Evaluation of the therapeutic effect of the plasma of recovered COVID-19 patients for treating the patients admitted to the intensive care unit

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Abstract

The novel coronavirus has infected about 141 million people around the world. So far, about 80.4 million people have been discharged, and nearly 3.01 million people have died (an estimated mortality rate of 2.13%). The study aimed to investigate the effect of plasma therapy from recovered COVID-19 patients to treat the patients hospitalized in the intensive care unit (ICU) of the Shahid Mostafa Khomeini Hospital of Ilam in 2020.

The present prospective study was conducted in 2019–2020. Overall, 57 cases of plasma therapy were analysed using the Cox proportional hazard regression model in STATA 12 software.

The results showed in patients receiving plasma treatment, the hazard ratio was (HR = 0.68, 95% CI, 0.45–1.04), indicating a 32% lower risk of death in the COVID-19 patients who received plasma therapy compared to those who did not. However, this relationship does not reach statistical significance (p = 0.07).

Plasma therapy seems to yield some efficacy among patients with severe COVID-19 and those who have no underlying diseases. It is recommended to be used in combination with pharmaceutical interventions, for example, Actemra, to assess its therapeutic efficiency.

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Introduction

The novel coronavirus has so far infected about 141 million people worldwide, of who 80.4 million have been discharged, and about 3.01 million have died, rendering an estimated mortality rate of about 2.13% [1]. In Iran and until 21st April, 2020, 2.26 million people have been infected so far; 1.8 million of whom have improved, and 67,130 have died (an estimated mortality rate of 3.72%) (2). So far, many therapeutics methods have been tried globally to treat the disease, such as using injectable drugs, antibiotics, IVIG, etc. [1] One of these
treatments has been plasma therapy from recovered COVID-19 patients, which is infused to the patients suffering from active disease. Therefore, the aim of this study was to investigate the effect of plasma therapy from recovered COVID-19 patients on the improvement of the patients admitted to the intensive care unit (ICU) of the Shahid Mostafa Khomeini Hospital of Ilam in 2020.

Methods

The present prospective study was conducted in 2019–2020. The registered data of the patients with COVID-19 disease admitted to the Shahid Mostafa Khomeini Hospital of Ilam was used. In this study, the effect of plasma therapy from recovered COVID-19 patients was investigated on mortality in 566 COVID-19 patients admitted to the ICU. Among these, 57 patients received plasma therapy, and their mortality rate was analysed using the Cox proportional hazard regression model in STATA 12 software.

Results

The mean age of the patients receiving plasma therapy was 57.8 years, and the mean age in the control group was 63 years. Thirty patients who received plasma therapy died, and 27 survived. In addition, 53% of the patients who received plasma therapy were intubated, and 70% of these patients had an underlying disease (Table 1).

Based on the results of the univariate Cox regression analysis considering death due to COVID-19 as the main outcome, many variables, including plasma therapy, were significantly associated with death among COVID-19 patients. Hazard ratio (HR) for plasma therapy was 0.72 with a 95% confidence interval of 0.49 to 1.06 (P = 0.09, Table 2). The Schoenfeld residuals test was performed for the variables, indicating that the proportional hazard assumption was met. All variables with p-value<0.2 from the univariate analysis were included in the multivariate proportional hazard Cox regression model models. In the multivariate model, the effect of plasma therapy was adjusted according to the main variables known to be related to COVID-19 mortality, such as cardiovascular diseases, hypertension, chronic lung diseases, smoking, age, sex, and other significant variables (Table 3). The HR for the effect of plasma therapy on death was obtained 0.68 with a 95% confidence interval of 0.45 to 1.04. This indicated that the risk of death due to COVID-19 was 32% lower in the patients who received plasma therapy than in those who did not. However, this relationship does not reach statistical significance (p = 0.07, Table 3).

