Annals of Medicine and Surgery 71 (2021) 102920

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Case Series

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

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ARTICLE INFO

Keywords:
COVID 19 pneumonia
Therapeutic plasma exchange
Cytokine strom
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

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https://doi.org/10.1016/j.amsu.2021.102920
Received 18 August 2021; Received in revised form 3 October 2021; Accepted 3 October 2021
Available online 7 October 2021

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 Guideline [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 scenographic 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 *30 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 57years. 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 leucocytes (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 filtred 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 Tahrane 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

Table 2
Laboratory findings of patients infected with COVID-19 on admission to ICU (n = 7).

Variable	Before	After	Pvalue
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 lenght
1	M	48	Without co-morbidity	O2 Saturation was 75%, while receiving 100%of O2 with high flow oxygen therapy	>75%	3	SaO2 88–90% AAA	13
2	M	38	Asthma	O2 Saturation was 75%, while receiving 100%of O2 with high flow oxygen therapy	10–25%	3	SaO2 88% AAA	34
3	F	57	Diabetes Hypertension	O2 Saturation was 89%, while receiving 100% of O2 with high flow oxygen therapy	50–75%	5	SaO2 90% AAA	28
4	F	59	Without co-morbidity	O2 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	O2 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	O2 Saturation was 89%, while receiving 80% of O2 with high flow oxygen therapy	>75%	3	SaO2 88%AAA	15
7	M	77	Without co-morbidity	O2 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, Jakhjoukh 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.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Consent

The requirement of patient consent has been lifted. Data anonymity was respected in accordance with national and international guidelines.

Declaration of competing interest

The authors state that they have no conflicts of interest for this case series.

Acknowledgments

We would like to thank the medical and nursing teams of Mohammed VI University Hospital for their significant involvement in the management of the patients included in our study. Particular thanks to the director of Mohammed VI University Hospital Prof. AbdelKarim Daoudi for his successful management of this outbreak.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102920.

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