Convalescent Plasma Transfusion Results in Clinical Improvement in Critically Ill Patients with COVID-19: San Luis Potosí, México

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ABSTRACT
The outbreak of the novel coronavirus disease (COVID-19) caused by the new SARS-CoV-2 virus is indeed a pandemic threat to global public health. The disease has spread worldwide and millions of lives have been affected not only by the disease but by the economic consequences of compulsory isolation and quarantine. We designed protocols to treat patients with severe forms of COVID-19 in México with convalescent plasma. Currently we already have vaccines, however the objective of this article is to publicize the results obtained in the state of San Luis Potosí, with the use of convalescent plasma. The use of convalescent plasma reduces complications and length of stay in intensive care units.

KEYWORDS
CoPla, Convalescent Plasma, Coronavirus disease, COVID-19.

Introduction
The outbreak of the novel coronavirus disease (COVID-19) caused by the new SARS-CoV-2 virus is indeed a pandemic threat to global public health. Although the pandemic’s epicenter was initially located in Wuhan, China in December 2019, the disease has spread worldwide and millions of lives have been affected not only by the disease but by the economic consequences of compulsory isolation and quarantine [1]. The use of convalescent plasma (CoPla) was recommended as empirical treatment of Ebola in 2014 and later, in the management of the Middle East respiratory syndrome, SARS-CoV, H5N1 avian influenza and H1N1 influenza [2-4]. CoPla has been recently used in the treatment of patients with COVID-19 in China and other countries [3-7] and was found to be safe and effective; in addition, it is affordable, a key requirement in low and middle-income economies. Based on these concepts, we designed protocols to treat patients with severe forms of COVID-19 in México with CoPla (Figure 1), [8-10]. Currently we already have vaccines, however the objective of this article is to publicize the results obtained in the state of San Luis Potosí, with the use of convalescent plasma.
Objective
To study the safety and outcomes of the administration of CoPla to individuals with severe COVID-19 in a medical center of San Luis Potosi, Mexico.

Methods
Twenty-five patients were prospectively treated with plasma from COVID-19 convalescent donors. Patients with confirmed laboratory evidence of COVID-19 by reverse transcriptase polymerase chain reaction of the upper respiratory tract, were eligible to receive CoPla provided the following criteria: a) Severe pneumonia with rapid progression, b) \( \text{PaO}_2/\text{FiO}_2 < 300 \) with or without mechanical ventilation support, c) admitted to the intensive care unit (ICU), d) more than 18 years and e) signed the informed consent form. ABO blood types were determined for donor compatibility and each patient received 200 ml ABO compatible CoPla. The selection of donors was carried out in accordance with the provisions of NOM 253-SSA1-2012, and the guidelines of the National Center for Blood Transfusion of Mexico. (The protocol authorization number was 203301410A0074).

Figure 1: Protocol to treat patients with severe forms of COVID-19 in México with CoPla. 1. Antibodies that bind a SARS-CoV-2 help patient recover. 2. Recovered patients donates CoPla by plasmaphoresis. 3. Plasma is treated for antibody strenght an number, an finally 4. Patient recieves donador CoPla. Taken and modified from Biorender Template.

Figure 2: Changes after plasma infusion in the 25 patients. Panel A depicts the significant drop of the SOFA index; panel B shows the significant increase in the Kirby index (p\( \text{O}_2/\text{FiO}_2 \)); panel C shows the significant decrease in body temperature.
Results
Over 21 days, the sequential organ failure assessment (SOFA) score dropped significantly in all patients, from 3.2 to 1.7 (p=0.01); the Kirby index (PaO\textsubscript{2}/FiO\textsubscript{2}) score increased from 120 to 250, (p<0.0001), body temperature decreased significantly from 38.7 to 37.0°C (p=0.001). Five of seven patients on mechanical ventilation support could be extubated, Thirteen were transferred to conventional hospital floors without ventilation support; four patients died (Figure 3). The administration of CoPla had no side effects and the 21-day overall survival was 70%. Previous studies have reported the merit of CoPla in several infectious diseases [2-4] and specifically, in COVID-19 [3]. In these studies, critically ill patients due to infection by the SARS-CoV-2 virus and with a Kirby index below 300 reflecting severe pulmonary injury, received CoPla. Most patients had a positive result, defined as the improvement in both their clinical course and in the surrogate markers of the disease [5]. Since the patients were receiving other treatments, it is difficult to conclude that the CoPla infusion was fully responsible for the improvement in pulmonary function and in the patients’ clinical course.

Be that as it may, these studies suggest that the administration of CoPla may result in improvement in both respiratory function and in the clinical course of COVID-19 patients. Although the numbers are small, the intervention confirms previous experiences [3]. Adding CoPla to the treatment of critically ill patients with COVID-19 may be useful and it is both affordable and safe, but we need more detailed information in order to define the role of this practical therapeutic intervention. In a recent study from China [6], patients were randomized for Copla and best therapy in comparison with just the best therapy available.

Conclusion
The results showed that there is no significant difference, but a potential benefit was observed in severely ill patients and there is a reasonable hope that high titer antibody against SARS-CoV-2 may have antiviral efficacy and a role in the treatment of COVID-19 patients. The use of convalescent plasma reduces complications and length of stay in intensive care units.

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