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VENO-VENOUS ECMO SUPPORT IN THE MANAGEMENT OF A JEHOVAH'S WITNESS WITH SEVERE COVID-19: A CASE REPORT AND LITERATURE REVIEW

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ABSTRACT

Background: Severe coronavirus disease 2019 (COVID-19) infection can lead to severe acute respiratory syndrome for which extracorporeal membrane oxygenation (ECMO) could be used in selected cases. Most Jehovah's witnesses (JWs) do not accept transfusion of blood and/or blood products. The use of ECMO for the management of JWs during the pandemic was challenging.

Case report: We present a case of a JW with severe COVID-19 infection and multiple organ failure necessitating ECMO support for 20 days. We discuss the management challenges in patients who do not accept blood transfusions. A significant drop in the patient's haemoglobin and platelet count was observed throughout ECMO duration. An anti-coagulation-free ECMO circuit was maintained, and we did not observe any major circuit or patient complications.

Conclusion: Management strategies to minimize blood loss, avoid bleeding, augment haemoglobin production, maintain ECMO circuit integrity without systemic anticoagulation, and reduce blood loss during ECMO decannulation are helpful in the management of JW followers on ECMO. We recommend treatment in such a situation at experienced centres with the involvement of a haematologist within an interprofessional team.

KEYWORDS

Jehovah's Witness, COVID-19, veno-venous extracorporeal membrane oxygenation, transfusion

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LEARNING POINTS

- Management of patients who are Jehovah's witnesses, who do not accept blood transfusion is challenging.
- Conservative transfusion strategies are feasible on selected patients supported by extracorporeal membrane oxygenation.
- Transfusion thresholds should be dynamic and reviewed daily.
- Mitigation of blood loss, rationalization of blood tests, and anticoagulation help reduce the need for transfusion.
- Transfusion targets and guidelines need revision, and it is best to adopt patient-specific targets tailored to each patient's needs.

INTRODUCTION

Haemorrhagic and thromboembolic events are common in severe coronavirus disease 2019 (COVID-19) infection. More than 30% of critically ill COVID-19 patients were found to have thrombosis. Endothelial dysfunction, hyperinflammation, immune system stimulation, pulmonary vessel microthrombi formation resulting in cytokine release, von Willebrand factor, and platelet activation could explain the disseminated intravascular micro-thrombosis and COVID-19-associated coagulopathy[1]. Extracorporeal membrane oxygenation (ECMO) support has been widely used for the treatment of severe acute respiratory distress disorder (ARDS) secondary to COVID-19 infection[2] and is thought to alter normal clotting[3]. Patients with severe COVID-19 on ECMO may develop coagulopathy and bleeding, requiring massive transfusion[3]. We present a case of a Jehovah's witness (JW) with severe COVID-19 infection complicated with multiple organ failure necessitating ECMO support. We also address the challenges of treating this patient who did not accept blood transfusions.

CASE DESCRIPTION

A 49-year-old male presented with fever and shortness of breath for 7 days. Upon admission, he was hypoxemic (peripheral oxygen saturation SpO_2 of 65% on room air), tachypnoeic with a respiratory rate of 35 breaths/minute, tachycardic, and had bilateral crackles on chest examination. Polymerase chain reaction testing confirmed COVID-19 infection. The patient developed peri-intubation cardiac arrest with pulseless electrical activity and was successfully resuscitated. The patient was admitted with a diagnosis of pneumonia and acute respiratory distress syndrome (ARDS) secondary to COVID-19.

The laboratory investigations on admission revealed a raised white blood cell count of 14.2 $\times 10^3$/µl, normal haemoglobin of 12.7 g/dl, and platelet count of 187.000/mm^3. The initial blood gas showed severe metabolic acidosis with a pH of 7.17, partial pressure of oxygen (PaO_2) of 60 mmHg, and partial pressure of carbon dioxide ($PaCO_2$) of 38 mmHg. Chest X-ray showed bilateral extensive heterogeneous infiltrates, as shown in *Fig. 1*. Computed tomography of the chest revealed bilateral extensive ground glass opacities and pleural effusions. The patient was maintained on infusions of sedation, neuromuscular blocking agents, and norepinephrine. Treatment of COVID-19 included anti-viral agents, steroids, and tocilizumab. Despite prone positioning, the oxygen saturation was 75%, and the patient remained hypoxic with a PaO_2/fraction of inspired oxygen (FiO_2) ratio of 50. Due to the failure of conventional mechanical ventilation and maximum ARDS management strategy, veno-venous (VV)-ECMO was initiated via a bifemoral percutaneous approach. The clinical course was complicated, with acute kidney injury requiring a few days of continuous renal replacement therapy. On days 2 and 3 of the ECMO run, the patient received three packed red blood cell (PRBC) units due to persistent hypoxia and hemodynamic instability associated with a drop of Hb to < 8 g/dl. No other blood products were administered. On day 4 of ECMO, the medical team was alerted by a nursing colleague that this patient was a JW and attended the same church as him. Interestingly, the patient had had multiple admissions to our hospital since 2017, but no indication of the religious state or advance directive was available in the medical records. Considering this emerging information, a management plan was formulated focusing on:

1) Minimizing blood loss was achieved by reducing the volume and frequency of routine laboratory testing and arterial blood gas analysis and using smaller (paediatric) collecting tubes;
2) Optimizing haemoglobin production was carried out by intravenous iron administration during the ECMO run, with a total of 1500 mg of ferric carboxy maltose in two separate doses of 750 mg, one week apart. This was



Figure 1. Chest X-ray on admission showing bilateral infiltrates of severe COVID- 2019 pneumonia.

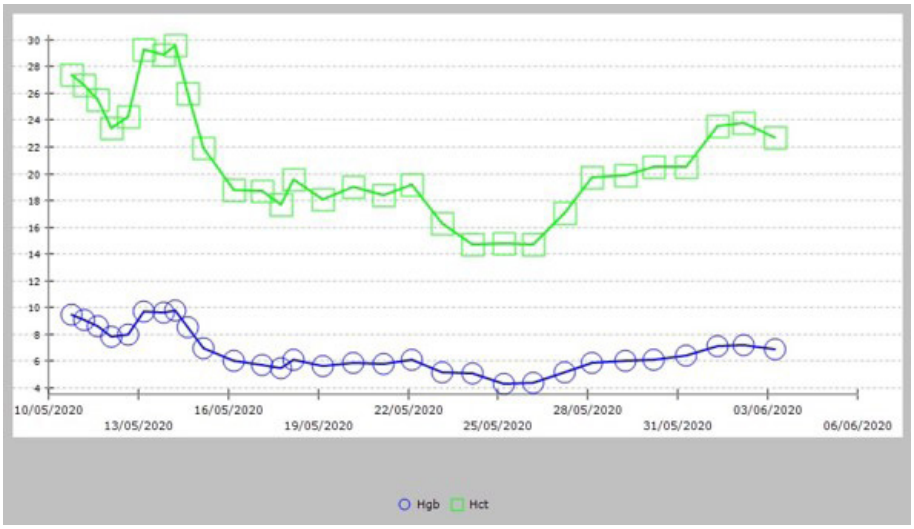


Figure 2. Graphic representation of haemoglobin (Hgb, in blue line) concentration and haematocrit (Hct, in green line) throughout veno-venous extracorporeal membrane oxygenation.

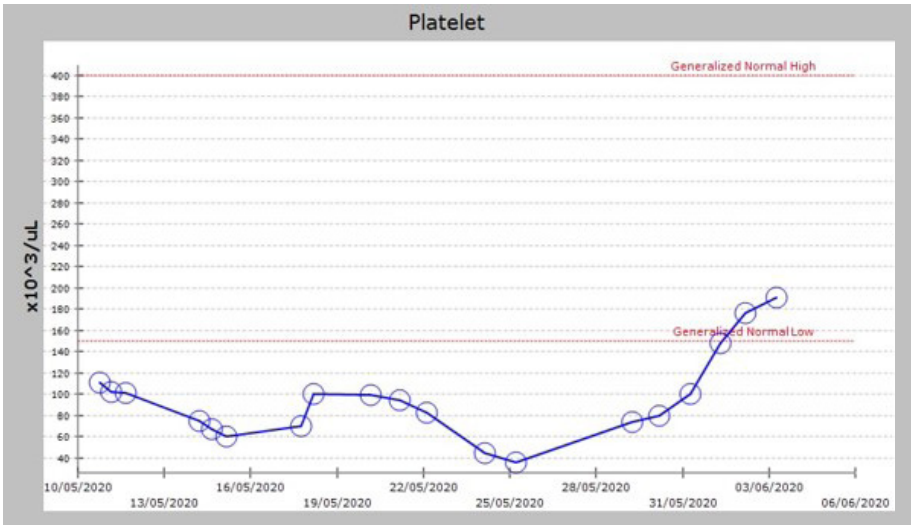


Figure 3. Graphic representation of platelet count throughout the course of veno-venous extracorporeal membrane oxygenation.

followed by the administration of erythropoietin (EPO) 50 units/kg three times per week;

3) An anticoagulation-free ECMO strategy is crucial to minimize bleeding and blood loss. It was maintained throughout the ECMO run, and we did not observe any indication of circuit malfunction or need for a circuit change;
4) Acceptance of lower SpO_2 >85% and PaO_2 >55 mmHg;
5) Reducing blood loss at decannulation.

