Case Series

Therapeutic plasma exchange in patients with COVID-19 pneumonia in intensive care unit: Cases series

Ikram Zaid a,b,*, Ounci Essaad a,b, Ghizlane El aidouni a,b, Mohammed Aabdi a,b, Samia Berrichi a,b, Salma Taouihar a,b, Manal Marbouh a,b, Houssam Bkiyer a,b, Naima Abda b,c, Brahim Housni a,b,d

a Department of Intensive Care Unit, Mohammed VI University Hospital, Oujda, Morocco
b Faculty of Medicine and Pharmacy, Mohammed 1st University, Oujda, Morocco
c Department of Community Medicine, Mohammed VI University Hospital, Oujda, Morocco
d Mohammed First University Oujda, FMP Oujda, LAMCESM, Oujda, Morocco

ARTICLE INFO

Keywords:
COVID 19 pneumonia
Therapeutic plasma exchange
Cytokine storm
Acute respiratory distress syndrome

ABSTRACT

Introduction: COVID 19 pneumonia can lead to an inappropriate inflammatory response, and can be complicated by acute respiratory distress syndrome, multivisceral failure with a high mortality rate.

Objective: To observe the effect of therapeutic plasma exchange on the excessive inflammatory response.

Materials and methods: In this study, we included 7 confirmed cases of COVID-19 in the intensive care unit (ICU) department of the university hospital of Oujda. COVID-19 cases were confirmed by RT PCR (reverse transcription-polymerase chain) and CT (computerized tomography) imaging according to WHO guidelines. Therapeutic plasma exchange was performed decrease cytokine storm-induced ARDS (Acute respiratory distress syndrome). Inflammation marker assays were performed before and after therapeutic plasma exchange to assess its efficacy.

Results: Levels of inflammatory cytokines (IL-6) and acute phase response proteins, including ferritin and CRP, were elevated before therapeutic plasma exchange.

After therapeutic plasma exchange, levels of acute phase reactants, inflammatory mediators, were significantly reduced (p < 0.05).

Conclusion: Our data suggest that therapeutic plasma exchange reduces the inflammatory response in patients with severe COVID-19 not undergoing mechanical ventilation. Further studies are needed to explore the efficacy of therapeutic plasma exchange in patients with COVID-19.

1. Introduction

The immunologic response to COVID-19 infection initiates an acute autoimmune disease by over-production of inflammatory cytokines leading to a cytokine storm leading to ARDS [1].

When the virus enters the body, it activates inflammatory cells such as neutrophils, macrophages, lymphocytes, dendritic cells, and natural killer cells, these cells produce different types of cytokines especially the inflammatory type, leading to an inappropriate overproduction of cytokines [2].

These patients are susceptible to develop ARDS defined as acute onset of severe hypoxemia less than one week with bilateral infiltrates in chest-X Ray, and lung edema not fully explained by left ventricular failure or liquid overload [3].

The procedure of therapeutic plasma exchange is considered as an adjunctive treatment for the management of cytokine storms and coagulopathy in respiratory viral pandemics [4].

2. Materials and methods

2.1. Study design

The study was conducted in the intensive care unit (ICU) department of the university hospital of Oujda, Morocco. Between 18 January and 16 March 2021. Written informed consent was obtained from all study participants, 7 adult patients with confirmed COVID-19 as determined by clinical criteria and positive RT-PCR assays. Critically ill patients were defined as those with clinical deterioration requiring admission to
the intensive care unit and who required non-invasive ventilation; the initial blood sample was measured immediately upon the patient’s admission to the ICU and prior to receiving any treatment.

This study was approved by the ethics committee for biomedical research of Oujda of the faculty of medicine and pharmacy of Oujda. Informed consent was obtained from the participants.

2.2. Inclusion criteria in patient selection

We report a case series of 7 patients with COVID-19 infection, who were in a clinical and biological cytokine storm, undergoing therapeutic plasma exchange.

