Transfusion Medicine

original paper

haematologica 2001; 86:749-752
http://www.haematologica.it/2001_07/0749.htm

Bedside leukoreduction of cellular blood components in preventing cytomegalovirus transmission in allogeneic bone marrow transplant recipients: a retrospective study

AIDA B. NARVIOS, BENJAMIN LICHTIGER
The University of Texas, M.D. Anderson Cancer Center, Houston, Tx, USA

Correspondence: Aida Narvios, M.D., UT M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, Texas, USA.
Phone: international +1.713.7922644. Fax: international +1.713.794. 1410. E-mail: anarvios@mdanderson.org

Background and Objectives. Cytomegalovirus (CMV) infection continues to be a major complication of bone marrow transplants (BMTs). Administration of leukoreduced unscreened cellular blood products at the bedside has been shown to be effective in preventing CMV transmission via transfusions in CMV-seronegative bone marrow transplant recipients who receive their transplants from CMV-seronegative donors. The aim of this study was to determine whether CMV infection occurred in CMV-seronegative BMT patients who received CMV-seronegative donor marrows and CMV untested blood products leukodepleted at the bedside.

Design and Methods. We collected data over a 2-year period from patients undergoing allogeneic transplantation who received leukoreduced cellular blood components that were not screened for CMV. All CMV-seropositive patients and donors were excluded from the study. The CMV status of both the donors and the patients was determined before the transplantations. CMV cultures of urine, blood buffy coat, bone marrow samples and bronchial washings were performed if necessary in patients.

Results. Thirty-six CMV-seronegative patient-donor pairs were included in the study. Five patients (13.89%) were serologically reactive, but their CMV cultures were negative and they did not show signs or symptoms of CMV infection. These patients received intravenous immunoglobulin and thus could have acquired anti-CMV passively.

Interpretation and Conclusions. The confidence interval in this study is 0/36 incidence of CMV infection. Our present findings support those of prior studies showing the effectiveness of filtered unscreened blood components as an alternative transfusion support for CMV-seronegative marrow transplant recipients. Studies in larger number of patients are warranted.

Key words: CMV prevention, leukoreduction, bone marrow transplantation, transfusion

Cytomegalovirus (CMV) infection may cause severe disease, which can be fatal in immunosuppressed patients. This continues to be a major complication of bone marrow transplants (BMTs). CMV transmission via blood transfusion has been associated with blood leukocytes. Reducing the white blood cell (WBC) content of cellular blood components can significantly diminish or nearly eliminate CMV transmission via transfusion.[1] Additionally, several extensive studies of the relationship between the leukocyte load in blood products and the risk of transfusion-acquired infection have been done.[1,2] Even with new therapeutic options, CMV infection still has a high mortality rate, especially if it develops into pneumonia.[3,4] CMV infection from seropositive blood components has been practically avoidable since the introduction of systematic, routine WBC reduction using filtration.[4-6] Based on several reports on the effects of WBC reduction, the risk of CMV is nearly eliminated by consistently reducing WBCs to a level less than 1 to 5×10^6 WBCs/unit. The *American Association of Blood Banks* has suggested that a residual leukocyte level less than 5×10^6 makes a blood product *CMV-safe*.[7] Currently available filters designed for use with either platelets or red blood cells (RBC), are even more efficient, achieving a 4-5 log reduction in leukocyte contamination of cellular blood components. In a previously published study, we

reported our experience with bedside leukoreduction of cellular blood components in CMV-negative BMT recipients and donors.[8] To validate the data of that study, we collected data over a 2-year period from patients who were serologically CMV negative, whose cultures were CMV-negative, and who received allogeneic BMTs from CMV-negative donors. All patients included in this study had received cellular blood products that had not been screened for CMV using leukoreduction filters at their bedside.[9]

Design and Methods

Patient population

From January 1995 through December 1996, 36 patients undergoing allogeneic bone marrow transplantation for hematologic and solid organ malignancies were included in the study. Data from all allogeneic BMT recipients and their normal BMT donors who were CMV-seronegative pairs were collected. Before transplantation, all CMV-seropositive patients and donors were excluded from the study. Also, none of the patients received ganciclovir prophylaxis. Most of the patients – 22 (62%) – had received intravenous γ globulin (IVIG). A summary of the characteristics of the study population can be seen in Table 1. The CMV status of both patients and donors was determined before transplantation using a latex agglutination assay (Becton, Dickinson and Co., Franklin Lakes, NJ, USA). CMV cultures of urine, blood buffy coat and bone marrow samples and bronchial washings were performed if indicated.

