The evaluation of the audit of Fresh-Frozen Plasma (FFP) usage in emergency department

Emine Emektar*, Seda Dagar, Seref Kerem Corbacioglu, Huseyin Uzunosmanoglu, Mehmet Veyssel Oncul, Yunsur Cevik
Kecioren Training and Research Hospital, Department of Emergency Medicine, Ankara, Turkey

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A B S T R A C T

Objectives: In our study, the aim is to evaluate the use of Fresh-Frozen Plasma (FFP) in our emergency department and to assess its audit for transfusion.

Methods: All the patients aged 18 and over who received FFP transfusion in the emergency department between March 1, 2013 and March 1, 2016 were included into the study. The audit of FFP use was evaluated by according to ‘British Committee for Standards in Hematology Guideline-2004’. Results: Total 141 patients were identified to receive FFP transfusion in our emergency department. When the audit of FFP use was evaluated, 59.6% of all the practices were regarded as improper use. We identified that while the rate of improper use was 40.2% in patients with bleeding, it rose to 90.7% in patients without active bleeding or in those who used FFP with the aim of bleeding prophylaxis.

Conclusion: We have determined that FFP transfusions were conducted with improper indications at high rate in our emergency department. Preparing an up-to-date transfusion guideline for the practices in emergency departments in our country and training and supervising the medical staff at regular intervals may help prevent the shortcomings in FFP practices.

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1. Introduction

Fresh-Frozen Plasma (FFP) is the component that is prepared by freezing various plasma factors from whole blood or from the plasma collected through aphaeresis at the temperature and duration at which they can keep their functions. FFP contains stable coagulation factors, immunoglobulins and albumin at the same level as that of typical plasma. This being the case, FFP can be considered a costly therapeutic component, the source of which is the human body.1

There are publications as regards the unnecessary and improper use of FFP transfusion in recent years, which can assume a life-saving role in cases that are really indicative of its use.2-6 With an increase in the awareness of this issue, many guidelines have been brought our concerning FFP transfusion, and the indications of FFP use are restricted.7,8 Unnecessary use of FFP is known to increase the risk of side effects from the transfusion in patients, as well as wasting sources and being costly. Excess volume replacement, anaphylaxis, diseases transmitted through transfusion and transfusion - based lung injury (TRALI) are the complications likely to develop out of the use of FFP.9 In our country, there are not sufficient data available about transfusion practices particularly in emergency departments. In our study, the aim is to analyze the use of FFP in our emergency department and to assess its audit for transfusion.

2. Material and methods

2.1. Study design and setting

Our study was conducted in an emergency department at the third step at which almost 250,000 patients are admitted annually. Prior to the study, the approval was obtained from the local ethical board. All the patients aged 18 and over who received FFP transfusion in the emergency department between March 1, 2013 and March 1, 2016 were included into the study. Pregnant women were
excluded the study. The demographic data of the patients, complete blood count (CBC) and coagulation parameters before the transfusion, FFP transfusion indications, bleeding areas if there was any, and coagulation parameters after FFP were obtained from the hospital automation system and from patient files through retrospective scanning. The patients who had missing data were excluded. The audit of FFP use was evaluated by an emergency physician according to the rules in ‘British Committee for Standards in Hematology, blood transfusion, FFP, cryoprecipitate and the use of cryosupernatant Guideline-2004’. The cases in which the use of FFP is appropriate are given at Table 1.

2.2. Statistical analysis

The SPSS 16.0 for Windows (SPSS Inc., Chicago, IL) software was used for the statistical analyses. The Kolmogorov–Smirnov test was used to assess the normal distribution of the variables. Regarding digital data obtained by measurement, data that conforms to normal distribution was shown as mean and standard deviation, and data that does not conform to normal distribution was shown as median and minimum - maximum. The categorical data obtained by counting was shown as number (n) and percentage (%).

