Original article

Calculation of fresh frozen plasma amount to correct high international normalized ratio

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Abstract:

Introduction: *Fresh frozen plasma (FFP) is the most widely-used blood component to correct high International Normalized Ratio (INR). However, little is known about the amount of FFP needed to correct high INR and factors related to normalized INR.* ***Methods:*** *A retrospective chart review study included 144 patients (96 warfarin and 48 nonwarfarin groups), aged over 18 years old, presenting high pretransfusion INR (PreINR; > 1.5) and receiving FFP with INR values after transfusion (PostINR) between September 1, 2019 and November 30, 2020.* Δ*INR (PreINR - PostINR) was calculated.* ***Results:*** *The median (range) PreINR was 2.67 (1.50-14.64) and median (range)* Δ*INR was 0.87 (-0.09-12.81). The mean (±SD) amount of FFP was 2.2±0.6 units. The median (range) time from FFP administration to PostINR testing was 4.59 hours (0-19). The median (range) time between PreINR and PostINR testing was 11.55 hours (3-33). Vitamin K was administered to 88 patients. The formula* Δ*INR after FFP 2 units = (0.91 x PreINR)-1.38 (R^2 = 0.96 between predicted INR and actual improvement INR; p < 0.001). The factors, correlated with normalized PostINR (INR < 1.5), were lower PreINR level (adjusted odds ratio [aOR] = 0.64, p = 0.017), intravenous vitamin K (aOR = 1.74, p = 0.025) and longer duration between PreINR and PostINR testing (aOR = 1.30, p = 0.001).* ***Conclusion:*** *This formula may be used to predict INR after FFP transfusion. Factors correlated with normalized INR after transfusion were lower pretransfusion INR, intravenous vitamin K and longer duration between pre- and posttransfusion INR measurements.*

Keywords : ● *Fresh frozen plasma* ● *INR* ● *Formula*

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นิพนธ์ต้นฉบับ

การคำนวณปริมาณพลาสมาสดแช่แข็งเพื่อแก้ไขภาวะการแข็งตัวของเลือดผิดปกติ

ลลาวรรณ์ พินิจทรัพย์สิน และ ยิ่งยง ชินธรรมมิตร์
คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล

