Section Editor: Theresa Wicklin Gillespie

QUALITY IMPROVEMENT

Improving Use of Cytomegalovirus Negative and Irradiated Blood Products in an Outpatient Oncology Clinic

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Author's disclosures of conflicts of interest are found at the end of this article.

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https://doi.org/10.6004/jadpro.2025.16.4.2

Abstract

Background: Indications for the use of cytomegalovirus (CMV)-negative and irradiated blood products (IRBP) are not standardized and are often poorly understood by providers. This project evaluated the use of a transfusion algorithm in an outpatient oncology clinic to reduce the risk of transfusion-associated graft-vs.-host disease (TA-GVHD) and eliminate the improper use of CMV-negative and irradiated blood products. **Objectives:** The aim of this project was to increase the correct use of CMV-negative and irradiated blood products at an outpatient oncology clinic by establishing a transfusion algorithm, to evaluate the effectiveness of clinical transfusion algorithms on the use of specialty blood products, and to educate providers on TA-GVHD. **Methods:** This quasi-experimental project compared 12 weeks of transfusion data before the implementation of a transfusion algorithm to 12 weeks of transfusion data after the algorithm was introduced. A pre- and post-test survey measured the satisfaction and the impact of the education. **Findings:** The transfusion algorithm resulted in a clinically significant increase in the correct use of both CMV-negative and irradiated blood products at an outpatient oncology clinic. The education in-services provided to staff about TA-GVHD and the indications for irradiated blood product resulted in a significant increase in provider knowledge on ordering specialty blood products.

Irradiation of blood products is the standard of care for the prevention of transfusion-associated graft-vs.-host disease (TA-GVHD). Transfusion-associated graft-vs.-host disease is a rare but fatal complication where engraftment of the donors' lymphocytes in the recipient eventually causes multisystem organ failure and death following the transfusion of blood products (Patel et al., 2010). Patients with hematologic malignancies are at an increased risk of developing TA-GVHD (Bahar & Tormey, 2018). While there is a low incidence (0.1%–1%) of developing

J Adv Pract Oncol 2025;16(4):137–142

TA-GVHD, the mortality rate is estimated at 87% to 100% (Gupta, 2016).

Cytomegalovirus (CMV) is a common viral illness that more than 85% of adults have been exposed to by the age of 40 (American Red Cross, 2022). CMV-negative blood products are indicated for immunocompromised patients and those undergoing hematopoietic stem cell transplant (HSCT; American Red Cross, 2022). CMV infection in the immunocompromised patient can cause significant complications, with high rates of morbidity and mortality (American Red Cross, 2022). Patients receiving transfusions containing the virus have a 40% to 60% chance of contracting CMV through transfusion (American Red Cross, 2022). Exposure is common, and many individuals have positive antibodies for CMV. Thus, obtaining CMV-negative blood products for CMV-negative patients is challenging. In addition, indications for using CMV-negative and irradiated blood products (IRBP) are not standardized, and clinical practice differs between countries and specialties (Bahar & Tormey, 2018).

Clinical features of TA-GVHD include fever, erythematous rash, liver dysfunction, diarrhea, and pancytopenia. Symptoms develop quickly and can progress rapidly into multisystem organ failure, often presenting within the first 11 days following transfusion (Foukaneli et al., 2020).

Two populations are most at risk of developing TA-GVHD: immunocompromised patients and transfusion recipients who share human leukocyte antigen (HLA) matching with the donor, such as between first-or-second-degree family members, and the Japanese population who have documented high rates of HLA sharing or homozygosity (Prokopchuk-Gauk & Solh, 2021).

RESEARCH DEFICITS

To date, no clinical trials have specifically evaluated TA-GVHD, and there is a paucity of literature establishing preventative measures. The number of lymphocytes necessary to provoke a reaction and cause proliferation is unknown (Foukaneli et al., 2020). Additionally, the level of immunosuppression at which one is at higher risk of developing TA-GVHD is unknown (Foukaneli et al., 2020). Transfusion practices and guidelines differ among countries (Foukaneli et al., 2020). Due to the rarity of this disease, this is often a diagnosis of exclusion.

