Supply with Platelet Concentrates from the Point of View of a Blood Donation Service of the Bavarian Red Cross

Franz Weinauer

Blutspendedienst des Bayerischen Roten Kreuzes, Institut München, Germany

Key Words

Apheresis platelets · Buffy coat platelets · Pooled platelets

Summary

Background: It is known that pooled platelet concentrates derived from buffy coat (PCs) have several disadvantages compared to platelet concentrates produced by platelet apheresis (APCs). Therefore, all blood products issued by the Bavarian Red Cross blood banks (BSD/BRK) (18,000 products/year) were produced by single donor apheresis. The main reason not to produce PCs was the elevated viral and bacterial infection risk during the last decade. But also the four-fold increased exposition to HLA and PLA antigens and the poor quality (in the sense of white and red cell contamination) of PCs (especially the ones produced with the platelet-rich plasma method) played a role to abstain from these products. **Material and Methods:** We performed a risk assessment to evaluate both products with regard to the actual testing and production methods, considering recently published data. However, a statistical calculation of the risks associated with the use of PCs or APCs with regard to different infectious agents with various prevalences was not done. **Results:** The dramatically reduced risk for the transmission of HIV, HBV or HCV accompanying the implementation of improved antibody tests and of NAT minipool testing, the introduction of 100% leukocyte filtration, the conversion of PC production from the platelet-rich to the buffy coat method, and recent data on the risk of transmission of bacterial infections resulted in a equal assessment of APCs and PCs. **Conclusion:** As a consequence of this revised risk assessment, we supply our hospitals with both products APCs and buffy coat-derived PCs (pools of 4 donors). For clinical use we considered both products as equally effective, except for patients who have multiple antibodies and need HLA-typed platelets.

Schlüsselwörter

Zellseparator-Thrombozytenkonzentrate · Buffy-coat-Thrombozytenkonzentrate · Gepoolte Thrombozytenkonzentrate

Zusammenfassung

Hintergrund: Der Blutspendedienst des Bayerischen Roten Kreuzes (BSD des BRK) hat aus Gründen der Produktqualität in der Vergangenheit den Bedarf an Thrombozytenkonzentraten (zirka 18 000 Einheiten/Jahr) zu 100% mit apheretisch gewonnenen Produkten gedeckt. Der Hauptgrund, keine gepoolten Thrombozytenkonzentrate (Pool-TK) zu benutzen, war in den 1990er Jahren das erhöhte Risiko der bakteriellen und viralen Kontamination des Endprodukts. Daneben spielte die vierfache Antigenexposition und die im Vergleich zu den maschinell hergestellten Produkten vielfach erhöhte Leukozyten- und Erythrozytenkontamination (besonders bei der Herstellung mit der Methode aus plättchenreichem Plasma) eine bedeutende Rolle. **Material und Methoden:** An unserem Institut wurde eine aktualisierte Risikobewertung zum Einsatz der beiden Produktlinien anhand der für die Produktqualität maßgebenden Parameter durchgeführt. Es erfolgte allerdings keine statistische Berechnung der produkttypspezifischen Risiken, die von verschiedenen infektiösen Agenzien mit unterschiedlicher Prävalenz ausgehen. **Ergebnisse:** Der dramatische Rückgang des Übertragungsrisikos für HIV, HBV und HCV durch die Einführung neuer bzw. verbesserter Antikörpertests und besonders der PCR-Testung, die Durchführung der 100%igen Leukozytenfiltration, die Umstellung der Pool-TK-Herstellung von der PRP (Gewinnung aus plättchenreichem Plasma)-Methode auf die Buffy-coat-Methode und nicht zuletzt neuere Daten zum Risiko der Übertragung bakterieller Infektionen führten in unserer aktualisierten Risikobewertung zu einer Gleichbewertung der beiden Produkte. **Schlussfolgerung:** Als Konsequenz aus der geänderten Risikobewertung werden beim BSD des BRK seit Ende 2006 neben Zellseparator-Einzelpreparaten auch Buffy-coat-Pool-TK hergestellt und vertrieben. Für den klinischen Einsatz sehen wir beide Produkte als gleichwertig an, mit Ausnahme der Versorgung refraktärer Patienten, die eine Versorgung mit HLA-typisierten Produkten benötigen.