### TABLE 1. Distribution of Demographic and Clinical Qualitative and Quantities Variables among the Patient Groups

| Characteristics | Plasma (yes) | Plasma (no) |
|-----------------|--------------|-------------|
| Total patients(N) | 57 | 509 |
| Age (years) (mean ± SE) | 57.8 (1.7) | 63.4 (0.7) |
| Sex (%) | Female | 26 (11) | 211 (89) |
| Male | 31 (9.4) | 296 (90.6) |
| BP (mean ± SE) | 28.6 (0.4) | 26.7 (0.3) |
| Smoking status (%) | Non-smoker | 54 (10.3) | 470 (89.7) |
| Ex-smoker | 1 (9.3) | 10 (90.7) |
| Smoker | 2 (8.7) | 21 (91.3) |
| Underling disease (%) | No | 17 (11.1) | 136 (88.9) |
| Yes | 40 (9.7) | 372 (90.3) |
| Intbation (%) | No | 27 (9.7) | 252 (90.3) |
| Yes | 30 (10.5) | 257 (89.5) |
| Lung lobe affected (mean ± SE) | 4.5 (0.1) | 4 (0.1) |
| hospital stay(mean ± SE) | 13 (0.9) | 8.2 (0.3) |
| Death (%) | No | 27 (9.3) | 262 (90.7) |
| Yes | 30 (10.8) | 247 (89.2) |
| Platelet(mean ± SE) | 208694.7 (9258.5) | 216244 (4161.8) |
| White blood cell (mean ± SE) | 127877.992 (5126) | 113247 (5423) |
| ESR (mean ± SE) | 4 (1.79) | 40 (1.74) |
| CRP (mean ± SE) | 918.2 (87.7) | 735.6 (28.2) |
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As shown in Fig. 1, the median survival for the patients receiving plasma therapy was 21 days compared to 17 days for the control group. Although the survival of plasma-treated patients was slightly higher, the survival curves became close at some points, rendering similar survival rates in plasma-treated and non-treated patients. As shown in Fig. 2, the risk function was ascending for both groups, with the risk being higher in the patients who did not receive plasma.

**TABLE 3. Cox Proportional Hazard analysis for related factors of mortality in COVID-19 disease in multivariate model**

| Characteristics     | Adjusted hazard ratio (95% CI) | PH assumption | P-value |
|---------------------|--------------------------------|---------------|---------|
| Age                 | 1.00 (0.99 – 1.01)             | met           | 0.72    |
| Sex                 | 1.32 (1.00 – 1.76)             | met           | 0.05    |
| Female              |                               |               |         |
| Male                |                               |               |         |
| Smoking status      |                               |               |         |
| Non-smoker          |                               | met           |         |
| Ex-smoker           | 1.30 (0.59 – 2.83)             |               | 0.51    |
| Smoker              | 1.15 (0.56 – 2.35)             |               | 0.71    |
| Intubation          |                               | met           |         |
| No                  |                               |               |         |
| Yes                 | 9.39 (5.98 – 14.46)            | <0.001        |
| Plasma therapy      |                               | met           |         |
| No                  |                               |               |         |
| Yes                 | 0.68 (0.45 – 1.04)             | 0.07          |
| White blood cells   |                               | met           |         |
| No                  | 1.01 (0.99 – 1.01)             | 0.19          |
| Yes                 | 1.09 (0.96 – 1.00)             | 0.09          |
| LDH                 | 1.00 (0.99 – 1.00)             | met           | 0.22    |

* = Proportional Hazard Assumption.
** = Significant.
*** = Borderline significant.
* = Reference category.
** = White blood cells/1000.
*** = Platelet/100000.

**Discussion**

In this study, we investigate the effects of plasma therapy on the COVID-19 patient’s mortality. The results showed that plasma therapy might help patients improve their clinical outcomes. In addition, the survival of the patients who were early diagnosed was higher; moreover, those who were hospitalized in the general ward and had lower lung involvement recovered sooner.

**New clinical experiences**

If performed continuously, plasma therapy can help in the relative recovery of COVID-19 patients with severe pulmonary involvement.

**Conclusion**

Plasma therapy in severe COVID-19 patients might improve the clinical outcome of the patients with a severe condition admitted to the intensive care unit and can be used to improve the recovery rate of these patients.

**Recommendations**

It is recommended to combine plasma therapy along with other medications such as Actemra and assess its therapeutic efficiency in COVID-19 patients with moderate lung involvement.
Limitations

Due to the novelty of the subject and the fact that there are a few studies on the subject, we could not perform comparative analyses for variables such as the level of lung involvement, recovery rates, and the effects of other therapeutic methods.

Ethical considerations

The ethical was approved by Ilam University Medical Science IR.MEDILAM.REC.1398.212.

Transparency declaration

The authors declare that they have no conflicts of interest.

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