INFORMATION BRIEF (RAPID REVIEW)

EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) FOR TREATMENT OF INFLUENZA A WITH MYOCARDITIS – AN UPDATE

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032/2020

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Rapid Review
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DISCLOSURE: The author of this report has no competing interest in this subject and the preparation of this report is entirely funded by the Ministry of Health Malaysia.

TITLE: EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) FOR TREATMENT OF INFLUENZA A WITH MYOCARDITIS – AN UPDATE

PURPOSE

To provide updated evidence on the use of extracorporeal membrane oxygenation (ECMO) for the treatment of influenza A with myocarditis following a request from the Director of Medical Practice Division, Ministry of Health Malaysia.

BACKGROUND

Influenza A is a type of seasonal influenza virus which are further classified to common subtypes A(H1N1) and A(H3N2) currently circulating in humans. Seasonal influenza epidemics lead to approximately 3-5 million cases of severe illness, and 290,000-650,000 respiratory deaths each year globally.[1] Myocarditis is a rare but life-threatening complication of influenza infection. The frequency of myocarditis secondary to seasonal influenza ranges from 0%-11%, depending on the diagnostic criteria; however, the prevalence of influenza A with myocarditis remains unclear.[2] The clinical severity of the influenza A infection ranges from asymptomatic to fulminant myocarditis. Myocarditis resulting in cardiogenic shock, a critical condition of haemodynamic instability with compromise of end-organ and tissue perfusion, requires extracorporeal membrane oxygenation (ECMO).[3] A review by Ukimura et al. (2012) on cases of myocarditis associated with the 2009 influenza A(H1N1) pandemic found that out of 58 patients (52% females; mean age 32 years), 12 (21%) required ECMO; mortality rate was 24%; and 36 (62%) had fulminant myocarditis with mortality rate of 39%.[4]

ECMO is a portable medication of cardiopulmonary bypass, providing mechanical circulatory support to critically ill patients with refractory cardiopulmonary failure for days to weeks, as a bridge to recovery or definitive treatment. Deoxygenated blood from the venous system is withdrawn by the closed ECMO circuit through one or multiple drainage cannulae, pumped through an oxygenator where gas exchange occurs, and returned to the venous (VV) or arterial (VA) circulation through a reinfusion cannula. The VV-ECMO provides support for the lungs; whereas VA-ECMO provides both haemodynamic and respiratory (heart and lungs) support.[3] According to the United States Food and Drug Administration (FDA), extracorporeal circuits and accessories for long-term respiratory/cardiopulmonary failure (>6 hours) are a system of devices and accessories regulated under 21 CFR 870.4100 (device class II with special controls) that provide assisted extracorporeal circulation and physiologic gas exchange of the patient's blood in patients with acute respiratory failure or acute cardiopulmonary failure, where other available treatment options have failed, and continued clinical deterioration is expected or the risk of death is imminent.[5]

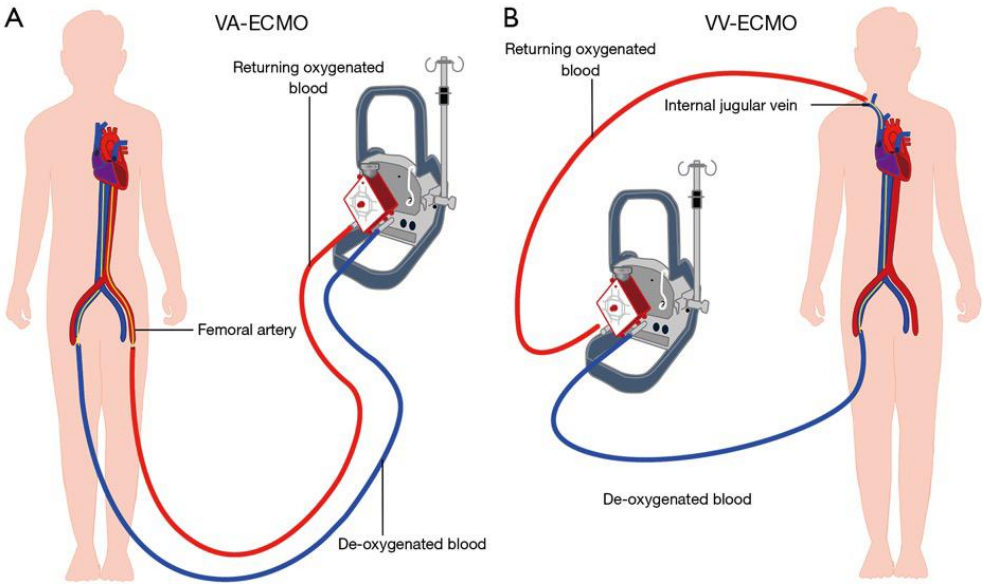

Figure 1: Extracorporeal Membrane Oxygenation (ECMO) system.
A) Veno-arterial (VA-) ECMO. B) Veno-venous (VV-) ECMO.[6]

