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Reversal of warfarin-coagulopathy: How to improve plasma transfusion practice in a community hospital setting?

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Abstract:

BACKGROUND: Plasma is often given inappropriately to reverse warfarin-induced coagulopathy, wasting health-care resources and exposing the patients to transfusion-associated risks.

AIMS: The clinical practice at our institution was evaluated in order to reduce the number of unnecessary plasma transfusions.

MATERIALS AND METHODS: Retrospective audit of plasma transfusions was done (July 2014 to June 2015).

DESIGN: To improve the clinical practice, a two-prong strategy was implemented: (1) in-service was given to clinicians on the warfarin-reversal guidelines and (2) for a 30-day period, plasma orders were placed on the approval list of the Transfusion Medicine Service.

RESULTS: Of the 729 units of plasma, 189 (26% of total) were given for the reversal of warfarin-induced coagulopathy. The medical charts of these patients were reviewed: 46 units of plasma (~25%) were given inappropriately (e.g., patients with minimally elevated international normalized ratio, no evidence of bleeding, and no surgery within 24 h). To check the effectiveness of our intervention, two audits of plasma transfusions were done. During the first audit (January 1–February 29, 2016), 24 patients received plasma to reverse warfarin-coagulopathy. Medical chart review revealed that the vast majority of plasma orders (96.66%) followed the guidelines. A second audit was carried out a year later (January 1–March 31, 2017): during this 3-month period, 47 patients were transfused with plasma for warfarin reversal with a 94% adherence to the guidelines.

CONCLUSION: We conclude that plasma transfusion practices may be improved by a combination of education and active enforcement of warfarin reversal guidelines.

Keywords:

Audit of transfusion practices, plasma, physician education, warfarin reversal

Introduction

Plasma is a commonly transfused blood product. According to the National Blood Collection and Utilization Survey, in the US, plasma transfusions had changed little between 2006 (4 million units)[1] and 2011 (3.8 million units),[2] and the American Red Cross still estimates a daily plasma use of 10,000 units.[3] Most of the plasma (~75%) is transfused as fresh frozen plasma, whereas the rest is 24 h plasma. For most indications, these products are interchangeable. The main indications of plasma transfusions in the US include replacement of clotting factors in acquired coagulopathies[4] (including reversal of

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warfarin-induced coagulopathy[5]) and use in therapeutic plasma exchange procedures.[6] In community hospitals, ~90% of plasma is transfused in the management of patients with acquired bleeding disorders.[5]

Like any other blood product, plasma transfusions are associated with risk of adverse effects. Indeed, before 2004, switch to all male donor base plasma transfusion was a leading cause of transfusion-associated lung injury.[7] Other common adverse effects include transfusion-associated circulatory overload and allergic/anaphylactic reactions.

Considerably, controversy surrounds the use of plasma for the reversal of warfarin-induced coagulopathy given the poor correlation between International Normalized Ratio (INR) and bleeding risk (reviewed in reference[8]). The current American College of Chest Physicians (ACCP), American College of Cardiology (ACC), and American Heart Association (AHA) guidelines emphasize the futility of plasma transfusions in patients on warfarin when the INR is <2.0 and the patient is not bleeding or when there is sufficient time (24 h or more) to reverse warfarin effects by Vitamin K injections.[9] Yet, audit after audit from North America[10,11] to Pakistan[12] and India[13] shows that these guidelines are oftentimes not followed and patients receive plasma for warfarin-reversal inappropriately.

Our institution is a community-based teaching hospital with over 500 beds, several residency programs, and an annual number of patient admissions that exceeds 20,000. We use an electronic blood order system (CERNER) which, along with the availability of electronic medical records, makes accurate and timely audits possible. Recently, the activity-based cost of plasma transfusion in "real-world US inpatient setting" was estimated to be $400.[14] During the past 10 years, we transfused 8796 units of plasma at an estimated cost of $3.5 million. To evaluate the clinical practice of using plasma for the reversal of warfarin-induced coagulopathy at our institution, we performed a retrospective audit of plasma transfusions during a 12-month period between July 1, 2014, and June 30, 2015. Generally speaking, transfusion practice changes require a combination of education, active enforcement, and monitoring. In this study, we report our experience with this blood utilization project.

Materials and Methods

After approval by the Monmouth Medical Center Institutional Review Board (IRB Study# 15–031), a retrospective search of the blood bank records was conducted for plasma transfusions done between July 1, 2014, and June 30, 2015 (preintervention phase). The study population included all adult patients of both sexes above the age of 18 years who received plasma. We identified 729 plasma transfusions, of which 183 were ordered by checking the indication "emergency reversal of warfarin sodium." The medical charts of these patients were reviewed for appropriateness of the transfusion including pretransfusion INR value, presence or absence of active bleeding, and plans for surgery (within 24 h or not). These factors were compared to the ACCP/ACC/AHA guidelines [Table 1] for warfarin reversal.

