


Blood component use in critical care in patients with COVID-19 infection: a single-centre experience

Andrew J. Doyle,¹  Anicee Danaee,¹
Charlene I. Furtado,¹ Scott Miller,¹
Tim Maggs,² Susan E. Robinson¹ and
Andrew Retter³

¹Department of Clinical Haematology, NHS Foundation Trust, Guy's and St Thomas, ²Viapath Analytics LLP, St Thomas Hospital, and ³Department of Critical Care, NHS Foundation Trust, Guy's and St Thomas, London, UK

Received 13 May 2020; accepted for publication 25 May 2020

Correspondence: Dr Andrew Retter, Department of Critical Care, 1st Floor East Wing, St Thomas' Hospital, Westminster Bridge Road, London SE1 7EH, UK.
E-mail: Andrew.Retter@gstt.nhs.uk

Summary

There has been a significant surge in admissions to critical care during the coronavirus disease 2019 (COVID-19) pandemic. At present, the demands on blood components have not been described. We reviewed their use during the first 6 weeks of the outbreak from 3 March 2020 in a tertiary-level critical care department providing venovenous extracorporeal membrane oxygenation (vv-ECMO). A total of 265 patients were reviewed, with 235 not requiring ECMO and 30 requiring vv-ECMO. In total, 50 patients required blood components during their critical care admission. Red cell concentrates were the most frequently transfused component in COVID-19-infected patients with higher rates of use during vv-ECMO. The use of fresh frozen plasma, cryoprecipitate and platelet transfusions was low in a period prior to the use of convalescent plasma.

Keywords: COVID-19, transfusion, critical care, bleeding.

Since the outbreak of the coronavirus disease 2019 (COVID-19) pandemic, there has been a surge in admissions to intensive care departments. At present it has not been described whether there is an increased blood component requirement in patients with COVID-19 infection. Coagulopathy is present in 20–55% of cases and is related to disease severity and worse survival outcomes.¹ Prothrombotic markers, such as fibrinogen and D-dimer, are increased with COVID-19 infection, with an absence of significant rates of disseminated intravascular coagulation (DIC), but higher incidence of thrombosis.^{2,3}

Restrictive transfusion practice of red blood cells in critical care and extracorporeal membrane oxygenation (ECMO) has similar survival outcomes to liberal transfusion practice.^{4–6} There is concern that COVID-19 infection disproportionately affects the Black, Asian and Minority Ethnic (BAME) population.⁷ Blood group disparity between donors and recipients in the UK, particularly from different ethnic groups affected by COVID-19, may therefore be a potential issue.⁸

Our centre provides extensive regional critical care facilities including venovenous ECMO (vv-ECMO). Patients requiring ECMO have increased use of blood components particularly if they bleed.^{4,9} In anticipation of increased hospitalisations and a decline in blood donation due to social distancing measures, elective major surgery has largely been postponed in accordance with nationwide policy. In the

present study, we aimed to evaluate the current blood product usage, the demographics of those requiring blood components and their requirements and indications.

Patients and methods

A prospective database of patients with COVID-19 infection admitted to critical care was reviewed to identify appropriate patients. Dates of inclusion were from 3 March 2020 to 14 April 2020 inclusive. Blood traceability is maintained on WinPath Laboratory Integrated Management System (Chertsey, UK) with transfused blood components identified from this during critical care admissions. Blood components included were red cell concentrate (RCC), platelets, fresh frozen plasma (FFP) and cryoprecipitate. Blood groups were identified from the iSOFT Clinical Manager Electronic Patient Records software (Sydney, Australia). Data were screened on 21 April 2020. Indications for blood component transfusion were evaluated against the National Blood Transfusion Committee (NBTC) Indication Code for Transfusion (June 2016). As transfusion during ECMO is not included in the NBTC policy, a RCC transfusion trigger of haemoglobin <80 g/l is adopted locally. All patients received weight- and renal function dose-adjusted chemical thromboprophylaxis, unless actively bleeding or required therapeutic anticoagulation.