บทคัดย่อ

บทนำ *พลาสมาสดแช่แข็ง (Fresh Frozen Plasma; FFP) เป็นส่วนประกอบเลือดที่มักใช้เพื่อแก้ไขภาวะการแข็งตัวของเลือดผิดปกติที่มีค่า INR (International Normalized Ratio) ยาว แต่ยังมีหลักฐานการศึกษาจำนวนน้อยเกี่ยวกับปริมาณที่เหมาะสมของ FFP ในการแก้ไขภาวะการแข็งตัวของเลือดผิดปกติ และปัจจัยที่มีผลต่อการทำให้ค่า INR กลับมาอยู่ในเกณฑ์ปกติ* ***วัตถุประสงค์*** *เพื่อหาสูตรที่สามารถคำนวณหาปริมาณ FFP ที่เหมาะสมในการแก้ไขภาวะการแข็งตัวของเลือดผิดปกติ และหาปัจจัยที่มีผลทำให้ค่าการแข็งตัวของเลือดกลับมาอยู่ในเกณฑ์ปกติ* ***วิธีการ*** *เป็นการศึกษาข้อมูลย้อนหลังจากเวชระเบียนผู้ป่วยทั้งหมด 144 คน ในโรงพยาบาลศิริราช ที่มีอายุมากกว่า 18 ปี โดยมีค่าการแข็งตัวของเลือดผิดปกติ (INR > 1.5) ร่วมกับได้รับ FFP และมีการบันทึกค่าของ INR หลังการได้รับ FFP โดยเก็บข้อมูลตั้งแต่วันที่ 1 กันยายน พ.ศ. 2562 ถึง วันที่ 30 พฤศจิกายน พ.ศ. 2563 โดยผู้ป่วยแบ่งเป็นสองกลุ่ม คือ กลุ่มที่ได้รับยาวาร์ฟาริน 96 คน และไม่ได้รับยาวอร์ฟาริน 48 คน และเก็บข้อมูลเพื่อนำมาวิเคราะห์ค่า INR ก่อน (PreINR) และหลังการได้รับ FFP (PostINR) และคำนวณค่า INR ที่เปลี่ยนแปลงไป (ΔINR = PreINR - PostINR)* ***ผลการศึกษา*** *ค่ามัธยฐานของ PreINR และ ΔINR คือ 2.67 (พิสัยตั้งแต่ 1.50 ถึง 14.64) และ 0.87 (พิสัยตั้งแต่ -0.09 ถึง 12.81) ค่าเฉลี่ยของปริมาณ FFP (±ส่วนเบี่ยงเบนมาตรฐาน) คือ 2.2±0.6 ยูนิต ค่ามัธยฐานของช่วงเวลาหลังจากได้รับ FFP ถึง PostINR คือ 4.59 ชั่วโมง (พิสัยตั้งแต่ 0 ถึง 19 ชั่วโมง) ค่ามัธยฐานของช่วงเวลาระหว่างการเจาะเลือดค่า PreINR และ PostINR คือ 11.55 ชั่วโมง (พิสัยตั้งแต่ 3 ถึง 33 ชั่วโมง) มีผู้ป่วยได้รับวิตามินเคทั้งหมด 88 คน สูตรของ ΔINR (หลังได้รับ FFP 2 ยูนิต) = (0.91 x PreINR) - 1.38 (ค่าสัมประสิทธิ์การถดถอย [R^2] = 0.96 และค่าความแม่นยำ [p-value] < 0.001) โดยปัจจัยที่มีผลต่อการทำให้ค่าการแข็งตัวของเลือดกลับมาอยู่ในเกณฑ์ปกติ คือ ค่า PreINR ที่ต่ำ [ค่าปรับแต่งอัตราส่วนออด (adjusted odds ratio; aOR) = 0.64, p-value = 0.017] การได้รับวิตามินเคฉีดเข้าทางหลอดเลือดดำ (aOR = 1.74, p-value = 0.025) และระยะเวลาระหว่าง PreINR และ PostINR ที่นานขึ้น (aOR = 1.30, p-value = 0.001)* ***สรุป*** *สูตรที่ได้จากการศึกษานี้อาจนำไปคาดคะเนค่าของ INR หลังจากได้รับ FFP และปัจจัยที่มีผลต่อการทำให้ค่าการแข็งตัวของเลือดกลับมาอยู่ในภาวะปกติ คือ ค่า PreINR ที่ต่ำ การได้รับวิตามินเคทางหลอดเลือดดำ และระยะเวลาระหว่างค่า PreINR และ PostINR ที่นานขึ้น*

คำสำคัญ : ● *พลาสมาสดแช่แข็ง* ● *INR* ● *สูตร*

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต. 2565;32:341-50.

Introduction

Fresh Frozen Plasma (FFP) can be prepared from healthy blood donors. FFP contains plasma proteins consisting of coagulation factors, natural anticoagulants and ADAMTS13. FFP is commonly used to replace among patients with various protein deficiencies such as coagulopathy in cirrhosis, antithrombin deficiency and ADAMTS13 deficiency in thrombotic thrombocytopenia purpura.[1]

Coagulograms are used to reflect coagulation capability in clinical practice, whereas prothrombin time is commonly used to reflect a part of the liver functions and to monitor the effect of warfarin in which the International Normalized Ratio (INR) is used as an internationally standardized value. When INR is above the therapeutic range, bleeding risk increases. FFP is the most widely-used blood component[2,3] to correct high INR.[4] However, many inappropriate uses[5] up to 25 to 30% of all transfused FFP units were noted in the US and the UK.[6,7] Normally, the amount of FFP to correct high INR is 10 to 15 mL/kg without any calculation of predicted INR change.[8] Whether INR is high or not, FFP is usually transfused in the same amount without any evidence to confirm that posttransfusion INR (PostINR) could be normalized. Furthermore, no standard formula is available to calculate the amount of FFP to correct high INR. Overall, little evidence exists about factors relating to normalized INR after FFP transfusion.[9,10] This study aimed to develop a formula to calculate the appropriate amount of FFP to be used and determine factors related to normalized INR after transfusion.