Treatment recommendations for TA-GVHD are therefore limited. The literature recommends preventing TA-GVHD with irradiation of blood products using gamma rays or X-rays to damage the T cells and prevent them from proliferating (Prokopchuk-Gauk & Solh, 2021). It has been proposed that leukoreduction is an equally effective intervention (Foukaneli et al., 2020). However, it is worth noting that even after universal leukoreduction, there were still 66 cases reported between 2000 and 2013 (Foukaneli et al., 2020). Irradiation remains the only recognized preventative tool for TA-GVHD.

CLINICAL GUIDELINE RECOMMENDATIONS

All red blood cells, platelets, and granulocyte products should be irradiated (Foukaneli et al., 2020). The most recent guideline for preventing TA-GVHD was published in 2020 by the British Society for Haematology (BSH). This guideline was the only relevant source identified in the review of the literature. It is recommended that patients undergoing allogeneic hematopoietic stem cell transplant (HSCT) receive IRBP from the initiation of chemotherapy and "should be continued until the following criteria are met: > 6 months have elapsed since the transplant date, the lymphocyte count is > 1.0×10^9, the patient is free of active chronic GVHD, and the patient is off all immunosuppression" (Foukaneli et al., 2020, p. 713). Patients undergoing autologous HSCT require IRBP at the initiation of chemotherapy and for 3 months following transplant.

All patients with Hodgkin lymphoma regardless of stage should receive IRBP indefinitely throughout their course of treatment due to their immunocompromised status (Foukaneli et al., 2020). Patients receiving chemotherapy with purine analogs such as fludarabine, cladribine, bendamustine, clofarabine, and pentostatin should also receive IRBP, as purine analogs can cause significant lymphocytopenia (Foukaneli et al., 2020). Additionally, patients with hematologic malignancies who receive alemtuzumab or other T-lymphocyte-depleting therapy should receive IRBP due to their severely immunocompromised status

(Foukaneli et al., 2020). For patients undergoing chimeric antigen receptor (CAR) T-cell therapy, it is recommended that they receive IRBP 7 days before infusion and 3 months following CAR T-cell therapy (Foukaneli et al., 2020). Transfusion of CMV-negative blood is recommended for all patients who have received an HSCT or are potential candidates for HSCT (Elemary, 2017).

METHODS

This project aimed to assess the impact of a transfusion algorithm on the use of CMV-negative products and IRBP.

Design and Setting

A quasi-experimental study design was used to assess the first aim, the impact of the transfusion algorithm on the use of CMV-negative products and IRBP. This approach was chosen since the intervention in this context could not be randomized (Harris et al., 2006).

This project took place at an outpatient oncology clinic comprised of four clinics. Patients diagnosed with hematologic malignancies were included in the project, as this population is most often affected by the improper use of CMV-negative products and IRBP (Bahar & Tormey, 2018).

Sample

The site's clinical support staff created a 2022 report using the site's electronic medical record (EMR) to identify patients with hematologic malignancies who warranted the use of specialty blood products. A total of 1,841 patients served as the total population (*N*). Stratified sampling was utilized to obtain a representative sample from the population. A power analysis using G*Power software determined a required sample size of $n = 40$, with an effect size of 0.5. This analysis was conducted using a one-tailed *t*-test with an alpha level of 0.05, with actual power estimated at 81%.

A gap analysis that was administered to the medical oncologists and advanced practice providers (APPs) at the site identified a decreased understanding of TA-GVHD as a barrier to the appropriate administration of IRBP. Often, staff did not understand the critical importance of ordering IRBP for patients at risk for developing TA-GVHD. Educational in-services were provided to all APPs and chemotherapy nurses. There were two sessions provided at the project start and following implementation. Each session was 15 minutes long. The pathogenesis of TA-GvHD, prevalence, prevention strategies, and an overview of CMV infections were detailed during the in-service. Current indications for IRBP and CMV-negative blood products were discussed, and an algorithm was introduced. The handout on TA-GVHD and the transfusion algorithm were also provided in an email to all applicable staff.