Table I. Clinical characteristics of patients with COVID-19 infections requiring critical care support who required blood components.

Clinical feature	All patients N = 50	Not requiring ECMO n = 33	Requiring vv-ECMO n = 17
Age, years, median (range)	53 (26–85)	53 (26–85)	52 (34–66)
Gender, n male (%)	32 (64)	21 (63.6)	11 (36.7)
Died in Critical Care, n (%)	19 (38)	13 (39.4)	6 (35.3)
Ethnicity, n (%)			
White	13 (26)	6	7
Black	21 (42)	17	4
Asian	11 (22)	7	4
Mixed	1 (2)	0	1
Not specified	4 (8)	3	1
Therapeutic anticoagulation, n (%)	12 (24)	9 (27.2)	3 (17.6)
Fibrinolytic agents, n	0	0	0
Red cell antibodies, n	6*	2	4
Platelet antibodies, n	0	0	0
Special requirements, n	2	2†	0
ABO and Rh D Group, n (%)			
O and R&D+/R&D–	25/2 (54)	21/0	4/2
A and R&D+/R&D–	13/1 (28)	6/1	7/0
B and R&D+/R&D–	7/2 (18)	3/2	4/0
AB and R&D+/AB R&D–	0/0	0/0	0/0

*All red cell antibodies detected were non-specific IgG antibodies with no allo-antibodies detected.

†For exchange transfusion in patients with sickle cell disease.

Results

A total of 265 patients were identified for review in the above time period; 30 required the use of vv-ECMO and 235 were admitted to critical care but did not require ECMO support. In all, 17 patients (56.7%) requiring ECMO used blood components in comparison to 33 patients (14.0%) not requiring ECMO. The clinical and transfusion details of patients requiring blood components during critical care admission with COVID-19 infection are shown in Table I.

In total, the blood component use over this 6-week period included 204 RCC, 23 platelets, 24 FFP and 10 cryoprecipitate (0.77, 0.09, 0.09 and 0.04 units per patient admission respectively). Of all the patients in critical care with COVID-19 infection, 52 (19.6%) required ≥ 1 unit RCC transfusion, eight (3.0%) required ≥ 1 unit platelets, five (1.9%) required ≥ 1 unit FFP and five (1.9%) required ≥ 1 pooled unit of cryoprecipitate. Table II compares the blood component use by patients requiring ECMO to those who did not. Convalescent plasma was not available at our Centre during the period of review.

The NBTC indications for the blood component transfusions given over the time period are shown in Table III. RCC was the predominant blood component used. There was low use of platelets, FFP and cryoprecipitate in both ECMO and non-ECMO patients. There were three episodes of non-intracranial major haemorrhages (6% of transfused patients and 1% of all patients). There was a mean use of 11 units RCC, 4 units FFP and 0.3 pooled unit

Table II. Comparison of the number of patients with COVID-19 infection transfused with blood components and the number of units in critical care with and without ECMO.

Blood component	No. of ECMO patients using blood component (%) [median use, range]	No. of non-ECMO patients using blood component (%) [median used, range]
RCC	15 (50) [0.5, 0–23]	33 (14) [0, 0–9]
Platelets	3 (10) [0, 0–3]	5 (2) [0, 0–9]
FFP	3 (10) [0, 0–10]	2 (1) [0, 0–5]
Cryoprecipitate	4 (13) [0, 0–2]	1 (<1) [0, 0–2]

cryoprecipitate in these patients during the bleeding episodes with no platelets transfused. Two episodes of exchange transfusion occurred for patients with sickle cell disease (each requiring 8 units RCC). The highest utilisation of platelets was in a patient with acute myeloblastic leukaemia who remained severely thrombocytopenic with sepsis following induction chemotherapy (9 units used).