Despite the above strategies, the haemoglobin level was 4.4 g/dl on day 8 of ECMO. However, other clinical parameters were satisfactory, and the haemoglobin at decannulation was 6 g/dl. On day 19 of the ECMO support, the patient demonstrated clinical improvement, passed an ECMO weaning trial, and met the decannulation criteria. However, the medical team opted for continuing zero sweep ECMO for 24 hours to be more confident that the patient would remain stable off-ECMO and would not require re-cannulation. ECMO cannulas were successfully removed on day 20 using the circuit blood return technique by infusing saline into the drainage limb after clamping the drainage cannula. Supplemental iron, vitamins, and EPO administration was maintained. Liberation from mechanical ventilation was successful and the tracheostomy tube was removed on day 40, and the patient was subsequently transferred to a rehabilitation facility. Upon home discharge on day 60, the patient's haemoglobin was at 13.4 g/dl with oral iron therapy. The trend of haematocrit, haemoglobin, and platelet concentration during ECMO is shown in *Fig. 2 and 3*.

DISCUSSION

In critically ill patients, a restrictive transfusion strategy has been associated with better outcomes[4]. The requirement for blood transfusion on ECMO can be related to anaemia, thrombocytopenia, and coagulopathy. Anaemia is one of the most common indications. Anaemia in patients with ECMO is multifactorial and can be attributed to several causes, such as blood sampling, bleeding as a complication of anticoagulation, circuit change, direct insult by the ECMO machine secondary to clotting factor consumption, bone marrow suppression, and haemolysis. There are many potential risk factors for bleeding in patients receiving ECMO[5]. The ECMO-associated coagulation cascade's activation impacts fibrinolysis, thrombin formation, and platelet function due to the systemic inflammatory response syndrome and contact between the patient's blood and the ECMO circuit. With both thrombotic and haemorrhagic risk, the outcomes of these alterations to haemostatic balance

are challenging. Anticoagulation is still a standard practice in ECMO patients to balance the thrombotic risks associated with the circuits themselves[3]. Bleeding is the most common complication of ECMO and is associated with increased mortality[3]. The Extracorporeal Life Support Organization guidelines recommend continuous anticoagulation and haemoglobin levels greater than 12 g/l during ECMO support. However, a multicentre randomized trial recommended a haemoglobin level of only 6-7 g/dl[6]. ECMO is a blood and blood products-consuming intervention, and frequent transfusions are common. VV-ECMO recipients generally require less transfusion than veno-arterial (VA)-ECMO-supported patients. Adult patients on VA-ECMO required up to 5 units of PRBC and 9 units of platelets. A large prospective study demonstrated a very high prevalence of transfusion among critically ill patients on VV-ECMO to maintain a mean haemoglobin concentration at 9.1 g/dl. The impact of restricted transfusion and less mortality was demonstrated at a transfusion threshold of less than 7 g/dl[7]. In addition, ECMO decannulation may be associated with significant blood loss.

We described a challenging case of a JW who required prolonged extracorporeal lung support for COVID-19-induced severe ARDS. During treatment, there was a significant drop in his haemoglobin level, which was managed with no blood or blood product transfusion once the clinical team was made aware of the patient's faith. There are no guidelines for such complex cases[8]. JWs are a religious group that does not allow blood transfusion. Although some JWs would accept separate/some blood component transfusion, most would decline it, leading to clinical challenges in the management of JW patients[9]. To support a JW patient with ECMO, particularly during a pandemic, raises a multitude of clinical and ethical concerns due to the blood-consuming characteristic of ECMO, the patient's refusal of blood and blood components replacement, the scarcity of resources during pandemics and the need to ration ECMO for those most likely to benefit from it. Given the multiple transfusions often required during ECMO support, the refusal of transfusion by JW may be considered a relative contraindication for ECMO[9]. In addition, managing such patients on ECMO is challenging, and substantial evidence or consensus is lacking. However, the growing management experience, has improved equipment functionality, and adoption of blood conservation practice challenge this viewpoint[10]. Strict blood conservation strategy is required and repeated and routine laboratory investigations should be avoided. Paediatric collecting tubes and closed in-line systems allow for less blood loss. When appropriate, human recombinant EPO, intravenous iron, and supplementation with folate and vitamin B12 should be considered[10].

CONCLUSION

The management of JW patients who do not accept blood transfusion is challenging and requires an interprofessional approach, careful planning, and meticulous attention to detail to minimize blood loss and preserve the patient's blood. The widely accepted red blood cell transfusion threshold of 7g / dl may be challenged, and a lower haemoglobin and platelet target accepted on a case-by-case basis. The involvement of a haematologist is crucial in such complex cases. The concept of more permissive anaemia and hypoxia can be considered and tailored to individual patients. Experienced ECMO centres are ideally placed to provide better care for JW patients. It is crucial to establish what patient's wishes are and what they would (not) accept. Religious beliefs and refusal of blood transfusion should not be a contraindication to VV-ECMO.

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