2.3. Data collection

We collected the epidemiological, biological, and radiological data of those patients. The medical and surgical history, as well as the therapeutic and evolutionary data, was well collected from the electronic files available.

2.4. Statistical analysis

The data were analyzed using the statistical package SPSS version 24.0 and descriptive statistics. P values < 0.05 were considered significant. Our study was registered in Research Registry under the number: 6573.

This case series has been reported in line with the PROCESS Guide [5].

3. Results

In our study, we included 7 patients with COVID-19 infection confirmed by RT-PCR. All patients received 10 days of dexamethasone at a dose of 6 mg.

Initial scencographic damage was greater than 75% in 3 patients, between 50 and 75% in 2 patients; one patient had involvement between 25 and 50% and one patient between 10 and 25%.

Four patients had initially received a 400 mg dose of Tocilizumab, without clinical or biological improvement. Plasma exchanges were performed with fresh frozen plasma (FFP), with a quantity of 1.5 ml/kg at a rate of 3–5 sessions successive, with a plasma filtration flow rate of 20 ml/min, four patients had blood type A+, two had O+ and one had AB-.

Table 1 shows the demographic information of participating COVID-19 infected patients. The mean age of the patients was 57 years. Three (42.9%) patients were male and 4 (57.1%) were female. One of the patients has a history of hypertension (HTN), 14.3%, one has a history of diabetes (14.3%), and one has a history of asthma (14.3%) (Table 1). All patients had respiratory compromise at admission.

The 2nd table shows a very significant decrease after plasma exchange of IL6 with P-value 0.0004, a decrease of ferritinemia (P-value 0.011), of fibrinogen level (0.015), of leukocytes (0.017) (Table 2).

4. Discussion

Plasma exchange was efficient in our seven critically ill patients by decreasing the cytokine storm, reducing pro-inflammatory cytokines. It also improved the respiratory status of the patients and increased the number of lymphocytes.

In our study, all our patients had a very high inflammatory balance before plasma exchange, with a good clinical and biological evolution afterward. This good evolution can be explained by early management and the practice of therapeutic plasma exchange on the first day of the cytokine storm and before the necessity of intubation.

The four patients who received tocilizumab initially had a favorable outcome after therapeutic plasma exchange.

In a similar study, carried out by Seyed H et al. in IRAN in March 2020, therapeutic plasma exchange was practiced in 8 patients with good evolution, only one patient died, due to the delay of the practice of plasma exchange. Therapeutic plasma exchange was as follows: 2 L of plasma filtered every day, exchanged with 4 units of FFP, 5 vials of albumin with calcium gluconate, and the rest of the volume was replaced with saline serum. The remaining volume was replaced with normal saline serum, according to the patient volume status [6].

Another study done in Tahran by Hashemian et al. in March 2020 on 15 patients who were in critical respiratory condition, showing that after therapeutic plasma exchange, there has been a decrease in levels of inflammatory mediators, liver enzymes after one week, with a survival rate of 75%.

Table 2

| Variable                      | Before | After | P-value |
|-------------------------------|--------|-------|---------|
| Arterial blood gas analysis   |        |       |         |
| PaO2                          | 57,1 ± 7 | 59,1 ± 11 | 0,74    |
| Infection and immunity        |        |       |         |
| C-reactive protein, mg/dl     | 149 ± 104 | 16 ± 10 | 0,066   |
| Ferritin, ng/ml               | 1322 ± 902 | 601 ± 404 | 0,011   |
| Lymphocyte, /mm3              | 997 ± 585 | 1421 ± 1210 | 0,046   |
| Fibrinogen, g/l               | 3,7 ± 2,1 | 3,1 ± 1,5 | 0,015   |
| Leucocyte, /mm3               | 13780 ± 6700 | 12050 ± 6000 | 0,017   |
| Biochemical test              |        |       |         |
| LDH, U/L                      | 993 ± 333 | 646 ± 271 | 0,073   |
| Inflammatory mediators        |        |       |         |
| IL-6 pg/ml                    | 779 ± 1400 | 205 ± 412 | 0,0004  |