Aims and Instruments

The goal of this QI project was to improve the correct use of CMV-negative products and IRBP. This project had two specific aims. The first aim was to introduce and implement a standardized transfusion algorithm developed from current literature to measure the use rate before and after implementation. The second aim was to educate providers about TA-GVHD, CMV infection through transfusion, the current indications for the use of specialty blood products, and the recommendations for IRBP.

The instruments used included the transfusion algorithm for IRBP and CMV-negative blood products (Table 1), and the provider survey (Table 2). The study instruments were developed by the team for specific use in this project. The impact of the education for providers was evaluated with a survey given to all APPs during the pre-implementation phase and before education sessions. The survey was created using Qualtrics, which consisted of five questions gauged on a Likert scale. The survey addressed reported confidence in ordering specialty blood products. Additionally, there were three clinical scenarios to assess existing knowledge. To ensure reliability, the same survey was administered following the intervention and allowed for consistency following the test-retest reliability method. To maintain validity, the survey questions were unambiguous. The transfusion algorithm was created to mirror current clinical practice guidelines as established by the BHS in 2020.

Data Collection

Data collection consisted of completing a chart audit ($n = 40$) spanning 12 weeks before

Table 1. Transfusion Algorithm for IRBP and CMV-Negative Blood Products

Irradiated blood products (platelets and PRBCs only)
1. Hematologic malignancy? Yes____ No____
If NO, IRBP not indicated.
If YES, does the patient meet one or more indications?
AML____ Hodgkin lymphoma____ Treatment with purine analogues____
PMH: HSCT/preparing for HSCT____ Treatment with alemtuzumab or ATG____
PMH: CAR-T or preparing for CAR-T____
If patient meets indications → order irradiated blood products.
CMV-negative blood products (platelets and PRBCs only)
1. Hematologic malignancy? Yes____ No____
If NO, CMV-negative blood products not indicated.
If YES, does the patient have a PMH: HSCT or preparing for HSCT? Yes____ No____
If NO, CMV-negative blood products not indicated.
If YES, the patient meets indications for CMV-negative blood products.
2. Does the patient have a CMV antibody on file? Yes____ No____
If NO, order a CMV AB test.
If YES, AND CMV negative:
If > 12 months, order repeat CMV AB and flag recorder to order CMV AB annually.

Note. IRBP = irradiated blood products; CMV = cytomegalovirus; PRBCs = packed red blood cells; PMH = past medical history; AB = antibody; HSCT = hematopoietic stem cell transplant; ATG = anti-thymocyte globulin; CAR-T = chimeric antigen receptor T-cell.

implementation to review all transfusion orders in the past 3 months to determine current transfusion practice and the correct use of specialty blood products. The transfusion data and percentage of correct transfusion orders for 3 months post-algorithm implementation were compared to pre-implementation data. The chart audits performed pre- and post-intervention were conducted similarly using the same sample demographics. The clinical informaticist assisted in chart audits of transfusion orders and patient CMV status integration in the EMR. Data collected from chart audits were independently reviewed by all members of the practice group to ensure accuracy. The educational material was reviewed and verified by the site before the presentation.

Data Analysis

Data analysis included descriptive and inferential statistical methods to analyze results from the project using Excel. A Chi-squared test of homogeneity was conducted to determine whether the frequency of correctly used IRBP and CMV-negative products was evenly distributed between the pre- and post-algorithm groups. The impact of the education provided during staff in-service was measured with a pre- and post-survey that revealed that participants scored higher on the survey post education. An ANOVA with one within-subjects factor was conducted to determine whether significant differences exist among pre- and post-survey results.

RESULTS

For aim 1, the transfusion algorithm resulted in the increase of correctly utilized IRBP from 60% to 79% following implementation (Figure 1). A Chi-squared test of homogeneity determined that this was not significant based on an alpha value of .05, with a p value of 0.057. This finding suggests that while clinically significant, the transfusion guideline did not result in a statistically significant difference in the distribution of the frequency of IRBP used correctly between the pre- and post-groups. The use of CMV-negative blood increased

Table 2. Provider Survey

Please rate your agreement with the following statements and scenarios:	Strongly disagree	Somewhat disagree	Neutral	Somewhat agree	Strongly agree
I am comfortable ordering CMV negative and irradiated blood products.					
I am aware of the current indications for irradiated blood products.					
I understand why it is necessary to order CMV negative and irradiated blood products.					
A 67-year-old female with Hodgkin lymphoma presents with symptomatic anemia and thrombocytopenia. The patient was ordered to have CMV negative and irradiated blood and irradiated platelets. Do you agree with current medical management?					
A 61-year-old male with relapsed AML treating with FLAG-Ida is found to have a hemoglobin of 5 and platelets of 3. The patient is transfused with CMV-negative irradiated blood and CMV-negative and irradiated platelets. Do you agree with current medical management?					

