-19 came from 552 hospitals in mainland China[4]. This disease is mild to severe; fever (88%), cough (67%) and fatigue (34%) are the most common symptoms. COVID-19 patients; 3 creates a picture similar to infection caused by other respiratory viruses (Influenza A / B, respiratory syncytial virus and rhinovirus)[5]. Considering that the number of unreported and unconfirmed cases is higher than the reported cases, it can be predicted that the actual mortality may be similar (less than 1%) to seasonal influenza[6]. It has been found that the virus is transmitted from person to person[7].

Lung infections caused by COVID-19; It can progress to severe ARDS (acute respiratory distress syndrome) with a high mortality. Treatment strategies are not based on precise data, but the evidence is increasing day by day. Today, systemic glucocorticoids are used empirically to prevent serious complications[8]. However, there is no evidence from randomized clinical trials to support glucocorticoid therapy for COVID-19. For ARDS patients, methylprednisolone (1-2 mg / kg per day) is recommended to be as short as possible[9].

Coronavirus disease 2019 (Covidien-19) are associated with infections of bacteria and fungi is poorly understood. Isolated COVID-19 associated viral infection and possible bacterial and/or fungal infection are clinically challenging. 15% of the Covidien-19 case in Wuhan hospitalized reported secondary bacterial infections[10] and survival group was observed at a higher ratio than in survivors (50% vs. 1%).

The aim of this study; to investigate the effect of methylprednisolone on secondary infection rates in critically ill patients.

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Material and method

All patients with a diagnosis of covid-19 over the age of 18 who were hospitalized in the pandemic intensive care unit between March 2020 and September 2020 were retrospectively screened. A total of 1458 patients; According to pcr (polymerase chain reaction), antibody (ab), or CT (computed tomography) results, they were hospitalized in the intensive care unit due to covid-19-induced pneumonia.

Intensive care unit hospitalization indications; respiratory rate ≥ 30, signs of dyspnea and respiratory distress, SPO2 <90% (room air), PO2 <80 mmhg, PO2 / fio2 <300, Lactate> 4 mmol / L, bilateral infiltrations or multi-lobar involvement on chest radiography or tomography, organ dysfunction such as hypotension (systolic blood pressure <90 mmhg, mean arterial pressure <65 mmhg), skin perfusion disorder, renal function test, liver function test disorder, thrombocytopenia, confusion, presence of immunosuppressive disease, presence of multiple uncontrolled comorbidity, increased troponin was identified as arrhythmia.

Among these patients, those who had pcr +, ab + and developed ARDS were included in the study. Patients were divided into 2 groups as methylprednisolone and those not.

Patients; demographic data, hospitalization APACHE II scores, length of stay in hospital and intensive care, laboratory values (d-dimer, creatinine, CRP (C reactive protein)), culture results, mortality and morbidity, mechanical ventilator needs. It was recorded whether they took prednol or not. Laboratory values saved last day of hospitalization. On the first day of intensive care admissions, methylprednizalone was added to the treatment intravenously at 0.5 mg/kg/day for 5 days.

Inclusion criteria in the study; level 3 intensive care patients over 18 years of age with covid-19 positive and non-invasive and / or needing non-invasive mechanical ventilation.

Exclusion criteria are those under the age of 18, trauma and cancer patients, covid-19 negative patients.

Statistical analysis

In the statistical analysis made with Spss version 20; The distribution of the groups was determined by the Kolmogorov-Smirnov test. Assym sig. Values greater than 0.05 were considered as normal distribution, small values as abnormal distribution.

While parametric tests (T test) were applied to data with normal distribution, non-parametric tests were applied to data with a number of cases greater than 30 and not showing a normal distribution (Mann Whitney U). Pearson correlations were used in parametric data and spearman correlations were used in non-parametric data.

In the analysis of all statistical data, values with a p value less than 0.05 were considered statistically significant.

Statistical analysis was performed and the findings were discussed with tables and graphs in the light of the data.

Table I. Results of the study

	Yes (n)	%	No (n)	%
Gender (female)	90	44,8	111	55,2
IMV needs	99	49,3	102	50,7
Mortality	101	50,2	100	49,8
Methyprednizalone	94	46,8	107	53,2
Blood Culture	99	46,3	102	50,7
Staphylococcus	84	41,8		
Enterococcus	10	5		
Candida Albicans	2	1		
Klebsiella	2	1		
Psoudomonas Aeruginosa	1	0,5		
Acinetobacter	1	0,5		
Urine Culture	34	16,9	167	83,1
E.Coli	5	2,5		
Candida Albicans	22	10,9		
Enterococcus	2	1		
Klebsiella	1	0,5		
Psoudomonas Aeruginosa	1	0,5		
Acinetobacter	2	1		
ETA culture	8	4	193	96
Acinetobacter	4	2		
Staphylococcus	1	0,5		
Candida Albicans	3	1,5		