Methods

Patients and objectives

This observational clinical research constituted a retrospective chart review of patients older than 18 years, having high INR (> 1.5) and transfused with FFP from September 1, 2019, to November 30, 2020. The sample size was calculated using linear regression from the nQuery Advisor Program quoting data from the study of Sezik S, et al.[3] describing the relationship between delta INR and pretransfusion INR (PreINR). All 144 patients were classified in two groups; the warfarin group: 96 patients and the non-warfarin group: 48 patients. They were all evaluated for Pre- and PostINR. Patients transfused Prothrombin Complex Concentrate or recombinant activated Factor VII and whose duration between collecting pre- and PostINR was more than 12 hours were excluded. The primary objective was to develop a formula to calculate the appropriate amount of FFP to be used. The secondary objective was to study factors related to the normalized INR. This study was approved by the Siriraj Institutional Review Board (Si 632/2019) without funding support.

Data collection and analysis

Collected data included sex, age, comorbid diseases, principal diagnosis, PreINR, PostINR, ΔINR (PreINR to PostINR), date and time when blood samples were collected, vitamin K administration, amount of FFP transfused, and date and time when FFP was transfused.

Data were analyzed with descriptive statistics using SPSS Statistics for Windows, Version 26.0 (SPSS Inc., Chicago, IL, USA). The Mann-Whitney U test, Chi-square test and Kruskal Wallis test were used, as appropriate, to compare and identify associations of factors. Linear regression analysis was performed to develop a simple formula form of Delta INR (PreINR to PostINR) = a x preINR + b, where a and b are constants. The ΔINR and PreINR values were retrieved from patient medical records. Univariate logistic regression was employed to analyze the covariables on normalized INR (PostINR < 1.5). Significant factors were included in a multivariate analysis using the multiple logistic regression method. A *p*-value of < 0.05 was considered statistically significant.

Results

One hundred and forty-four patients were enrolled in this study with a mean (±SD) age of 68±14.9 years, and a mean (±SD) body weight of 60±12.4 kg. Among 96 patients in the warfarin group, 42.7% were men with

a mean (±SD) age of 71±12.5 years and a mean (±SD) body weight of 61±13.3 kg. Among 48 patients in the nonwarfarin group, 56.3% were men with a mean (±SD) age of 63±17.5 years and a mean (±SD) body weight of 58±10.4 kg. Warfarin overdose was the most common principal diagnosis (19.79%) in the warfarin group followed by gastrointestinal (GI) bleeding (18.75%), pneumonia (11.46%), intracranial hemorrhage (9.36%) and hematoma and mucosal bleeding (6.25%). In the warfarin group, indication for FFP transfusion was mostly bleeding (58.3%; GI bleeding and intracranial hemorrhage were the two most common sites of bleeding) followed by prophylaxis before invasive procedures (32.3%) and warfarin overdose (6.3%). In the non-warfarin group, pneumonia was the most common principal diagnosis (16.67%) followed by GI bleeding (6.25%), and valvular heart disease (6.25%). The potential causes of high INR in the nonwarfarin group were suspected to be multifactorial and related to systemic illnesses, e.g. sepsis, liver impairment, vitamin K deficiency and disseminated intravascular coagulation. Regarding comorbidities among 144 patients, hypertension was the most common comorbid disease (59.02%), followed by atrial fibrillation (46.53%), type 2 diabetes (28.47%) and chronic kidney disease (24.3%). Vitamin K was administered to 88 patients (oral 5, intravenous 83) which totaled 65.63% in the warfarin and 52.08% in the nonwarfarin groups. Bleeding was the most common indication for FFP transfusion in the warfarin group (58.33%). However, prophylaxis before any procedures was the most common indication for FFP transfusion in the nonwarfarin group (47.92%). The patients' characteristics, comorbidities, principal diagnosis, administration of vitamin K and the indications for FFP transfusion are summarized in Table 1.

