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Guidance

Proposal to allow recipients of convalescent plasma for treatment of infection with SARS-CoV-2 to donate plasma for treatment of SARS-CoV-2 infected individuals

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Contents

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1. Brief summary

Currently, individuals who have received a transfusion of blood or blood components since January 1980 are not allowed to donate as a risk reduction measure for vCJD. The UK blood services are about to begin collection of plasma donations from individuals recovering from COVID-19 for clinical trials. Convalescent plasma (CP) donations will be collected 28 days post recovery from individuals with a previous laboratory confirmed SARS-CoV-2 infection. If treatment with convalescent plasma is successful it is likely that many individuals treated for SARS-CoV-2 will receive CP. Once recovered, if these individuals cannot donate this may create a chronic shortage of CP donors. It is proposed that these individuals be allowed to donate CP plasma for further treatment of individuals with SARS-CoV-2 infection.

This would be a temporary measure, restricted to donation of plasma from individuals recovering from SARS-CoV-2 infection and will be reviewed in 6 months.

2. Proposal

NHS Blood and Transplant and other UK Blood Services are preparing to collect convalescent plasma (CP) from individuals recovered from infection with SARS-CoV-2. CP will be collected 28 days post recovery from individuals with a previous laboratory confirmed SARS-CoV-2 infection.

Trials for CP are due to start later this month. It is likely that the best donors (for example, those with the highest levels of neutralising antibody) are those who have been sickest and therefore those admitted to hospital and more likely to have been in receipt of CP. If the trials were to be successful, then there will be a dwindling number of suitable donors of CP unless the current restriction on blood donors who have previously received blood or a blood component since 1980 being allowed to donate as a risk reduction measure for vCJD is lifted.

Trial participants could receive up to 2 units of plasma from different donors (units would not be pooled). The majority of units will be collected by plasmapheresis, some by whole blood donation although the red cells would not be issued for clinical use. Also, plasma with a lower titre of neutralizing antibody could be offered to BPL for manufacture of a hyperimmune globulin (this measure is subject to approval of the Commission on Human Medicine) or considered for use as standard fresh frozen plasma. Donors with high levels of neutralizing antibody may give further donations

The recent risk assessment for vCJD transmission risk by plasma carried out by the Advisory Group for Dangerous Pathogens suggests that the transmission risk from plasma is low with an estimated 6 cases of vCJD over the next 50 years [1].

The SaBTO paediatric components group looked at the additional risk of stopping importation of around 110,000 units of plasma each year as a risk reduction measure for vCJD for individuals born after 1995. The additional vCJD risk was 1 to 2 cases of vCJD over the next 50 years [2].

It could be argued that, as trials for treatment of COVID-19 patients with convalescent plasma could reach a similar magnitude to the additional 110,000 units of plasma sourced from UK donors, the vCJD transmission risk to recipients would be similar. As CP treatment is expected to a short-term measure then the baseline risk would be very small. This argument comes with many caveats such as the potential opportunity for multiple exposure resulting from recipients of plasma having received CP from donors who may themselves have received CP and

so on. Each recipient could receive up to 2 donations. Also, donors with high levels of neutralizing antibodies could provide several donations. The true additional risk would need further modelling work although anticipated to remain very small. If CP treatment is successful, the benefit to patients would far outweigh this additional risk.

The proposal is that recipients of CP plasma be allowed to donate plasma for treatment of COVID-19 as the additional vCJD transmission risk from these individuals would remain low and be balanced against the considerable benefit to individuals who require CP to aid their recovery from COVID-19.

This would be a temporary measure and restricted to CP donations from individuals who have recovered from SARS-CoV-2 infection. The measure will be reviewed by SaBTO in 6 months.

After donation(s), it is proposed that individuals will then be deferred from future donation of blood or blood components for routine use. This would be consistent with the existing vCJD risk reduction measure deferring recipients of blood and or blood components since January 1980 for non-CP donors. However, if CP is widely used this could result in donor insufficiency so SaBTO may have to consider either a further derogation or removal of the deferral for all donors at some future stage.

