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Case Series

Correlation between the elevated level of interleukin-6 following actemra administration and the mortality rate of seven severe COVID-19 patients

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ABSTRACT

The escalation and involvement of Interleukin 6 (IL-6) in the pathogenesis of COVID-19 have been documented in numerous studies and are recognized as a diagnostic criterion, disease biomarker, and therapeutic objective. Our study aims to explore the correlation between the elevated level of IL-6 following actemra administration and the mortality rate of seven severe COVID-19 patients who were admitted to the special care department of Ardabil city hospital. In this case-series study, 7 patients with severe COVID-19 were admitted to the special care department of Ardabil city hospital were included in the study. Venous blood samples (3 cc) were taken in admission and after actemra injection. The demographic characteristics of the patients, including age, sex, duration of hospitalization, need for intubation, BMI, and interleukin 6 levels, were recorded in a checklist. The patients were then monitored for their clinical course, disease outcome, and complications. The mean IL-6 before and after actemra was 413.57±138.38 and 805.50±128.18, respectively and the difference was significant. After treatment by actemra, 71.4% of patients were discharged from hospital without mortality. Although elevated IL-6 levels have been associated with cytokine storms and unfavorable consequences in COVID-19 patients. This report indicates that high interleukin levels do not guarantee mortality. Young individuals without underlying conditions were ultimately discharged from the ICU despite severe inflammation, thanks to timely treatment and albeit with severe disability.

Keywords: IL-6, Actemra, COVID 19, Mortality

INTRODUCTION

In December 2019, the novel coronavirus disease (COVID-19) emerged in China and quickly spread worldwide. COVID-19 can present with a wide range of clinical symptoms, from asymptomatic to severe, requiring mechanical ventilation or resulting in death.[1]

Interleukin 6 (IL-6) is a cytokine that plays a crucial role in the immune response to infections. Studies have shown that patients with severe COVID-19 symptoms have higher levels of IL-6 in their blood compared to those with mild or no symptoms.[2] While IL-6 helps activate immune cells to fight infections, excessive production can lead to a cytokine storm, causing damage to healthy tissues and organs.[3]

In severe COVID-19 cases, the cytokine storm can cause severe inflammation in the lungs, leading to acute respiratory distress syndrome and other complications. Blocking IL-6 activity has been proposed as a potential treatment for severe COVID-19. IL-6 is a diagnostic index, disease biomarker, and therapeutic target as it has significant biological effects on the body.[4,5]

Actemra (tocilizumab) is a monoclonal antibody that targets the IL-6 receptor and blocks its activity. It is approved by the FDA for the treatment of rheumatoid arthritis and other autoimmune diseases. Tocilizumab has been suggested as a potential treatment for severe COVID-19 cases as it can reduce the cytokine storm and inflammation that can cause damage to the lungs and other organs.[6]

Several clinical trials have been conducted to test the efficacy of tocilizumab in COVID-19 patients. Some studies have shown that tocilizumab can improve clinical outcomes, reduce the need for mechanical ventilation, and shorten hospital stays in severely ill COVID-19 patients. However, other studies have reported conflicting results and potential side effects of tocilizumab, such as an increased risk of secondary infections and liver damage.[7,8]

Correlations have been observed between escalated levels of Interleukin 6 (IL-6) and mortality in patients diagnosed with COVID-19. This can result in severe inflammation, lung impairments, and multiple organ failures. Elevated IL-6 levels have been linked to cytokine storms and unfavorable consequences in COVID-19 patients. The present study aims to examine the association between high levels of IL-6 after actemra treatment and the mortality of six critically ill COVID-19 patients admitted to the Intensive Care Unit at Ardabil city hospital.

CASE SERIES

In this case-series study, 7 severe COVID-19 patients were hospitalized in the Intensive Care Unit at Imam Khomeini Hospital in Ardabil city, Iran. Diagnosis of COVID-19 was confirmed through RT-PCR, throat swab, and lung CT scan tests. Patients provided written consent, and their demographic information, clinical symptoms, comorbidities, and smoking history were recorded. Tocilizumab (Actemra) were prescibed for all patients treatment. Venous blood samples (3 cc) were taken from all patients to check all necessary laboratory findings and also check IL-6 levels in the first day of hospitalization and also 24 hours after receiving actemra to monitor any changes in the level of IL-6. Clinical course, response to treatment, need for intubation, arterial blood oxygen saturation, mortality, and related complications were monitored and recorded for all patients.