Once the preintervention phase was completed, the intervention phase was initiated which included the below two steps:

1. Education: In our hospital, plasma is primarily ordered by Internal Medicine followed by General Surgery, Orthopedics, and Emergency Medicine for the reversal of warfarin-induced coagulopathy. Education was focused on these departments using flyers, lectures, and conferences. Data from the preintervention study were used to demonstrate wastage and the need for improving clinical practice

Table 1: The American College of Chest Physicians/American College of Cardiology/American Heart Association Guidelines

Management of warfarin-induced coagulopathy
If INR >goal but <5 and no significant bleeding or risk of bleeding: lower the dose or skip next dose
INR ≥5 or ≤9 and no significant bleeding or risk of bleeding: skip next 1-2 doses or along with skipping give Vitamin K 1-2.5 mg PO. If the patient is at high risk of thrombosis (mechanical heart valves), omit 1-2 doses and use FFP 2 units IV and not to use Vitamin K
When INR ≥9 and no significant bleeding or low-moderate risk of bleeding: Hold warfarin, give 2 units of FFP, give Vitamin K (2.5-5 mg PO). In patients with mechanical heart valves after 2 units of FFP administration, administer only 1-2.5 mg PO of Vitamin K
Serious bleeding at any level of elevated INR or high risk of bleeding: Hold warfarin, give 4 units of IV FFP, give Vitamin K 10 mg by slow IV infusion. May repeat FFP and Vitamin K as needed. In patients with mechanical heart valves, FFP is preferred, administer only low dose of Vitamin K
Life-threatening bleeding: Hold warfarin, give 4 units of IV FFP, give Vitamin K 10 mg by slow IV infusion. Consider recombinant factor VIIa for unresolved coagulopathy. Repeat FFP and Vitamin K as needed
Preoperative management of warfarin-induced coagulopathy
If INR ≥1.5 or ≤1.9: Administer FFP for urgent surgery/procedure. Give Vitamin K 1 mg PO if surgery is scheduled in 24-48 h
If INR >1.9 but ≤5 with no significant bleeding: Administer FFP and Vitamin K 1-3 mg slow IV infusion for urgent surgery/procedure. Give Vitamin K 1-2.5 mg PO if surgery scheduled in 24-48 h. If INR continues to be elevated in 24 h, repeat PO Vitamin K
If INR >5 but <9 with no significant bleeding: Administer FFP and Vitamin K 2-5 mg slow IV infusion for urgent surgery/procedure. Give Vitamin K 2.5-5 mg PO if surgery scheduled in 24-48 h. If INR continues to be elevated in 24 h, repeat PO Vitamin K 1-2 mg PO
Vitamin K should be used with caution in patients with mechanical heart valves

INR = International normalized ratio, FFP = Fresh frozen plasma

2. Active enforcement: Our blood bank is covered by a pathology resident 7/24. For a 1-month period, plasma orders for the "emergency reversal of warfarin sodium" were placed on the approval list. The ordering physician was contacted and advised if the ACCP/ACC/AHA criteria were not met.

Monitoring (postintervention)

The charts of all patients who received plasma for "emergency reversal of warfarin sodium" between January 1, 2016, and February 28, 2016, and January 1–March 31, 2017, respectively, were checked for adherence to the ACCP/ACC/AHA guidelines.

Data were collected and stored in a password-protected secure hospital computer in compliance with HIPAA regulations and our IRB standards. InStat 3 GraphPad software (GraphPad, San Diego, CA) was used for statistical analysis. Statistical significance was determined by the Fisher's exact test.

Results

Over a 12-month study period (from July 1, 2014, to June 30, 2015), a total of 729 units of plasma were issued from our blood bank (this corresponds to our average annual plasma transfusion rate of 799 units). Of the 729 units, 183 (~25%) were given for the "emergency reversal of warfarin sodium." Comparing the medical charts of these patients to the ACCP/ACC/AHA guidelines [Table 1], the transfusion of 137 plasma units (~75%) was deemed "appropriate," and the use of 46 units of plasma (~25%) was classified as "inappropriate" [Table 2].

Table 2: Data from the pre- and post-intervention phase

	Preintervention	Postintervention
Time period	12 months	2 months
Total number of FFP issued	729	67
FFP issued for warfarin-induced coagulopathy	183	24
Appropriate	137	23
Inappropriate	46	1

FFP = Fresh frozen plasma

In the appropriate plasma transfusion category (137 units), 78 units (57%) were given for invasive procedure within 24 h; 27 units (~20%) were used for bleeding; 17 units (12%) were used for surgery within 24 h; and finally, 15 units (11%) were used for INR >9 [Table 3]. For the sake of completeness, it should be mentioned here that other indications for the plasma transfusions included elevated INR due to nonwarfarin causes (such as hepatic failure or disseminated intravascular coagulation), massive transfusion protocols, and plasma exchange procedures; such transfusions were not included in this study.

In the inappropriate plasma transfusion group (46 units), 24 units (52%) were ordered for INR in therapeutic range and no evidence of bleeding; 18 units (39%) were transfused for invasive and/or surgical procedures scheduled for >24 h; and somewhat perplexingly, 4 units were ordered for patients with no recent coagulation study results [Table 3].