Study definitions

CMV infection was defined as the presence of CMV-positive cultures from the suspected sites. CMV disease was defined as the presence of a positive culture associated with a clinical illness or a CMV-positive tissue biopsy. Patients who were serologically reactive according to the latex agglutination assay after transplantation but did not show signs of CMV infection and had repeated CMV-negative cultures were not considered to have CMV infection.

Transfusions

All patients in this study received leukoreduced cellular blood components that had not been screened for CMV. Sepacell PL-10A or PLS-10A leukocyte reduction administration sets (Baxter Healthcare Corp., Deerfield, IL, USA) were used to administer platelets and RBCs respectively, at the bedside (Table 2). Transfused random donor platelets were less than 2 days old, while the single donor platelets were less than 1 day old. RBCs were usu-

Table 1. Characteristics of BMT recipients and donors.

Characteristics	*Recipients*	*Donors*
Median age in years (range)	34 (8-59)	38 (6-72)
Sex (male/female)	25/11	11/12
Underlying diseases:		
Lymphoma	8	
CML	10	
ALL	6	
MDS	2	
CLL	3	
AML	2	
Multiple myeloma	1	
Aplastic anemia	1	
Hodgkin's disease	1	
Breast cancer	1	
Other	1	
Pre-transplant CMV:		
Positive	0	0
Negative	36	36

CML, chronic myelocytic leukemia; ALL, acute lymphoblastic leukemia; MDS, myelodysplastic syndrome; CLL, chronic lymphocytic leukemia; AML, acute myeloblastic leukemia.

Table 2. Number of blood products, mean and range, transfused before and after bone marrow transplantation.

Component	*No. of patients*	*Transfusions*	*CMV screened*	*CMV not screened*
		Mean (range)		
PRBCS	36	12 (1-35)	08 (2-16)	14 (1-35)
RDPs	32	30 (4-164)	17 (4-36)	36 (4-164)
SDPs	36	10 (1-39)	05 (1-13)	9 (1-39)
Cryoprecipitate	9	12 (1-30)	0	12 (1-30)
FFP	12	10 (2-96)	0	10 (2-86)
WBCs	1	1	0	1
IVIG	28	06 (1-18)	0	6 (1-18)

Abbreviations: PRBCs, packed red blood cells; RDPs, random donor platelet concentrates; SDPs, single donor platelet concentrates; FFP, fresh frozen plasma; WBCs, white blood cell concentrates; IVIG, intravenous γ globulin.

ally less than 30 days old. Fresh frozen plasma and cryoprecipitate were not leukoreduced.

Results

Our retrospective study showed that five patients (13.89%) were serologically reactive according to the latex agglutination assay. Two were CMV-reactive after 3 months, one after 4 months, and the remaining two 5 months following transplantation. These five patients did not show any signs or symptoms of CMV infection and all the CMV cultures performed were consistently negative. These patients had, however, received IVIG, and thus could have acquired anti-CMV passively.

Discussion

Prevention of CMV infection requires donor testing or filtration of cellular blood components. Leukoreduction has a significant effect on reducing the risk of transmission of cell-associated viruses such as CMV, human lymphotropic virus, Epstein-Barr virus, and human herpes virus 6, 7, and 8.[10-12] There have been significant advances in the removal of WBCs from blood using centrifugation and filtration techniques. Our experience with bedside filtration in our institution has been reported previously.[8] We showed high removal efficiency of WBCs in a quality control analysis of the components being transfused to BMT recipients. Likewise, in the past we have reported data showing the effectiveness of using leukoreduction filters at the bedside for all cellular blood components transfused to CMV-seronegative patients who received BMTs from CMV-seronegative donors.[9] Bedside leukoreduction is not a very common practice for a number of reasons: inconsistency of the leukoreduction procedure due to nursing staff rotation, new nurses who may not be familiar with the nuances of leukoreduction, and problems with quality control monitoring. However, at The University of Texas M. D. Anderson Cancer Center, leukoreduction at the bedside has been in effect for the past 5 years without any observable difficulties or untoward effects. In addition the fact that we transfuse relatively fresh blood components has greatly contributed to the effective removal of residual WBCs. Our quality control records of bedside leukoreduction consistently show residual WBC contamination of less than 10^5 cells as determined by flow cytometric studies.[9] The present study failed to show any CMV infection in the BMT recipients following transplantation despite using blood products that had not been screened for CMV. One confounding factor that must be taken into consideration is that some of these patients received infusion of IVIG. Our studies and those of others have shown that IVIG lots may have variable titers of CMV antibodies which may produce false-positive results in an otherwise uninfected patient.[13] Thus, it is of paramount importance that information about the patient's therapy protocol be readily available to the transfusion service in order to elucidate factors that may induce false-positive test results and thus avoid carrying out more expensive and unnecessary testing to rule out CMV infection.