3. Results

Total 161 patients were identified to receive FFP transfusion in the emergency department in the course of the study. Twenty patients that had missing data were excluded, and the remaining 141 patients were included in the study. We determined that 311 units of FFP transfusion in total were carried out. When side effects are evaluated in the study, we determined allergic reactions in four units of FFP transfusion in total were carried out. When side effects were evaluated in the study, we determined allergic reactions in four units of FFP transfusion in total were carried out. When side effects were evaluated in the study, we determined allergic reactions in four units of FFP transfusion in total were carried out. When side effects were evaluated in the study, we determined allergic reactions in four units of FFP transfusion in total were carried out.

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The patients on whom FFP was practiced most frequently were those in whom warfarin overdose (n = 99, 70.2%) was detected. We also determined that the rarest indication of FFP use was the FFP transfusion (n = 5, 3.5%) carried out due to TTP and DIC (Table 2). When the audit of FFP use was evaluated, 59.6% of all the practices were regarded as improper use. We identified that while the rate of improper use was 40.2% in patients with bleeding, it increase to 90.7% in patients without active bleeding or in those who used FFP with the aim of bleeding prophylaxis (Table 3).

Table 1

Clinical indications for use of FFP.

| Single-factor deficiencies where a specific or combined factor concentrate is not available | Multiple-factor deficiencies and/or disseminated |
|---------------------------------------------|-----------------------------------------------|
| Intravascular coagulopathy | Thrombotic thrombocytopenic purpura |
| Need for urgent reversal of warfarin effect | Following massive transfusion in presence of bleeding and prolonged coagulation |
| Liver disease in presence of bleeding or prolonged prothrombin time (PT)-partial thromboplastin time (PTT)-international normalized ratio (INR) in the settings of invasive procedures |

| Sex [n (%)] | Female | 63 (44.7%) |
|-------------|--------|------------|
| Age [median (min–max)] | 74 (18–92) |
| Active bleeding [n (%)] | 87 (61.7%) |
| Sites of bleeding [n (%)] | |
| Intracranial | 16 (18.4%) |
| Thorax | 2 (2.3%) |
| Gastrintestinal tract | 30 (34.5%) |
| Hematuria | 3 (3.4%) |
| Epistaxis | 17 (19.5%) |
| Vaginal | 4 (4.6%) |
| Intraabdominal | 8 (9.2%) |
| Other | 7 (8%) |

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Table 2

Demographic characteristics and laboratory parameters of patients.

| Outcome in ED [n (%)] | Alive | 132 (93.6%) |
|------------------------|-------|------------|
| Exitus | 9 (6.4%) |

Indications of FFP usage in ED [n (%)]

| Hepatic diseases | 11 (7.8%) |
| Warfarin overdose | 99 (70.2%) |
| Massive transfusion/trauma | 18 (12.8%) |
| Prophylaxis for surgical procedures | 8 (5.7%) |
| TTP/DIC | 5 (3.5%) |

Table 3

Appropriateness of FFP use.

| FFP use | Appropriate n (%) | Inappropriate n (%) | Total n (%) |
|---------|-------------------|---------------------|-------------|
| Patients with bleeding | 52 (59.8%) | 35 (40.2%) | 87 (61.7%) |
| No bleeding or prophylaxis for surgery | 5 (9.3%) | 49 (80.7%) | 54 (36.3%) |
| Total | 57 (40.4%) | 84 (59.6%) | 141 (100%) |

4. Discussion

FFP, which came into use in the 1940’s, has gained more importance in the clinic, and significant rises are reported in its use. For this reason, several guidelines have been published to avoid unnecessary use and to establish a standard while clinicians are deciding on the use of FFP. But, it is still reported in literature that improper use of FFP is common despite these guidelines. Proper use of FFP is appropriate are given at Table 1.
Appendix 1

Appropriate and inappropriate use of FFP in various conditions.

| Indication                      | Appropriate n (%) | Inappropriate n (%) |
|---------------------------------|-------------------|---------------------|
| Warfarin overdose               | 33 (57.9%)        | 66 (78.6%)          |
| Hepatic diseases                | 5 (8.3%)          | 6 (7.1%)            |
| Massive transfusion/trauma      | 14 (24.6%)        | 4 (4.8%)            |
| Prophylaxis for surgery         | 3 (5.3%)          | 5 (6%)              |
| TTP/DIC                         | 2 (3.5%)          | 3 (3.6%)            |
| Total                           | 57 (100%)         | 84 (100%)           |

FFP: Fresh frozen plasma.
TTP: Thrombotic thrombocytopenic purpura.
DIC: Disseminated intravascular coagulation.