EVIDENCE SUMMARY

A total of 205 titles were retrieved from scientific databases (Ovid Medline, EBM Reviews and PubMed) and general search engines (Google Scholar and FDA). Last search was conducted on 5th November 2020. The systematic search for evidence did not retrieve high level evidence that demonstrated the effectiveness of using ECMO specifically in cases of influenza A with myocarditis. However, 12 case reports (mean age 24.3 years) describing the use of ECMO in the management of H1N1-related myocarditis in six adult patients (4 females; 2 males) and six paediatric cases (4 females; 2 males) were identified.

EFFICACY/ EFFECTIVENESS

The use of ECMO was associated with successful management of H1N1-related myocarditis in five adult patients;[7-11] and five paediatric patients.[12-16] One adult case progressed to death while waiting for cardiac transplant with placement of ECMO following refractory cardiogenic shock.[17] One paediatric case progressed to death on third day of admission despite initiation of ECMO following refractory cardiogenic shock.[18] Early implantation of ECMO helped to ensure adequate peripheral perfusion, re-establish haemodynamic stability and promote recovery.[9] The ECMO functions as a bridge to recovery which can be weaned off upon recovery of heart function;[9-12,14] as well as a bridge to definitive treatment, permitting recovery of multi-organ injury and allowing time to complete a transplant evaluation before long-term circulatory support with an implantable LVAD or heart transplantation was considered.[7] Other than maintaining cardiac output and organ perfusion, ECMO minimised the need for inotropic support until myocardial recovery.[11] In a case of cardiac arrest refractory to prolonged cardiopulmonary resuscitation (CPR), the timely application of ECMO achieved sustained return of spontaneous circulation, which allowed further treatment, leading to good recovery with intact cerebral performance.[8]

SAFETY

Complications were reported in two adult cases[11,16] and four paediatric cases.[12-15] Montcriol et al. (2008) reported that anuric renal failure was observed during ECMO but renal functions recovered following 20 days of continuous veno-venous haemofiltration.[11] Subramanian et al. (2010) reported that the patient experienced an episode of severe pulmonary haemorrhage, necessitating reinstitution of high-frequency oscillatory ventilation.[16] Gross et al. (2011) described a case which was complicated by left lower extremity limb ischaemia, rhabdomyolysis, and acute renal failure that required continuous renal replacement therapy.[12] Kumar et al. (2011) reported that multilimb compartment syndrome occurred 24 hours following initiation of ECMO even though there were adequate systemic blood flow and lack of vascular obstruction from the ECMO cannulas. Despite multiple bilateral upper and lower limb fasciotomies, the patient continued to have ongoing significant rhabdomyolysis resulting in anuric acute renal failure which eventually improved at post-admission day 77, allowing cessation of haemodialysis.[13] Mohite et al. (2011) reported that left above knee amputation had to be performed due to continued deterioration of ischaemic left leg upon weaning of ECMO despite fasciotomy (following compartment syndrome three days after insertion of ECMO) and revision surgery.[14] Oda et al. (2010) found that spinal infarction occurred as a complication, likely due to chest compression during electrical storm, which might be avoided if cardiac function was not overestimated and VA-ECMO was applied instead of VV-ECMO as mechanical support in the beginning.[15] Other case reports observed recovery without any complications.[7-10]

COST / COST-EFFECTIVENESS

There was no retrievable evidence on cost-effectiveness of ECMO for the treatment of influenza A with myocarditis. However, a cost analysis was performed by Higgins et al. (2011) where the cost of ECMO was considered as one component of overall costs of care for patients with influenza A(H1N1) who were admitted to intensive care unit in Australia and New Zealand in 2009 (n=762; 7% required ECMO) using a "ground-up" costing method including supplies, labour and capital costs in a multicenter cohort study. The mean [standard deviation (SD)] additional cost of providing ECMO was AU$13,646 (AU$5,488) per patient. Treatment costs for patients who received ECMO were more than five times those who did not receive ECMO (ICU costs AU$160,735 vs AU$30,807, $p<0.001$).[19]

CONCLUSION

Based on the above review, there was limited evidence (case reports) to suggest the efficacy/effectiveness of ECMO for the treatment of influenza A with myocarditis. In terms of safety, few complications were reported. However, ECMO may be essential as a bridge to recovery or definitive treatment in critically ill patients with refractory cardiogenic shock due to myocarditis secondary to influenza A.