Introduction

In the past it was demonstrated that pooled platelet concentrates derived from buffy coat (PCs) have several disadvantages compared to platelet concentrates produced by plateletpheresis (APCs) [1]. The main disadvantage of pooled products was the elevated bacterial [2] and viral infection risk in the last decade. The four-fold increased risk of transmitting viral diseases was generally accepted, but never demonstrated in a risk calculation, taking into consideration different prevalences of the different infectious agents. The four-fold increased exposition to HLA and PLA antigens and the poor quality (in the sense of white and red cell contamination) of pooled products (especially the ones produced with the platelet-rich plasma method) led to a higher alloimmunization risk [3].

Recently the risk of transmitting the variant Creutzfeld-Jacob disease (vCJD) was another reason to avoid pooled products because of a suspected four-fold risk of transmitting the disease.

Material and Methods

In the blood donation service of the Bavarian Red Cross (BSD/BRK), we performed a risk assessment taking into consideration the different aspects influencing the outcomes of platelet transfusions of both products. However, a statistical calculation of the risks associated with the use of PCs or APCs with regard to different infectious agents with various prevalences was not done.

Results

The risk of transmitting HIV, HBV or HCV by transfusion of blood products was dramatically decreased by the implementation of NAT testing, and only a few cases in which viral transmission by transfusion occurred were observed in Germany since then [4].

In general the risk of transmitting an infectious agent is dependent on

- the incidence of missing a positive result (window period),
- the frequency of donations during the window period,
- the number of components transfused, and
- the size of the pool and the number of patients receiving products out of the pool.

Thus, an infectious agent with a very high prevalence and incidence (for example 1 in several hundreds, as it was in case in non-A/non-B hepatitis) would cause a four-fold risk for the recipient when giving PCs if there is no test available to detect the infection. At the moment such a transfusion-relevant and not reliably detectable infectious agent is not known within our donor population so that this is a only theoretical risk.

At a modest risk of e.g. <1 in 0.8 million, as in hepatitis B [4], it cannot be easily defined whether the residual risk of transmit-

ting HBV is higher with PCs or with APCs. The outcome of this risk assessment is predominantly affected

- by the question if pooling is relevant as there is still only 1 recipient (and therefore not comparable to elevated risk caused by agents in plasma pools) or
- by the influence of possible late seroconversion (median 45 days with mini-pool NAT [4]) and repeated donations during that period of time.

In the case of very low infection risks as in HIV or HCV infections (residual risk for HIV or HCV transmission <1 in 4.5 million [4], causing at maximum one case of transfusion-transmitted infection per year in Germany), it seems to be obvious: Pooling the one positive product with 3 negative ones still results in one PC causing viral transmission (augmented by the risk of a second transmission caused by the packed RBC if RBC and PC recipient are not the same person); in the manufacturing of APCs usually 2 APCs are produced in one apheresis procedure, thus resulting also in 2 viral transmissions (if the recipient of both products is not the same person).

In the case of very low (HCV, HIV) or even extremely low prevalence (vCJD) it must be considered what would happen if a donor would be infected with an agent having a very long incubation period, which is not detectable by testing. The repeated donation of regular apheresis donors who donate approximately 12 times per year in the BSD/BRK, would turn into a very risky procedure as considerations to the vCJD risk demonstrate: In APCs regular donations of an infected person could result in as much as 168 infected recipients (12 donations with 2 products each per year $\times$ 6–8 years (incubation phase)) if a regular APC donor is infected.

Even if we still do not have exact mathematical calculations, it seems to be obvious that there is no additional risk on the side of PCs.

During PC production it is not very likely that a donation of an infected PC donor will be repeatedly used in PC production because the median whole blood donation rate/year in Bavarian donors is 2.1 donations per year, and less than 14% of whole blood donors would suffice for PC production (out of a total of 520,000 whole blood units per year, 68,000 whole blood-derived buffy coats would be needed if 100% of the platelet concentrates produced by the BSD/BRK (18,000 PC products) would be covered by PC production.

Summarizing these results, there seems to be no difference between both products with regard to the risk of transmitting virus or prion diseases.

A large prospective multicenter study performed by the German Red Cross blood banks recently demonstrated that there is no difference with respect to the bacterial contamination risk of both types of platelet concentrates [5]. Thus, there is no reason to avoid use buffy coat-derived platelet concentrates for this reason.

Another argument not to use PCs is the risk of alloimmunization. However, after switching from the platelet-rich plasma

method to buffy coat-derived platelet concentrates which showed a better product quality in the sense of residual red cell and white cell contamination, and finally after the introduction of 100% leukodepleted products, there is no clinical demonstrable difference in the transfusion outcome [6, 7] between APCs and PCs.