Table II. Methylprednizalone

	Mp0	Mp1	Total	P value	
Age	67,7±14,9	66,7±12,9	67,3±14	,102	NS
Hospital day	16,1±11,2	15,1±9,4	15,6±10,4	,637	NS
ICU day	9,4±8,8	8,9±6	9,1±7,6	,069	NS
CRP	100,4±119,4	96,5±115	98,6±117,1	,488	NS
D-dimer	3173,9±3703,2	4945,2±5157,4	3946±4468,9	,013*	S
Kreatinine	1,9±2,9	1,5±1,4	1,7±2,3	,033*	S
APACHE II score	27,5(19-32)	26,5(20-33)	27(19-33)	,42	NS

Mp 1: Group using methylprednizalone, Mp 0: Group without methylprednizalone, NS:Not Statistically Significant, S: Statistically Significant, APACHE: Acute Physiology and Chronic Health Evaluation

Table III. Length of stay according to culture results

	-culture	**+culture**	**P value**	
Blood				
Hospital day	13,5±8	17,9±11,9	,029	S
ICU day	7,4±5,4	10,9±9,1	,028	S
Urine				
Hospital day	14,3±9	22,4±13,9	,003	S
ICU day	7,9±5,7	15,3±11,9	,000	S

S: Statistically Significant, ICU: Intensive care unit

Results

A total of 201 patients hospitalized in adult level 3 intensive care were included in the study. All patients were PCR positive. 44.8% of the patients were female (n: 90), 55.2% were male (n: 111). 102 (50.7%) patients received invasive mechanical ventilation (IMV) support. 101 patients died (50.2%). 46.8% of the patients were those using methylprednizalone (n: 94). Growth was detected in the blood culture in 49.3% of the patients, in the urine culture in 16.9%, in the endotracheal aspiration (ETA) culture in 4%. The mean age was calculated as 67.3 ± 14 years. The length of stay in the hospital was 15.6 ± 10.4. The mean intensive care hospitalization was found to be 9.18 ± 7.6 (Table I).

When the patients were divided into two groups as methylprednisone and those not; between groups; No significant differentiation was observed in terms of IMV need, mortality, age, APACHE II score, length of hospital and intensive care stay, blood, urine and ETA cultures. However, creatinine and d-dimer values were significantly different from the laboratory values obtained on the last day of hospitalization (p value <0.05) (Table II).

Blood, urine and ETA cultures; There was no statistically significant relationship between gender, IMV need, mortality and prednol use. Hospital and intensive care unit stay of patients with positive blood and urine cultures were found to be higher than those without growth (p value <0.05) (Table III).

Discussion

COVID-19 is a viral infectious disease that manifests mainly as fever and pneumonia. Anti-viral and respiratory supportive therapies are the main part of treatments for severe cases. The course of infections with COVID-19 is different for each patient. The disease may progress from mild clinical findings to severe ARDS, even resulting in death. Anti-inflammatory therapy can be applied in critically ill patients with ARDS and multiple organ damage.

Corticosteroid therapy; in addition, it includes the following risks: hyperglycemia, poor wound healing, psychosis, pancreatitis, and prolonged muscle weakness in impaired functional status[11]. In this study, infection rates and complications due to methylprednisolone use were not examined.

In their multicenter randomized controlled study, Confalonieri et al. Found that hydrocortisone treatment significantly reduced mortality in severe pneumonia[12]. In a retrospective study by Garcia-Vidal et al., Mortality decreased in patients who were given systemic steroids in addition to antibiotics in severe pneumonia[13]. Studies have been published showing that it reduces hospital mortality, length of stay in intensive care, duration of hospitalization, incidence of shock, and chest radiography findings[14].

In a meta-analysis published in 2012, nine randomized controlled trials, 1001 patients were included. Consequently, the use of corticosteroids did not decrease mortality. In the

subgroup analysis, prolonged survival was found in cases of severe pneumonia. It was determined that the use of corticosteroids for a period exceeding 5 days decreased mortality. Hyperglycemia was detected as a side effect. There was no risk of superinfection or gastrointestinal (GIS) bleeding[15].

As a result, the use of steroids in ARDS is a controversial issue. Studies supporting the use of low doses of steroids stand out in the literature findings. In this study; There was no effect of metiprednisone on mortality, infection rates and length of stay in intensive care patients due to COVID-19. Significant decrease in creatinine values suggested that prednisolone may have nephroprotective effects. Hospital and intensive care stay were longer, as expected, in patients with culture positive.

Referances

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