Note. CMV = cytomegalovirus; AML = acute myeloid leukemia; FLAG-Ida = fludarabine, cytarabine, G-CSF, and idarubicin chemotherapy regimen; G-CSF = granulocyte colony-stimulating factor.

from 43% to 64% following the implementation of a transfusion algorithm. A Chi-squared test of homogeneity determined this was statistically significant based on an alpha value of .05, with a p value of .047.

For aim 2, results indicated there was a statistically significant difference between the values of pre- and post-survey results, with a p value of 0.016. The providers reported higher levels of knowledge of TA-GVHD and CMV infections and confidence when ordering specialty blood products.

DISCUSSION

The strengths of the project include the low cost to implement and the minimal resources required. This project resulted in a more cohesive transfusion practice, prevention of TA-GVHD, and decreased the risk of CMV infection through transfusion. This project can be easily applied in other similar practice settings and can serve to bridge the gap between evidence and professional practice.

Limitations

Alternative explanations for the results were considered along with exterior forces. Such explanations include the possibility that providers received supplemental education from educational activities or conferences that influenced their use of specialty blood products. Some team members were employed at the site. The project's success may be biased based on preexisting relationships with the staff. Additionally, the small sample size of $n = 40$ could potentially pose a threat to both validity and reliability. Additional efforts are needed in the future to increase the frequency with which providers order a CMV antibody when appropriate.

While CMV-negative blood products were utilized more efficiently according to the guidelines outlined in the algorithm, it is worth noting that providers frequently did not order a CMV antibody test. This study is limited by the outcome measures applied at the beginning of the project. When ordering CMV-negative blood, the provider at that time must assume the patient is CMV negative until proven otherwise. While this is the correct way to utilize the algorithm, the process does not account for when a provider neglects to order a CMV antibody test and the patient is CMV positive. Despite identified limitations, the usefulness of the findings is still significant.

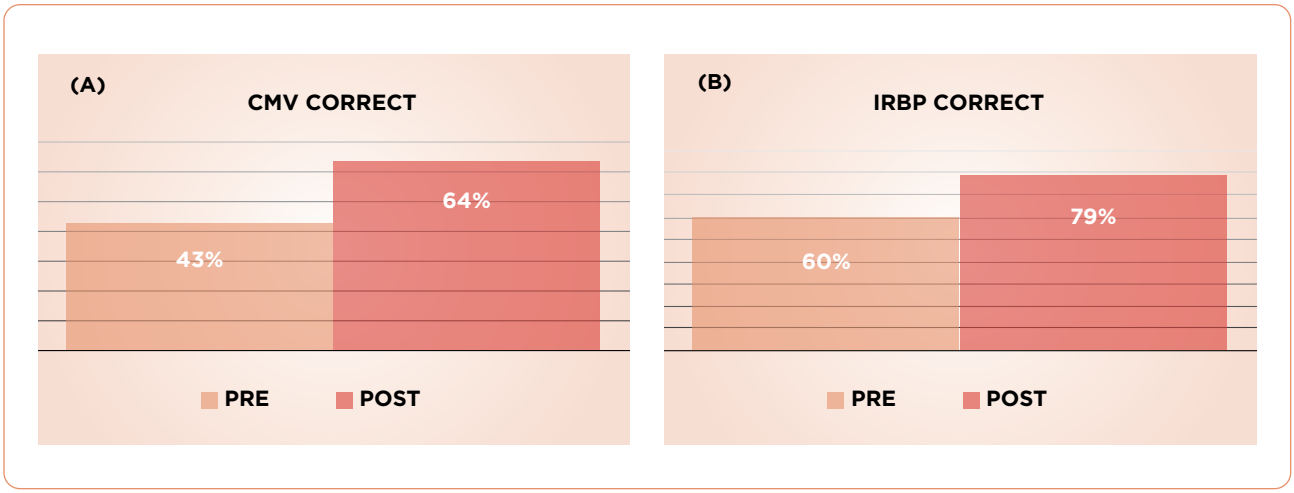

Figure 1. (A) Statistically significant based on an alpha value of .05, *p* value of .047. (B) Not significant based on an alpha value of .05, *p* value of .057.