REFERENCES

1. World Health Organisation (WHO). Influenza (seasonal). [online] 2018. Available from: https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal) (Accessed 5 November 2020)
2. Mamas MA, Fraser D, Neyses L. Cardiovascular manifestations associated with influenza virus infection. Int J Cardiol. 2008;130(3):304-309.
3. Guglin M, Zucker MJ, Bazan VM, et al. Venoarterial ECMO for adults: JACC scientific expert panel. J Am Coll Cardio. 2019;73(6):698-716.
4. Ukimura A, Satomi H, Ooi Y, et al. Myocarditis associated with influenza A H1N1pdm2009. Influenza Res Treat. 2012.
5. United States Food and Drug Administration (FDA). CFR - Code of Federal Regulations Title 21, Volume 8 (21CFR870.4100). [online] 2019. Available from: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=870.4100 (Accessed 5 November 2020)
6. Pillai AK, Bhatti Z, Bosserman AJ, et al. Management of vascular complications of extra-corporeal membrane oxygenation. Cardiovasc Diagn Ther. 2018;8(3):372.
7. Cobas M, Abbo L, Santos M, Baccini-Jauregui C, Pham S. Successful management of fulminant influenza A subtype H1N1 myocarditis. BMJ case reports. 2010.
8. Chiu CW, Yen HH, Chiu CC, et al. Prolonged cardiac arrest: successful resuscitation with extracorporeal membrane oxygenation. Am J Emerg Med. 2013;31(11):1627.e5-1627.e6.
9. Jiménez-Méndez C, Díez-Villanueva P, Bastante T, et al. Venoarterial extracorporeal membrane oxygenation as a bridge to recovery in refractory cardiogenic shock secondary to fulminant influenza A myocarditis complicated with cardiac tamponade. Archivos de cardiología de México. 2020;90(2):216-218.
10. Liao YC, Hsieh YC, Chang WC, et al. Fulminant myocarditis in an adult with 2009 pandemic influenza A (H1N1 influenza) infection. J Chin Med Assoc. 2011;74(3):130-133.
11. Montcriol A, Wiramus S, Ribeiri A, et al. Successful management of Influenza A associated fulminant myocarditis: mobile circulatory support in intensive care unit: a case report. Cases journal. 2008;1(1):46.
12. Gross ER, Gander JW, Reichstein A, et al. Fulminant pH1N1-09 influenza-associated myocarditis in pediatric patients. Pediatr Crit Care Med. 2011;12(2):e99-e101.
13. Kumar K, Guirgis M, Zieroth S, et al. Influenza myocarditis and myositis: case presentation and review of the literature. Can J Cardiol. 2011;27(4):514-522.
14. Mohite PN, Popov AF, Bartsch A, et al. Successful treatment of novel H1N1 influenza related fulminant myocarditis with extracorporeal life support. J Cardiothorac Surg. 2011;6(1):164.
15. Oda T, Yasunaga H, Tsutsumi Y, et al. A child with influenza A (H1N1)-associated myocarditis rescued by extracorporeal membrane oxygenation. J Artif Organs. 2010;13(4):232-234.
16. Subramanian S, Clark JD, Jeffries HE, et al. Novel pH1N1 viral cardiomyopathy requiring veno-venous extracorporeal membrane oxygenation. Pediatr Crit Care Med. 2010;11(6):714-717.
17. Hamoudi A, Vais D, Taqi V. H1N1 Influenza Causing Fulminant Myocarditis Requiring Extracorporeal Membrane Oxygenation. Cureus. 2019;11(5):e4665.
18. Demir SÖ, Atıcı S, Kadayifci EK, et al. Influenza A (H1N1)-associated severe complications; hemolytic uremic syndrome, myocarditis, acute necrotizing encephalopathy. J. Infect. Dev. Ctries. 2019;13(01):83-86.
19. Higgins AM, Pettilä V, Harris AH, et al. The critical care costs of the influenza A/H1N1 2009 pandemic in Australia and New Zealand. Anaesth Intensive Care. 2011;39(3):384-391.

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10 November 2020