The median (range) PreINR was 2.67 (1.50 to 14.64), and the median (range) improved INR (ΔINR) was 0.87 (-0.09 to 12.81). The mean (±SD) amount of FFP was 2.2±0.6 units. The mean (±SD) volume of 1-unit FFP was 254±22 mL. The median (range) amount of FFP was 8.9 mL/kg (4.4 to 23.5), while the median (range) time from FFP transfusion to PostINR testing was 4.59 hours (0-19). The median (range) time between PreINR and PostINR testings was 11.55 hours (3-33). The median PreINR, PostINR, ΔINR, the time from FFP transfusion to PostINR testing, the time between PreINR and PostINR testings and the mean amount of FFP in warfarin and nonwarfarin groups are presented in Table 2.

The formula ΔINR among all patients = (0.91 x PreINR) to 1.38 (R^2 = 0.96 between predicted INR and actual improved INR; $p < 0.001$; Figure 1), was similar to the formula among patients transfused with FFP of 2 units. For example, when PreINR = 4 and 2 units of FFP were administered, ΔINR = (0.91x4) - 1.38 = 2.26, then predicted PostINR = 4 - 2.26 = 1.74. When 2 units of FFP were administered again, ΔINR = (0.91x1.74) - 1.38 = 0.2, then predicted PostINR = 1.74 - 0.2 = 1.54.

In the nonwarfarin group, the formula ΔINR after FFP 2 units = (0.57 x PreINR) - 0.68 (R^2 = 0.65 between predicted INR and actual improved INR; $p < 0.001$; Figure 2). Regarding vitamin K administration (Figure 3), in the warfarin group with vitamin K intravenously ≥ 5 mg, the formula ΔINR after FFP 2 units = (0.94 x PreINR) - 1.4 (R^2 = 0.97 between predicted INR and actual improved INR; $p < 0.001$). In the nonwarfarin group with vitamin K intravenously ≥ 5 mg, the formula ΔINR after FFP 2 units = (1.02 x PreINR) – 1.5 (R^2 = 0.72 between predicted INR and actual improved INR; p <0.001). All formulas are demonstrated in Table 3.

The factors correlated with normalized PostINR (INR < 1.5), from univariate analysis, were PreINR (OR=0.62, $p < 0.001$), time between PreINR and PostINR testings (OR=1.16, $p < 0.001$), intravenous vitamin K (OR=1.47, $p = 0.031$), treated with warfarin (OR=2.33, P=0.02), pneumonia (OR=0.21, $p = 0.007$), chronic kidney disease (OR=0.3, $p = 0.006$) and atrial fibrillation (OR=0.5, $p = 0.04$). From multivariate analysis, the factors that significantly correlated to normalized INR were PreINR [adjusted odds ratio (OR)=0.64, $p = 0.017$), intravenous vitamin K (adjusted OR=1.74, $p = 0.025$) and time between PreINR and PostINR testings (adjusted OR=1.30, $p = 0.001$) as demonstrated in Table 4.