Discussion

Despite the increased demands of healthcare resources at the time of the COVID-19 pandemic, it appears that the infection itself does not cause a significant increase in blood component use in comparison to previous data from critical care.¹¹ There was a lack of other blood requirements or presence of allo-antibodies in this cohort. There was a

Table III. Indications for transfusion of each blood component in patients with COVID-19 infection in critical care with and without vv-ECMO.

Blood component	No. of units transfused to vv-ECMO patients (<i>n</i> = 33)	No. of units transfused to non-ECMO patients (<i>n</i> = 17)
RCC	95	109
R1 – Acute bleeding	33	12
R2 – Hb ≤70 g/l stable patient	11	55
R3 – Hb ≤80 g/l if CVD	51	26
R6 – Exchange transfusion	0	16
Plt	8	15
P2 – Plt <10–20 × 10 ⁹ /l sepsis	0	9
P3a – Plt <20 × 10 ⁹ /l CVC insertion	0	1
P4a – Major haemorrhage plt <50 × 10 ⁹ /l	3	2
P5a – DIC pre-procedure or bleeding	5	3
FFP	16	8
F1 – Major haemorrhage	14	0
F2 – INR >1.5 with bleeding	0	8
F3 – INR >1.5 pre-procedure	2	0
Cryoprecipitate	8	2
C1 – Significant bleeding and fibrinogen <1.5 g/l	8	2

Hb, haemoglobin; CVD, cardiovascular disease; Plt, platelets; CVC, central venous catheter; DIC, disseminated intravascular coagulation; INR, international normalised ratio.

predominance of BAME patients being treated in comparison to the donor population of the UK, reflected in a higher than expected number of patients with blood group B. There were low rates of major haemorrhage over the period, confined to patients requiring ECMO. As described previously, the use of ECMO showed higher but similar levels of RCC usage, previously estimated at 0.44–0.66 units/day at our Centre.⁴ This is in comparison 0.46 units/day in patients not requiring ECMO in critical care prior to the COVID-19 outbreak.¹¹

The predominant blood component used was RCC in both patients requiring ECMO and those not requiring ECMO. The most common indications for their transfusion were for maintenance of haemoglobin targets (NBTC Codes R2 and R3) comprising of 64.6% and 73.8% respectively. Preliminary data from China suggest that anaemia is more prevalent in those with COVID-19 requiring critical care, with a progressive fall in haemoglobin over admission.¹² Although the mechanism of this remains unclear at present, iron dysregulation due to inflammation may be a potential cause. Alternative options to RCC transfusion to optimise

patient blood management can be considered, such as intravenous iron and recombinant erythropoietin, but their roles in critical care are not well established.^{13,14} Concern of the increased thrombotic rates and inflammatory states in COVID-19 infection in this setting may preclude their widespread use.^{1–3,15}

The use of platelet, FFP and cryoprecipitate transfusions remains low with COVID-19 infection in those who have not had episodes of major haemorrhage. Elevated levels of fibrinogen, factor VIII and platelets are demonstrated in critical illness in COVID-19 infection suggestive of why transfusion triggers for these components were not met in the present patient cohort.^{1,15} Given the prothrombotic tendency of COVID-19 infection, unnecessary transfusion of plasma components should be avoided in the absence of bleeding.

A significant decline in blood donation has been shown in China, although initial concerns of this in the UK have been offset by a fall in transfusion rates.^{16,17} Our present results suggest that blood component usage as a result of COVID-19 infection remains low, with a higher usage in ECMO. Optimisation of patient blood management in the critical care setting is one consideration to assist with potential shortages of blood component provision in the next few months.

Acknowledgements

We would like to acknowledge the dedication of the Critical Care Department at Guy's and St Thomas' NHS Foundation Trust during this period.

Funding information

No funding was required for this study.

Conflict of interest

All authors declare no conflict of interest.

Author contributions

Andrew J. Doyle designed the research study, performed the research, analysed the data and wrote the paper. Anicee Danaee designed the research study, analysed the data and wrote the paper. Charlene I. Furtado performed the research and reviewed the final submission. Scott Miller performed the research and reviewed the final submission. Tim Maggs analysed the data and reviewed the final submission. Susan E. Robinson designed the research study, analysed the data and wrote the paper. Andrew Retter designed the research study, analysed the data and wrote the paper.