CONCLUSION

The transfusion algorithm resulted in a statistically significant increase in the correct use of both IRBP and CMV-negative products at an outpatient oncology clinic. The education in-services provided to staff on TA-GVHD and the indications for IRBP resulted in a significant increase in provider knowledge comprehension and reported confidence in TA-GVHD and the use of specialty blood products. There is a need for uniform transfusion practice and universal guidelines for the use of IRBP as evidenced by the lack of benchmark data for comparison and scarcity of clinical trials. This transfusion algorithm can be applied in similar practice settings and can be used as a tool to guide advanced practice providers when ordering specialty blood products. The implementation of a transfusion algorithm improved overall transfusion practice and health-care quality by increasing the correct use of specialty blood products at an outpatient oncology clinic.

Disclosure

The author has no conflict of interest to disclose.

References

American Red Cross. (2022). *What is CMV negative blood? Why is it important*. https://www.redcrossblood.org/local-homepage/news/article/why-cmv-negative-blood-is-so-important.html

Bahar, B., & Tormey, C. A. (2018). Prevention of transfusion-associated graft-versus-host disease with blood product irradiation: The past, present, and future. *Archives of Pathology & Laboratory Medicine, 142*(5), 662–667. https://doi.org/10.5858/arpa.2016-0620-RS(Blood Bank Guy)

Elemary, M., Seghatchian, J., Stakiw, J., Bosch, M., Sabry, W., & Goubran, H. (2017). Transfusion challenges in hematology oncology and hematopoietic stem cell transplant: Literature review and local experience. *Transfusion and Apheresis Science, 56*(3), 317–321. https://doi.org/10.1016/j.transci.2017.05.022(SCIRP)

Foukaneli, T., Kerr, P., Bolton-Maggs, P. H. B., Cardigan, R., Coles, A., Gennery, A., Jane, D., Kumararatne, D., Manson, A., New, H. V., & Torpey, N. (2020). Guidelines on the use of irradiated blood components. *British Journal of Haematology, 191*(5), 704–724. https://doi.org/10.1111/bjh.17015(SpringerLink)

Gupta, S., Sengal, T., Sachdeva, M. W. S., Nasem, S., Das, F., & Nada, R. (2016). Transfusion-associated graft-versus-host disease with a non-fatal course. *Indian Journal of Hematology and Blood Transfusion, 32*(4), 326–328. https://doi.org/10.1007/s12288-016-0677-3

Harris, A. D., McGregor, J. C., Perencevich, E. N., Furuno, J. P., Zhu, J., Peterson, D. E., & Finkelstein, J. (2006). The use and interpretation of quasi-experimental studies in medical informatics. *Journal of the American Medical Informatics Association, 13*(1), 16–23. https://doi.org/10.1197/jamia.M1749(Johns Hopkins University)

Patel, K. K., Patel, A. K., Ranjan, R. R., & Shah, A. P. (2010). Transfusion associated graft versus host disease following whole blood transfusion from an unrelated donor in an immunocompetent patient. *Indian Journal of Hematology and Blood Transfusion, 26*(3), 92–95. https://doi.org/10.1007/s12288-010-0028-0

Prokopchuk-Gauk O, Solh Z. Irradiated, washed and CMV seronegative blood components. In: Khandelwal A, Abe T, editors. Clinical Guide to Transfusion [Internet]. Ottawa: Canadian Blood Services, 2021. Chapter 15. https://professionaleducation.blood.ca/en/transfusion/clinical-guide/irradiated-washed-and-cmv-seronegative-blood-components