Table 1 Characteristics of patients

Characteristic	Warfarin (n = 96)	Nonwarfarin (n = 48)	Total (n = 144)
Mean age, year (SD)	71 (12.5)	63 (17.5)	68 (14.9)
Female, n (%)	55 (57.3)	21 (43.8)	73 (50.7)
Mean weight, kg (SD)	61 (13.3)	58 (10.4)	60 (12.4)
Principle diagnosis, n (%)			
Warfarin overdose	19 (19.8)	-	19 (19.8)
Gastrointestinal bleeding	18 (18.8)	3 (6.3)	21 (14.6)
Acute liver failure	-	1 (2.1)	1 (2.1)
Intracranial hemorrhage	9 (9.4)	2 (4.2)	11 (7.6)
Cerebrovascular disease	3 (3.1)	-	3 (3.1)
Acute decompensated HF	5 (5.2)	-	5 (5.2)
Pneumonia	11 (11.5)	8 (16.7)	19 (13.2)
Coronary artery disease	4 (4.2)	2 (4.2)	6 (4.2)
Valvular heart disease	1 (1.0)	3 (6.3)	4 (2.8)
Hematoma & mucosal bleeding	6 (6.3)	2 (4.2)	8 (5.6)
Peripheral arterial disease	-	1 (2.1)	1 (2.1)
Others	20 (20.1)	26 (54.2)	46 (31.9)
Comorbid disease, n (%)			
Hypertension	62 (64.6)	23 (47.9)	85 (59.0)
Type 2 diabetes	32 (33.3)	9 (18.8)	41 (28.5)
Chronic kidney disease	32 (33.3)	3 (6.3)	35 (24.3)
Benign prostate hyperplasia	5 (5.2)	3 (6.3)	8 (5.6)
Cirrhosis	4 (4.2)	5 (10.4)	9 (6.3)
Peripheral arterial disease	1 (1.0)	1 (2.1)	2 (1.4)
Deep vein thrombosis	15 (15.6)	1 (2.1)	16 (11.1)
Atrial fibrillation	64 (66.7)	3 (6.3)	67 (46.5)
Administration of vitamin K, n (%)			
Oral	5 (5.2)	-	5 (3.5)
Intravenous	57 (59.4)	26 (59.1)	83 (57.6)
Indication for FFP transfusion, n (%)			
Bleeding	56 (58.3)	15 (31.3)	71 (49.3)
Prophylaxis before any procedures	31 (32.3)	23 (47.9)	54 (37.5)
Disseminated intravascular coagulation	2 (2.1)	9 (18.8)	11 (7.9)
Warfarin overdose	6 (6.3)	-	6 (6.3)

FFP, fresh frozen plasma; Kg, kilogram

Table 2 Median PreINR, PostINR, ΔINR, time from FFP transfusion to PostINR testing, time between PreINR and PostINR testings and mean amount of FFP

Type	Warfarin group	Nonwarfarin group	Total
PreINR; median (range)	3.79 (1.5-14.64)	1.79 (1.5-5.47)	2.67 (1.50-14.64)
PostINR; median (range)	1.61 (1.00-3.61)	1.42 (1.03-3.07)	1.73 (1.00-3.61)
ΔINR; median (range)	1.85 (0.03-12.81)	0.32 (-0.09-2.40)	0.87 (-0.09-12.81)
FFP, unit; mean (SD)	2.13 (0.55)	2.24 (0.69)	2.17 (0.6)
Time FFP to PostINR, hour; median (range)	4.40 (0-13)	4.98 (0-19)	4 (0-19)
Time between PreINR and PostINR, hour; median (range)	11.28 (1-8)	12.08 (3-33)	10 (3-33)

PreINR, Pretransfusion INR; PostINR, Posttransfusion INR; ΔINR = Improved INR after FFP transfusion (PreINR-PostINR)

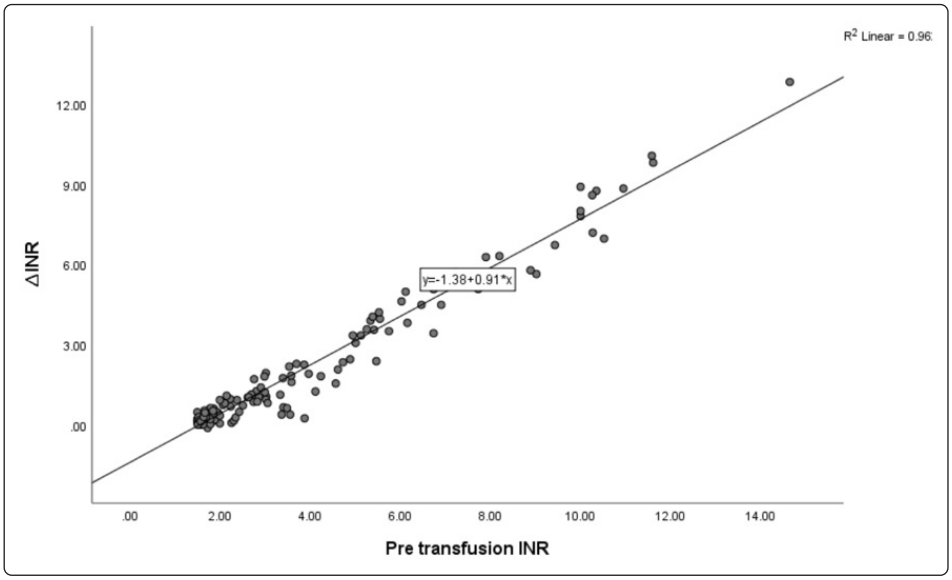

Figure 1. Relationship between actual INR before FFP administration (PreINR) and change of INR (ΔINR) values for patients receiving 2 units of FFP