References

- Lee SG, Fralick M, Sholzberg M. Coagulopathy associated with COVID-19. *CMAJ*. 2020;192:E583.

2. Klok, FA, Kruip, MJ, Van der Meer, NJ, Arbous, MS, Gommers, DA, Kant, KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res.* 2020;**191**:145–7.
3. Yin S, Huang M, Li D, Tang N. Difference of coagulation features between severe pneumonia induced by SARS-CoV2 and non-SARS-CoV2. *J Thromb Thrombolysis.* 2020 [Epub ahead of print]. <https://doi.org/10.1007/s11239-020-02105-8>
4. Doyle AJ, Richardson C, Sanderson B, Wong K, Wyncoll D, Camporota L. Restrictive transfusion practice in adults receiving venovenous extracorporeal membrane oxygenation. *Crit Care Explor.* 2020;**2**:e0077.
5. Hébert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. *N Engl J Med.* 1999;**340**:409–17.
6. Klein HG. Should blood be an essential medicine? *N Engl J Med.* 2013;**368**:199–201.
7. Laurencin CT, McClinton A. The COVID-19 pandemic: a call to action to identify and address racial and ethnic disparities. *J Racial Ethn Health Disparities.* 2020;**7**:398–402.
8. Lattimore S, Wickenden C, Brailsford SR. Blood donors in England and North Wales: demography and patterns of donation. *Transfusion.* 2015;**55**:91–9.
9. Agerstrand CL, Burkart KM, Abrams DC, Bacchetta MD, Brodie D. Blood conservation in extracorporeal membrane oxygenation for acute respiratory distress syndrome. *Ann Thorac Surg.* 2015;**99**:590–5.
10. Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC). National Blood Transfusion Committee (NBTC) indication codes June 2016v2. Available at: <https://www.transfusionsguidelines.org/document-library/documents/nb-tc-indication-codes-june-2016v2>. Accessed 2 May 2020.
11. Chohan SS, McArdle F, McClelland DB, Mackenzie SJ, Walsh TS. Red cell transfusion practice following the transfusion requirements in critical care (TRICC) study: prospective observational cohort study in a large UK intensive care unit. *Vox Sang.* 2003;**84**:211–8.
12. Sun S, Cai X, Wang H, He G, Lin Y, Lu B, et al. Abnormalities of peripheral blood system in patients with COVID-19 in Wenzhou, China. *Clin Chim Acta.* 2020;**507**:174–80.
13. Baron DM, Franchini M, Goobie SM, Javidrooz M, Klein AA, Lasocki S. Patient blood management during the COVID-19 pandemic: a narrative review. *Anaesthesia.* 2020;**75**:1105–13.
14. Litton E, Baker S, Erber WN, Farmer S, Ferrier J, French C. Intravenous iron or placebo for anaemia in intensive care: the IRONMAN multicentre randomized blinded trial: a randomized trial of IV iron in critical illness. *Intensive Care Med.* 2016;**42**:1715–22.
15. Panigada M, Bottino N, Tagliabue P, Grasselli G, Novembrino C, Chantarangkul Vea. Hypercoagulability of COVID-19 patients in intensive care unit: a report of thromboelastography findings and other parameters of hemostasis. *J Thromb Haemost.* 2020;**18**:1738–42.
16. NHS Blood and Transplant COVID-19 updates. Available at: <https://nhsbt.dbe.blob.core.windows.net/umbraco-assets-corp/18120/nhsbt-situation-update-26-march-2020-coronavirus-covid-19.pdf>. Accessed 2 May 2020.
17. Wang Y, Han W, Pan L, Wang C, Liu Y, Hu Wea. Impact of COVID-19 on blood centres in Zhejiang province China. *Vox Sang.* 2020;**115**(6): 502–6.