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Are SOFA score, PaO₂/FiO₂ ratio, lymphocytes levels, total bilirubin, lactate dehydrogenase, ferritin, C-reactive protein and interleukin-6 significantly normalized following TPE completion: Is this fact or fiction?



We read with great interest the study by Faqih et al. finding that therapeutic plasma exchange (TPE) demonstrates a potential survival benefit and low risk in life-threatening COVID-19 acute respiratory distress syndrome (ARDS) [1]. They also found that Sequential Organ Function Assessment (SOFA) score, PaO₂/FiO₂ ratio, lymphocytes levels, total bilirubin, lactate dehydrogenase, ferritin, C-reactive protein, and interleukin-6 normalized [1]. No adverse effects from TPE were observed. The patients received 5–7 TPE sessions. We are not sure that the authors have demonstrated the point that they intended to make. Misinterpretation of the results can lead to the wrong conclusions. PE has a cutoff of 1,000,000 Da (Da) and can therefore remove many substances [2]. Let us just take the example of the inflammatory mediators C-reactive protein (CRP) and interleukin-6 (IL-6). CRP, in its pentameric form, has a molecular weight of 120,000 Da and IL-6 has a molecular weight of 21,000 Da [2]. It stands to reason that these two inflammatory molecules will be easily removed by TPE. Reduction of the plasma level of inflammatory mediators via the use of PE does not necessarily equate to an improvement in the septic status of the patient. It is simply an artificial reduction, “treating the numbers” so to speak. The same is true for ferritin (474,000 Da) and lactate dehydrogenase (144,000 Da), where the observed reduction is simply a consequence of removal and not an improvement of the patient's condition [1]. In addition, TPE removes bilirubin by removing albumin [1]. It is also important to note that PE has the potential to cause harm by diluting or attenuating the patient's adaptive response to infection via depletion of immunoglobulins and complement components 3 and 4 in individuals treated with plasmapheresis [3,4]. Importantly, in the case of patients with COVID-19, PE will remove the protective antibodies formed by the patient, which is not desirable. Indeed, PE may not restore immune homeostasis but may rather aggravate immunoparalysis [5]. The authors stated that clinical improvements were achieved in the four patients, possibly indicating a direct pathophysiological influence of PE on the COVID-19-associated cytokine storm-like clinical syndrome [1]. The only positive effect seen is the control of temperature. Indeed, perhaps by inducing relative hypothermia, PE resulted in peripheral vasoconstriction maybe responsible for the weaning of vasopressors. It has also been shown that the extracorporeal removal of immunoglobulins had modulating effects on T-Helper cells balance [5]. Again, this could be only an artificial change in the balance of T-Helper lymphocytes linked directly to PE and not an improvement of the immune condition of the patient. The authors claims that TPE was associated with a marked clinical improvement with decrease in SOFA score and improvement in PaO₂/FiO₂ ratio [1]. Indeed, control of fever and

vasoconstriction induced by PE leads to reduction of vasopressors will lead to improvements in SOFA score and PaO₂/FiO₂ ratio but this is simply artificially, and PE does not necessarily equate to an improvement in the septic status of the patient.

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