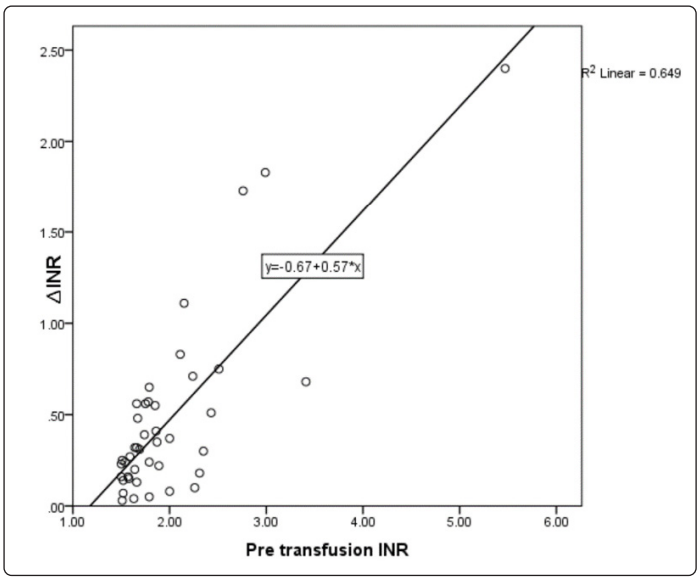

Figure 2. Relationship between actual INR before FFP administration (PreINR) and change of INR (ΔINR) values for patients in the *nonwarfarin group* receiving 2 units of FFP

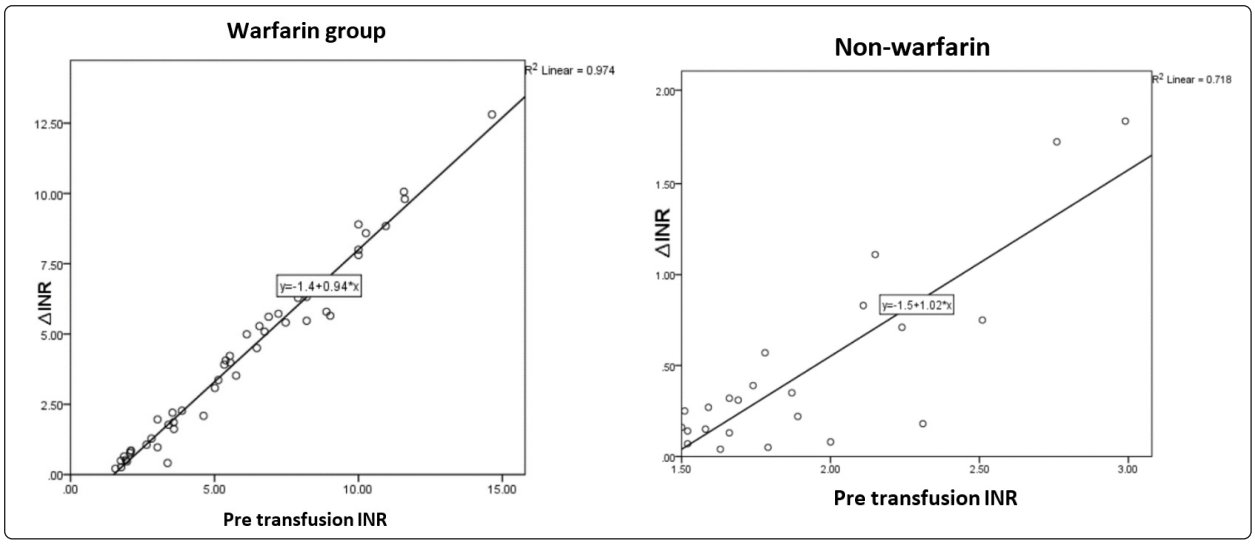

Figure 3 Relationship between actual INR before FFP administration (PreINR) and change of INR (ΔINR) values for patients receiving intravenous vitamin K ≥ 5 mg and two units of FFP