After completing the first phase of this study, in-service education on the ACCP/ACC/AHA guidelines was performed using flyers and lectures, focusing on medicine and surgery residents. For 1 month, plasma orders were also placed on the approval list of the pathology resident covering the blood bank. When an order was placed, the resident checked the patient's last INR value and then contacted the ordering clinician for bleeding history and plans for surgical intervention. When the ACCP/ACC/AHA criteria were not met, the clinician was advised not to transfuse the patient with plasma. Of course, no transfusion order was ever denied.

To evaluate the effectiveness of the intervention, two audits of plasma transfusions were conducted: the first covered 2 months (January and February) in 2016, and the second involved 3 months (January–March) in 2017. During the first audit, a total of 67 units of plasma were released from the blood bank, of which 24 units (36%) were ordered for "emergency reversal of warfarin sodium." According to the medical chart review, 23 of the 24 units were transfused appropriately, following the ACCP/ACC/AHA guidelines [Table 2]: 15 units were used for invasive procedure or surgery within 24 h; and 8 units were given for elevated INR and active

Table 3: Identified appropriate and inappropriate usage of FFP in the study

Appropriate usage of FFP	*n*1a (%)	*n*2a (%)	Inappropriate usage of FFP	*n*1b (%)	*n*2b (%)
Warfarin-induced coagulopathy	137 (22.35)	23 (37.71)	Warfarin-induced coagulopathy	46 (39.65)	1 (16.67)
Invasive procedure in 24 h	78	12	Without bleeding	24	0
Bleeding	27	8	>24 h before procedure	18	1
Surgery within 24 h	17	3	Not done coagulation studies	4	0
INR >9	15	0	Other inappropriate usage	70 (60.35)	5 (83.33)
Other appropriate usage	476 (77.65)	38 (62.29)			
Total	613 (100)	61 (100)		116 (100)	6 (100)

n = Number of FFP issued. *n*1a = Preintervention appropriate usage, *n*2a = Postintervention appropriate use, *n*1b = Preintervention inappropriate use, *n*2b = Postintervention inappropriate usage, % = Percentage of FFP issued out of total. FFP = Fresh frozen plasma, INR = International normalized ratio

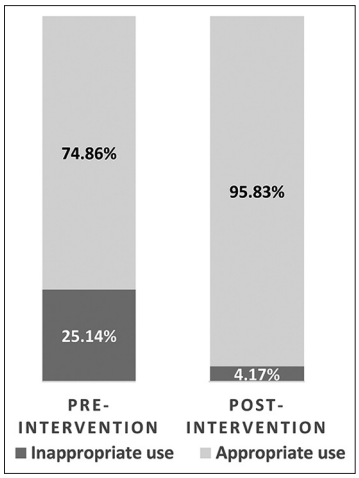

Figure 1: Inappropriate use of plasma for the reversal of warfarin-coagulopathy dropped from 25% to 4% after our intervention combining education with active enforcement of guidelines

bleeding. During the second audit, 44 of the 47 transfused patients (94%) received plasma appropriately for warfarin reversal.

Statistical analysis of the pre- and post-intervention plasma transfusion data revealed significant ($P < 0.001$) improvement in the clinical ordering practice after the intervention [Figure 1].

Discussion

Plasma transfusions can save life. When given inappropriately, they can also expose patients to unnecessary risks and may result in adverse clinical outcomes. Indeed, almost 20% of patients developed pulmonary complications after receiving plasma for warfarin reversal.[15] Furthermore, clinically not indicated plasma transfusions are wasting valuable resources and hurting the operating budget of the blood bank. There are guidelines for the appropriate use of plasma in the reversal of warfarin-induced coagulopathy.[9] Yet, study after study demonstrates that these guidelines are often not followed.[10-13] Clinical practice is hard, but not impossible, to change. One proven strategy combines education with active enforcement and monitoring.

During the audit of plasma transfusion practices at our institution, we found that plasma was frequently ordered inappropriately (46 out of 183 units) for patients on warfarin. The most common misuse was the transfusion of patients with INR in the therapeutic range in the absence of active bleeding. As corrective action, we performed in-service with flyers and lectures, educating clinicians about the appropriate use of plasma in the reversal of warfarin-induced coagulopathy. These efforts were focused on the Medicine and Surgery Department where most inappropriate orders originated from. The education efforts were coupled to active enforcement: for a month, the pathology resident covering the blood bank contacted the ordering physician to see if the guidelines were satisfied. This intervention almost completely eliminated the inappropriate plasma orders: from ~ 4/month in 2014/15 to <1/month in 2016.

Our study is not without limitations. Most important, the postintervention data were collected for a total of 5 months within a 2-year period following the education of medical staff. It remains to be seen if compliance with the ACCP/ACC/AHA guidelines will be maintained over time. Clearly, continued reinforcement is necessary. To do so, as of November 2, 2016, we implemented a real-time online transfusion support system in CERNER that checks the patient's pretransfusion INR level and reminds (with "pop-up" alert) the ordering physician to the plasma transfusion guidelines.[16]

Conclusion

Our study provides evidence that it is possible to improve plasma transfusion practices in a community hospital setting for the reversal of warfarin-coagulopathy by combining evidence-based education with active enforcement of the guidelines and continuous monitoring.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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