In our study, which aims to analyze the use of FFP and evaluate the audit of the transfusion in emergency departments, we determined that improper use of FFP had a rate of 59.6%. In a study conducted by Moylan et al in Australia, where there are more than one national guideline about blood and blood products, it was reported that 11% of the FFP transfusions were conducted with an improper indication and 18% with an uncertain indication.10 Luk et al. determined the improper use of FFP to be 45% in Canada, whereas, in Asian and European countries, the use of FFP with an improper indication ranged from 21% to 78%.4,11-12 In a study conducted in our country by Akkas et al, the rate of improper use was found to be 67%, which is similar to the result in our study.13 The discrepancy between the results of the studies may result from the differences in the national transfusion guidelines that are prepared according to the existing needs and sources and from the number of the centers included in the study. Besides, as a result of the inclusion of more than one clinic in the study at the center where the study was conducted, different clinical algorithms may have created a difference in FFP practices, thus affecting the final results of the study. The clinic that conducted FFP transfusion with the most appropriate indication in the study by Moylan et al was found to be a medical emergency clinic with a rate of 75%.10 The most commonly observed and the most significant complication of warfarin use is bleeding. In our study, we determined that the most common indication in the patients on whom FFP transfusion was conducted was warfarin overdose, with a rate of 70.2%. Warfarin overdose is one of the most commonly reported causes of FFP use in literature, similar to the result of our study.14,15 However, guidelines don’t recommend FFP transfusion to reverse the effect of warfarin without the presence of severe active bleeding.2 In our study, FFP transfusion in cases of warfarin overdose without active bleeding is regarded as improper use of FFP, and this indication is determined to be the most common reason for improper FFP practices, with a rate of 78.6%. In the study by Luk et al, the most common improper FFP use was reported to be present at active bleeding with PTT values normal or less than one and half times higher or at stages of preparation for surgical procedures. In the same study, the indication of the reversal of oral anticoagulant effect without bleeding was shown to be the rarest reason for improper FFP use, which is inconsistent with the results of our study.2 Similarly, in a study by Pahuja et al and in another one by Lingegowda et al, it was reported that no improper FFP use was seen to reverse warfarin effect in their patient groups.5,11 The hospital where our study was conducted is located in a densely populated area of settlement where the elderly are many in number; most of those who apply to the emergency department were of geriatric patient population. In this age group, warfarin is used more frequently due to atrial fibrillation, cerebrovascular disease, thromboembolism, which are more commonly seen with age, and more medical inspection is demanded from elderly patients during their emergency application. This was one of the reasons, in our study, that enabled us to identify warfarin overdose as the most common indication in improper FFP use, contrary to the data in literature. When the change in bleeding parameters with the transfusion of FFP was examined, we determined that the median INR value was 6.15 and PT value was 71.5 s prior to the transfusion in our study, whereas the median INR value decreased up to 2.46 and the PT value up to 27.4 s after the transfusion. Stanworth et al reported the decrease to be 0.2 s for INR and 1.9 s for PT after the FFP transfusion in adult patients in a wide series of 4635 diseases. Also, they determined that, in mild and moderate INR and PT increases, the effect of FFP transfusion on bleeding parameters were slight and that, in sharp contrast with this, there was greater reduction in extremely high INR and PT values with FFP transfusion.2 Likewise, Abdel-Wahab et al reported in their study that FFP transfusion had no effect on many patients for moderate PT values.15 In our study, we had patients who are INR, PT and PTT values couldn’t be read by the devices in the lab or whose values were too high to be read (38 patients for INR, 35 for PT and 27 for PTT). The highest reference values that our lab gave for these patients were accepted as parameters. The higher number of these patients in our study than in other studies could account for the higher rate of reduction in bleeding parameters after the transfusion in our study.