Table 3 Formulas of ΔINR classified by subgroup analysis

	N	Formula (A = PreINR)	R^2	*p* -value
All patients	144	0.908A - 1.378	0.962	< 0.001
Subgroup				
FFP 1 unit	3	0.617A - 0.718	1.000	0.006
FFP 2 units	126	0.908A - 1.375	0.964	< 0.001
FFP 3 units	4	1.126A - 2.343	0.978	0.011
FFP 4 units	10	0.971A - 1.527	0.967	< 0.001
Warfarin group	96	0.92A - 1.444	0.962	< 0.001
Warfarin group with FFP 2 units	84	0.921A - 1.455	0.962	< 0.001
Nonwarfarin group	48	0.526A - 0.586	0.589	< 0.001
Nonwarfarin group with FFP 2 units	42	0.573A - 0.675	0.649	< 0.001
Administration of vitamin K				
Warfarin group with FFP 2 units and Vit K IV ≥ 5 mg	48	0.941A - 1.404	0.974	< 0.001
Warfarin group with FFP 2 units and Vit K IV < 5 mg or oral vit K or without Vit K	36	0.780A - 1.168	0.936	< 0.001
Nonwarfarin group with FFP 2 units and Vit K IV ≥ 5 mg	23	1.024A - 1.496	0.718	< 0.001
Nonwarfarin group with FFP 2 and Vit K IV < 5 mg or oral vit K or without Vit K	19	0.476A - 0.521	0.786	< 0.001

FFP, fresh frozen plasma; Vit, vitamin; IV, intravenous

Table 4 Factors correlated to normalized PostINR (INR < 1.5)

Factor	Univariate OR (95%CI)	*p*-value	Multivariate Adjusted OR (95%CI)	*p*-value
PreINR	0.62 (0.5-0.76)	< 0.001	0.64 (0.438-0.922)	0.017
Time between PreINR and PostINR	1.16 (1.08-1.25)	< 0.001	1.30 (1.12-1.51)	0.001
Intravenous vitamin K	1.47 (1.036-2.01)	0.031	1.736 (1.07-2.81)	0.025
Treated with warfarin	2.33 (1.15-4.73)	0.019	0.82 (0.16-4.35)	0.816
Pneumonia	0.21 (0.07-0.65)	0.007	0.17 (0.21-1.37)	0.095
Chronic kidney disease	0.30 (0.13-0.71)	0.006	0.57 (0.13-2.56)	0.464
Atrial fibrillation	0.50 (0.25-0.97)	0.04	1.35 (0.33-5.81)	0.685