The mean age of patients was 41.57±16.41 (Range:21-72 years). Four patients were male and rest of them were female. The average duration of stay in the intensive care unit was 29.43±15.57 days, and two patients died due to their illness. The mean IL-6 levels before and after Tocilizumab (Actemra) administrations were 413.57± 138.38 and 805.50±128.18, respectively and the difference was significant (p=0.02) (Table 1). The demographic characteristics and underlying diseases of the patients are mentioned in Table 2. After treatment by Tocilizumab (Actemra) most of patients (n=5, 71.4%) discharged from hospital.

Table 1: Clinical and laboratory findings of patients.

Variable	Minimum	Maximum	Mean±SD
Age (in years)	21	72	41.57±16.41
BMI	19	31	24.86±5.01
HR	98	120	109.71±8.1
SAT	60	88	77.71±10.14
SBP	100	140	122.86±18.9
DBP	60	90	78.57±8.99
GCS	15	15	15.00±0.00
Ferritin	380	2000<	953.33±573.92
CRP	2	3	2.29±0.48
IL6 at admission time	238	582	413.57±138.38
IL6 at 24 hour after receiving Tocilizumab (Actemra)	650	989	805.50±128.18
Stay in the intensive care unit	10	50	29.43±15.57

Table 2: Demographic characteristics and underlying diseases of the patients.

Variable		Frequency	Percentage
Gender	Male	4	57.1
	Female	3	42.9
Blood pressure	Yes	1	14.3
	No	6	85.7
Asthma	Yes	2	28.6
	No	5	71.4
Diabetes	Yes	1	14.3
	No	6	85.7
Outcome	Discharge	5	71.4
	Death	2	28.6

Continued.

Variable		Frequency	Percentage
Vaccination	No	1	14.3
	1	1	14.3
	2	5	71.4
CRP	2++	5	71.4
	3++	2	28.6
Morbidity	Yes	5	71.4
	No	2	28.6

DISCUSSION

Tocilizumab is a medication that has been studied for its potential use in treating COVID-19. It is a monoclonal antibody that targets the IL-6 receptor, which plays a role in the body's immune response.[9]

Various studies, including randomized controlled trials and uncontrolled clinical trials, have evaluated the effectiveness of blocking IL-6.[10,11] This study describes the relationship between high levels of IL-6 after actemra treatment and the mortality of six severely ill COVID-19 patients hospitalized in the Intensive Care Unit.

In this study, the interleukin levels of seven hospitalized patients were high, which was consistent with the clinical condition and severity of COVID-19. Despite receiving actemra, the interleukin levels remained high due to the cytokine being released from its receptors. However, five patients with severe COVID-19 and high interleukin 6 levels were discharged from the hospital alive.

The systematic study and meta-analysis conducted by Mojtabavi et al demonstrate a dependable correlation between IL-6 and COVID-19 severity, regardless of age and gender.[12] In the meta-analysis done by Coomes et al, it was found that the level of IL-6 increased significantly in patients with COVID-19, and this was linked with unfavorable clinical outcomes.[2]

The study conducted by Udomsinprasert et al, reveals that the levels of IL-6 and IL-10 in circulation hold immense promise as biomarkers for assessing disease severity and mortality in patients afflicted with COVID-19.[13]

The findings of Pour et al's study demonstrated that the administration of Tocilizumab had an effect on the outcomes of COVID-19 patients, such as the need for mechanical ventilation and length of hospitalization in the case group, despite the presence of poor biological symptoms like severe lymphopenia upon admission. This showed a significant difference compared to the control group. However, Tocilizumab did not affect the patient's discharge condition or mortality rate.[14] It is consistent with the results of our report.

Several clinical trials have been conducted to investigate the safety and efficacy of tocilizumab in COVID-19 patients. Some studies have suggested that tocilizumab may be effective in reducing the risk of death or need for mechanical ventilation in patients with severe COVID-19. However, other studies have not found significant benefits.

CONCLUSION

The serum levels of IL-6 appear to serve as a valuable prognostic biomarker in COVID-19 pneumonia patients. Although elevated IL-6 levels have been associated with cytokine storms and unfavorable consequences in COVID-19 patients. Despite the increase in the amount of interleukin-6, we expected that most of the patients would die, but as the results of the data analysis indicates that high interleukin levels do not guarantee mortality. Young individuals without underlying conditions were ultimately discharged from the ICU despite severe inflammation, thanks to timely treatment, albeit with severe disability. Doing more new studies with big sample size is recommended in the future to confirm the result of this study

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