In our study, the number of cases is one of the limitations in our study. In addition, there is the possibility of having missing and faulty information in the record files of the patients in our study, which was conducted retrospectively.

5. Limitations
Our study is a single centered, retrospective study. The low number of cases is one of the limitations in our study. In addition, there is the possibility of having missing and faulty information in the record files of the patients in our study, which was conducted retrospectively.

6. Conclusion
We have determined that FFP transfusions were used with improper indications at a rate of high in the emergency department. As well as causing a serious economic burden and loss of sources, unnecessary FFP may be risky for the patients in terms of complications. Preparing an up-to-date transfusion guideline for the practices in emergency units in our country and training and supervising the medical staff at regular intervals may help prevent the deficit in FFP practices.

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Conflicts of interest
None declared.

References
1. Stanworth SJ. The evidence-based use of FFP and cryoprecipitate for abnormalities of coagulation tests and clinical coagulopathy. Hematol Am Soc Hematol Educ Program. 2007:179–186.
2. Luk C, Eckert KM, Barr RM, et al. Prospective audit of the use of fresh-frozen plasma, based on Canadian Medical Association transfusion guidelines. CMAJ. 2012;166:1539–1540.
3. Kakkar N, Kaur R, Dhanoa J. Improvement in fresh frozen plasma transfusion practice: results of an outcome audit. Transfus Med. 2004;14:231–235.
4. Moiz B, Avif FM, Hashmi KZ. Appropriate and inappropriate use of fresh frozen plasma. J Pak Med Assoc. 2006;56:356–359.
5. Stanworth SJ, Grant-Casey J, Lowe D, et al. The use of fresh-frozen plasma in England: high levels of inappropriate use in adults and children. Transfusion. 2011;51:62–70.
6. Pahuja S, Sethi N, Singh S, et al. Concurrent audit of fresh frozen plasma: experience of a tertiary care hospital. Hematology. 2012;17(5):306–310.
7. Crosby E, Ferguson D, Hume HA, et al. Guidelines for red blood cell and plasma transfusion for adults and children. Can Med Assoc J. 1997;156:1–24.
8. O’Shaughnessy DF, Atterbury C, Bolton Maggs P, et al. British Committee for Standards in Haematology. Blood Transfusion Task Force. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. Br J Haematol. 2004;126:11–28.
9. Kleinman S, Caulfield T, Chai P, et al. Toward an understanding of transfusion-related acute lung injury: statement of a consensus panel. Transfusion. 2004;44:1774–1789.
10. Moylan S, Szabo F, Scott H, et al. Use of fresh-frozen plasma at Royal Darwin Hospital: a retrospective audit. Intern Med J. 2008;38:686–691.
11. Lingegowda JB, Jeyakumar JD, Muddegowda PH, et al. An audit of requests for fresh frozen plasma in a tertiary care center in South India. J Lab Physicians. 2016;8:41–46.
12. Iorio A, Basileo M, Marchesini E, et al. Audit of the clinical use of fresh-frozen plasma in Umbria: study design and results of the pilot phase. Blood Transfus. 2008;6:211–219.
13. Akkas¸ M, Ataman DK, Akman C, et al. Inappropriate fresh frozen plasma use in coagulation disorder. Eur J Surg Sci. 2011;2:38–41.
14. Hui CH, Williams I, Davis K. Clinical audit of fresh-frozen plasma and platelets in a tertiary teaching hospital and the impact of a new transfusion request form. Intern Med J. 2005;35:283–288.
15. Ozgonenel B, O’Malley B, Kirshen P, et al. Warfarin reversal emerging as the major indication for fresh frozen plasma use at a tertiary care hospital. Am J Hematol. 2007;12:1091–1094.
16. Abdel-Wahab OI, Healy B, Dzik WH. Effect of fresh-frozen plasma transfusion on prothrombin time and bleeding in patients with mild coagulation abnormalities. Transfusion. 2006;46:1279–1285.