PreINR, Pretransfusion INR; PostINR, Posttransfusion INR

Discussion

Calculating the appropriate amount of FFP would help prevent the unnecessary transfusion of FFP in hospital settings. The formula, derived from the relationship between PreINR and ΔINR would be a helpful tool to predict improved INR after FFP transfusion. According to our results, the formula for all patients in this study was ΔINR after FFP 2 units = 0.91 x PreINR - 1.38, which could be used to predict improved INR among patients experiencing prolonged INR and receiving FFP 2 units. According to Table 1, the population had an average weight of 60 kg. Thus, this formula was the most suitable for a patient weighing about 60 kg. Most patients (87.5%) in our study received FFP of 2 units. That may have been because most Thai physicians learned that the proper amount of FFP used was about 10 ml/kg and believed that most Thai adult patients' weighed around 50 kg. Therefore, the amount of FFP was around 500 mL, which is about 2 units of FFP. Additionally, younger physicians experienced the practice from senior physicians and imitated the pattern of ordering 2 units of FFP for all degrees of coagulopathy. According to the 2020 ACC expert consensus, warfarin reversal should be 4-factor prothrombin complex concentrate (4F-PCC) or FFP of 10 to 15 mL/kg.[10] In our study, the median amount of FFP was 8.9 mL/kg, which was slightly lower than the suggested dose. Because most patients in our study received FFP of 2 units, we were interested in analyzing patients receiving FFP of 2 units. Concerning vitamin K administration, the effect of vitamin K on INR is usually delayed compared with FFP. Vitamin K can be given orally, subcutaneously, or intravenously. Slow intravenous administration effects a more predictable and rapid reduction in INR (4 to 6 hours) compared with oral (18 to 24 hours) or subcutaneous (unpredictable and not recommended) administration.[10] Thus, the shorter interval between FFP transfusion and repeated INR testing after transfusion (time FFP to PostINR) could be interpreted as vitamin K would minimally interfere with the effect of FFP to correct high INR. In this study, "time FFP to PostINR" was short (mean, 4.6 hours). However, the median (range) time between PreINR and PostINR testings was 11.55 hours (3 to 33), whereas vitamin K was usually given early before FFP administration. Therefore, this could affect the postINR value in a time-dependent pattern. We derived multiple formulas, which were compatible with specific patients. For example, amomg patients treated with warfarin, the formula was ΔINR after FFP 2 units = 0.92 x PreINR - 1.46, among patients not treated with warfarin, the formula ΔINR after FFP 2 units = 0.57 x PreINR - 0.68, and patients treated with vitamin K, were classified in 2 groups (warfarin and nonwarfarin), as demonstrated in Table 3. When the formula for warfarin users with intravenous vitamin K > 5 mg (0.941A to 1.404) was used, the ΔINR would be higher than that calculated from the formula for warfarin user without vitamin K (0.780A to 1.168) implying that vitamin intravenous K increased the ΔINR in this study.

This study represents a more specific and practical formula than related proposals. Rashidi et al.[2] derived the following formula: ΔINR after 1 FFP = 0.6 x PreINR - 0.7 with multiple variables (PreINR, body weight, FFP-to-PostINR interval and administration of vitamin K) using a sample of 956 patients treated with warfarin only and receiving FFP 1 unit. Moreover, the formula predicted 83% of the total variation in PostINR and repeated application of the FFP1 formula to the FFP2 in 4 subsets to increase predictive power to 95% (in 2 to 4 units of FFP). Although the sample size was smaller than the related study, the predictive power of our formula (R^2 =0.96) was higher than the formula by Rashidi et al.[2] Similarly, Frazee et al.[11] and Holland and Brooks[12] derived the formula using 91 patient samples which predicted 57% for Frazee et al.[11], and using 140 patient samples to calculate the improved INR with 2 units of FFP predicting 82%.

Currently, no standard formula has been established. We derived the formulas which were specific and practical for patients. Using these formulas should be based on clinical judgement for each patient. In multivariate analysis, three factors significantly correlated to normalized INR including PreINR, intravenous vitamin K and time between PreINR and PostINR. We interpreted that lower PreINR level (adjusted OR 0.64, *p*-value < 0.01) and longer duration between PreINR and PostINR (adjusted OR 1.3, *p*-value < 0.001) would be associated with normalized INR after FFP transfusion. Regarding intravenous vitamin K, more than 60% of our patients in this study were treated with warfarin, constituting a vitamin K antagonist substance; therefore, receiving vitamin K would directly correct prolonged INR.

Several limitations encountered in our study included the retrospective nature that might lead to missing data, especially among patients transfused with one unit and more than 2 units of FFP, and limited study number, which might have prevented some parameters from achieving statistical significance in the analysis.

In summary, this retrospective study demonstrated a practical formula to predict INR after FFP transfusion, especially for FFP 2 units. Using the formula could determine how many units of FFP were required to correct high INR to normalized INR and might prevent using unnecessary amounts of FFP. These formulas could be used among specific patients treated with or without warfarin and vitamin K. The factors correlated to normalized INR after FFP transfusion would serve as a guide predictor for a clinician to estimate the chance of normalized PostINR after FFP transfusion. Those included lower INR before correction, intravenous vitamin K and longer duration between pre- and post-transfusions.

Abbreviation and Acronyms: ΔINR = INR change after FFP transfusion; FFP = fresh frozen plasma; INR = international normalized ratio; PreInR = INR before FFP transfusion; PostINR = INR after FFP transfusion

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