Conclusions

The findings of the present study confirm those of our prior study[9] as well as earlier findings by Bowden *et al.*[6] regarding the effectiveness of using leukoreduced cellular blood products as an alternative to CMV-negative blood components in bone marrow transplantation.

Contributions and Acknowledgments

Both authors contributed equally to the work.

Disclosures

Conflict of interest: none.

Redundant publications: no substantial overlapping with previous papers.

Manuscript processing

This manuscript was peer-reviewed by two external referees and by Dr. Paolo Rebulla, who acted as an Associate Editor. The final decision to accept this paper was taken jointly by Dr. Rebulla and the Editors. Manuscript received April 23, 2001; accepted June 4, 2001.

Potential implications for clinical practice

Bone marrow patients who are CMV antibody non-reactive and receive transplants from donors who are CMV antibody non-reactive can safely be transfused with CMV unscreened cellular blood components leukoreduced by bedside filtration.

References

1. Hillyer CD, Emmens RK, Zago-Novaretti M, Berkman EM. Methods for the reduction of transfusion–transmitted cytomegalovirus infection: filtration versus the use of seronegative donor units. Transfusion 1994; 34:929-34.
2. Andreu G. Role of leukocyte depletion in the prevention of transfusion–induced cytomegalovirus infection. Semin Hematol 1991; 28:26-31.
3. Meyers JD, Flournoy N, Thomas ED. Risk factors for cytomegalovirus infection after human marrow transplantation. J Infect Dis 1986; 153:478-88.
4. Forman SJ, Zaia JA. Treatment and prevention of cytomegalovirus pneumonia after bone marrow

transplantation: where do we stand? Blood 1994; 83:2392-8.
5. Gilbert GL, Hayes K, Hudson IL, et al. Prevention of transfusion acquired cytomegalovirus infection in infants by blood filtration to remove leukocytes. Lancet 1989; 1:1228-31.
6. Bowden RA, Sayers MH, Cays M, et al. The role of blood product filtration in the prevention of cytomegalovirus (CMV) infection after bone marrow transplant. Transfusion 1989; 29:57S.
7. Smith DM Jr. Leukocyte reduction for the prevention of transfusion–transmitted cytomegalovirus (TT-CMV). Am Assoc Blood Banks 1997; 97:10-1.
8. Lopez A, Lichtiger B. Bedside platelet leukoreduction is as effective as that performed in the blood bank. Am J Clin Pathol 1995; 103:521.
9. Narvios AB, Przepiorka D, Tarrand J, Chan KW, Champlin R, Lichtiger B. Transfusion support using filtered unscreened blood products for cytomegalovirus-negative allogeneic marrow transplant recipients. Bone Marrow Transplant 1998; 22:575-7.
10. Freedman JJ, Blajchman MA, McCombie N. Canadian Red Cross Society symposium on leukodepletion: report of proceedings. Transfus Med Rev 1994; 8:1-14.
11. Lane TA. Leukocyte reduction of cellular blood components. Effectiveness, benefits, quality control, and costs. Arch Pathol Lab Med 1994; 118:393-402.
12. Goldman M, Delage G. The role of leukodepletion in the control of transfusion-transmitted disease. Transfus Med Rev 1996; 9:9-19.
13. Lichtiger B. Laboratory serologic problems associated with administration of intravenous IgG. Curr Iss Transfus Med 1994; 3:1-7.