3. Background

Variant Creutzfeldt-Jakob disease (vCJD) is an incurable neurodegenerative disease, part of a group of diseases which can affect humans and other animals known as Transmissible Spongiform Encephalopathies (TSEs) or prion diseases. vCJD arose for the consumption of meat from cattle infected with Bovine Spongiform Encephalopathy (BSE). Stringent measures were put in place to remove BSE from the food supply by the end of 1995. There have been 178 deaths in the UK from vCJD, the last case was in 2016. However, based on evidence from other prion diseases, vCJD could have a very long incubation period in some individuals, possibly lasting decades.

Following the first documented case of transmission of vCJD from blood in 2004 the Committee on the Microbiological Safety of Blood & Tissues (MSBT) made recommendations to the Department of Health to reduce the risk of transmission of vCJD from blood or blood component donation. This included the exclusion from donation of anyone who had previously received a blood transfusion anywhere in the world after 1 January 1980. This measure was later extended to previously transfused apheresis donors and donors who were unsure if they had received a blood donation.

The permanent deferral of these individuals was, and still is, an important part of management of vCJD. After, the removal of BSE from the human food chain, the most likely route of serial transmission of vCJD is blood transfusion.

To date, there have been 4 documented cases of transmission of the infectious agent that causes vCJD, 3 resulting in disease. The last case was in 2006. All recipients had received non-leucoreduced red cells; leucoreduction was introduced in 1999 as a risk-reduction measure for vCJD based on data from animal studies that suggested that the white cells contained the highest levels of the infectious agent.

A significant problem with preventing transmission of vCJD from blood donation is the lack of routine diagnostic assays with sufficient sensitivity to detect the very low levels of vCJD prion in blood. Assays which can detect vCJD prion in blood have been recently developed but require specialised laboratories and take too long to complete for routine use. These assays can detect prion in all components, including plasma from individuals with clinical vCJD [3] [4] and one group has detected prion in plasma from 2 individuals who were asymptomatic at the time of donation [3]. Studies on primates have detected vCJD prion in plasma well before the clinical phase [5] [6].

These studies show that plasma donation cannot be excluded as a vCJD transmission risk. It should be noted however, that all plasma samples reactive for vCJD prion had not been leucoreduced so the impact of this measure is not known.

The Advisory Committee on Dangerous Pathogens (ACDP) have conducted periodic risk assessments on the transmission risk of vCJD from blood. Early risk assessments had estimated that there was a significant transmission risk from blood but subsequent assessments have consistently revised downwards the risk as the number of cases has been lower than anticipated and with improved understanding of the disease progression and experimental studies. The last risk assessment, published in 2019, specifically included the transmission risk from plasma donation. Based on current plasma use in the UK, the assessment indicated there could be 6 cases of vCJD (0-31 95%CI) from plasma transfusion over the next 50 years[1].

It should be noted that the ACDP risk assessment makes assumptions about the population prevalence of vCJD derived from immunohistochemical analysis of appendix samples. The latest appendix study has recently been published [5]. All the appendix studies indicate a UK population of 1:2-4000 per million individuals with the potential to transmit vCJD. However, this does not appear to reflect clinical cases of vCJD so the risk assessment may be very conservative.

The UK blood services are anticipating collecting around 100,000 units of CP per year for treatment of SARS CoV-2 infected individuals. Transfusions on this scale would only be anticipated if CP is a successful treatment. The ACDP risk assessment looked at the vCJD transmission risk for plasma based on current use, so an increase of plasma use in the UK would increase the vCJD transmission risk. The SaBTO paediatric components working group looked at the additional risk of stopping importation of plasma for individuals born on or after 1 January 1996. Using the ACDP risk assessment, they estimated the additional risk, based on stopping importation of 110,000 units of plasma each year, could result in an additional 1 to 2 cases (0-6 95%CI) of vCJD over the next 50 years[2].

As the SaBTO modelling work was conducted on a similar number of units as anticipated for CP use, the model could be used to provide a baseline risk for CP treatment. However, there would be an additional risk for using CP donors who had received CP if they became serial CP donors (those with high levels of neutralizing antibody). Additionally, it is possibly that a chain of supply may become established where recipients of CP donate to recipients of CP who then, themselves donate and so on multiplying transmission risk. Without further consideration of these factors it would be important to restrict the use of CP donation to restricted to CP use where there would be a significant benefit to recipients compared to the increased vCJD risk.

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