When deciding between these two products, finally the following 'minor disadvantages' has to be taken into consideration:

APCs

- ABO compatible products not always available,
- additional donors needed and exposed to extracorporeal circuit,
- functional impaired platelets (induced by drugs or platelet disorders) may result in poor clinical outcome [8],
- increased risk of TRALI (if not female donors and donors which ever have received transfusion are excluded or tested against TRALI-causing antibodies),
- limited availability of donors,
- higher production costs (at least in our setting).

PCs

- CMV/Rh-negative products difficult to obtain,
- HLA-matched products not available,
- testing for functionally impaired platelets not feasible (but

on the other hand only 25% of the platelets of one product would likely to be impaired),

- packed red cells have a lower content of red cells due to the preparation of the buffy coat.

Conclusion

There are no evidence based data to make a decision on the inferiority of PCs or APCs in the clinical setting or with respect to the infection risk. To supply the needs of the patients both products are needed.

The only reason to exclusively use APCs in our view is that multisensitized patients need HLA-matched platelets.

Taken all these facts together, we decided to switch from 100% use of APCs to the use of both products (APCs and PCs), depending on the demands of the hospitals, except for patients who have multiple antibodies and need HLA-typed platelets. This is also in accordance with the recommendations of the German Platelet Working Group [9].

As no calculation is available on the influence of the infection risks of pooling vs. window period donations of the two products, a statistical calculation should be performed how the risk to be infected with a certain known or so far unknown infectious agent is influenced by its prevalence and window period and how the decision between APCs and PCs affect this risk.

References

- 1 Strindberg J, Berlin G: Transfusion of platelet concentrates – clinical evaluation of two preparations. *Eur J Haematol* 1996;57:307–311.
- 2 Ness P, Braine H, King K, Barraso C, Kickler T, Fuller A, Blades N: Single-donor platelets reduce the risk of septic platelet transfusion reactions. *Transfusion* 2001;41:857–861.
- 3 Williamson LM, Stainsby D, Jones H, Love E, Chapman CE, Navarrete C, Lucas G, Beatty C, Casbard A, Cohen H: The impact of universal leukodepletion of the blood supply on hemovigilance reports of posttransfusion purpura and transfusion-associated graft-versus-host disease. *Transfusion* 2007;47:1455–1467.
- 4 Offergeld R, Ritter S, Hamouda O: The risk of transfusion transmitted infections – current aspects. *Transfus Med Hemother* 2006;33:130–134.
- 5 Schrezenmeier H, Walther-Wenke G, Müller TH, Weinauer F, Junis A, Holland-Letz T, Geis G, Asmus J, Bauerfeind U, Burkhart J, Deitenbeck R, Förstemann E, Gebauer W, Höchsmann B, Karakassopoulos A, Liebscher U-M, Sängler W, Schmidt M, Schunter F, Sireis W, Seifried E: Bacterial contamination of platelet concentrates: results of a prospective multicenter study comparing pooled whole blood-derived platelets and apheresis platelets. *Transfusion* 2007;47:644–652.
- 6 Akkök CA, Brich L, Lauritzen GF, Solheim BG, Kjeldsen-Krah J: Clinical effect of buffy coat vs. apheresis platelet concentrates in patients with severe thrombocytopenia after intensive chemotherapy. *Vox Sang* 2007;93:42–48.
- 7 McFarland J, Menitove J, Braine H, Kickler T, Ness P, Fuller A, Slichter SJ, Gernsheimer T, Townsend-McCall D, Kao KJ, Noyes W, Weinauer R, Hudson S, Waldman-Slone A, Schiffer C, Lee E, Norris D, McCullough J, Enright H, Lennon S, Clay M, Woodson R, Meisch M, Noordsij P, Davis K, Mickel M, Millespie MJ, Parker S, Corley S, Rodey G, Sell J, Nemo G, Follmann D, Hernandez M, Hollingsworth C, Klein H, Dutcher J, Fratonini J, Kruskall M, Macklin R, Strauss R, Wittes J: Leukocyte reduction and ultraviolet B irradiation of platelets to prevent alloimmunization and refractoriness to platelet transfusions. *N Engl J Med* 1997;337:1861–1869.
- 8 Norden AT: Qualitative disorders of platelets and megakaryocytes. *J Thromb Hemost* 2005;3:1773–1782.
- 9 Greinacher A, Kiefel V, Klüter H, Pötsch B, Riess H: Empfehlungen zur Thrombozytentransfusion der Thrombozytenarbeitsgruppe der DGTI, GTH und DGHO. *Transfus Med Hemother* 2006;33:528–543.