Table 1

| Demographics and baseline characteristics of patients infected with COVID-19 (n = 7). |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Gender  | Age  | Co-morbidities                  | Respiratory status before plasmapheresis | Lung damage in CT scan | Plasmapheresis sessions | Respiratory status after plasmapheresis | Hospitalisation length |
|---------|------|-------------------------------|------------------------------------------|------------------------|-------------------------|----------------------------------------|------------------------|
| 1       | M    | 48                            | Without co-morbidity                      | 02 Saturation was 75%, while receiving 100% of O2 with high flow oxygen therapy | >75%                    | 3                        | SaO2 88-90% AAA                    | 13                     |
| 2       | M    | 38                            | Asthma                                   | 02 Saturation was 75%, while receiving 100% of O2 with high flow oxygen therapy | 10-25%                  | 3                        | SaO2 88% AAA                      | 34                     |
| 3       | F    | 57                            | Diabetes                                 | 02 Saturation was 89%, while receiving 100% of O2 with high flow oxygen therapy | 50-75%                  | 5                        | SaO2 90% AAA                      | 28                     |
| 4       | F    | 59                            | Hypertension                              | 02 Saturation was 87%, while receiving 10L of O2/min with oxygen Mask with reservoir bag | >75%                    | 3                        | SaO2 88% AAA                      | 6                      |
| 5       | M    | 63                            | Without co-morbidity                      | 02 Saturation was 80%, while receiving 100% of O2 with high flow oxygen therapy | >75%                    | 5                        | SaO2 92% AAA                      | 23                     |
| 6       | F    | 57                            | Without co-morbidity                      | 02 Saturation was 89%, while receiving 100% of O2 with high flow oxygen therapy | >75%                    | 3                        | SaO2 88% AAA                      | 15                     |
| 7       | M    | 77                            | Without co-morbidity                      | 02 Saturation was 89%, while receiving 100% of O2 with high flow oxygen therapy | 50-75%                  | 5                        | SaO2 88 sous 2L                    | 23                     |
rate of 60% in patients with non-invasive positive-pressure ventilation (NIPPV) [7].

Various studies published about Previous therapeutic plasma exchange showed that it can be a useful tool helping in the management of patients with acute respiratory failure undergoing mechanical ventilator and play a key role to reduce the mortality rate in patients with covid-19 infection [8,9].

Our study has several limitations. Only 7 patients with Covid-19 disease were studied. This is a study that is uncontrolled; Hence the need to conduct a randomized controlled study to better assess the effectiveness of therapeutic plasma exchange in seriously ill patients due to Covid-19.

5. Conclusion

This study showed that therapeutic plasma exchange is very effective in eliminating inflammatory mediators, acute phase proteins and improves tissue oxygenation.

Therapeutic plasma exchange should be used earlier in critically ill patients with acute respiratory distress syndrome. However, randomized clinical trials are needed to draw definitive conclusions.

Ethical approval

This is a retrospective case series that does not require a formal ethical committee approval. Data were anonymously registered in our database. Access to data was approved by the head of the department.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution

Zaid Ikram: study concept, Data collection; data analysis; writing review & editing, Essaad Ounci: Study conception, writing review, El aidouni Ghizlane: Study conception, writing review and editing, Aabdi Mohammed: Study conception, writing review and editing, Berrichi Samia: contributor, Jakhjouk Douae: contributor, Taouihar Salma: contributor, Marbouh Manal: contributor, Bkiyar Houssam: supervision and data validation, Abda Naima: Data analysis, supervision and data validation, Housni Brahim: supervision and data validation.

Trial registry number

Research registry 6573.

Guarantor

Zaid Ikram.
Essaad Ounci.