

VITAMIN K INSTEAD OF FRESH FROZEN PLASMA

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Summary

The educational effect on the use of vitamin K and fresh frozen plasma (FFP) for the treatment of coagulation disorders in patients with solid tumors was monitored. The use of FFP was reduced and that of vitamin K increased by 39% and 137.5%, respectively, without any evidence of consequent increase in patient bleeding. The ratio of FFP and vitamin K unwanted side effects and price was 30:0 and 50:1, respectively. The rational administration of both FFP and vitamin K is more efficacious and cost-effective than the use of FFP alone.

KEYWORDS: *vitamin K, fresh frozen plasma, coagulation disorder*

VITAMIN K UMJESTO SVJEŽE SMRZNUTE PLAZME

Sažetak

Praćen je edukacijski učinak na potrošnje vitamina K i svježe smrznute plazme (SSP) u liječenju koagulacijskih poremećaja bolesnika sa solidnim tumorima. Smanjena je potrošnja SSP za 39% i povećana potrošnja vitamina K za 137,5%. U bolesnika zbog toga nije bilo povećanog krvarenja. Odnos neželjenih nuspojava SSP i vitamina K bio je 30:0. Cijena SSP i vitamina K bila je u omjeru 50:1. Racionalna primjena SSP i vitamina K je efikasnija i isplativija, nego sama uporaba SSP.

KLJUČNE RIJEČI: *vitamin K, svježe smrznuta plazma, koagulacijski poremećaj*

INTRODUCTION

The deficiency of coagulation factors results in the prolonged coagulation time. This occurs in liver disease, bowel disease, cholestasis, malabsorption, malnutrition, during therapy with coumarins, warfarins, antiepileptics, antibiotics and sulfonamides. Disregarding international guidelines, fresh frozen plasma (FFP) transfusions rather than vitamin K or clotting factor concentrate infusions are often used in coagulation factor deficiency. In about 50% of the cases worldwide, FFP is administered inappropriately (1-7). The FFP request forms are often placed for 1 to 2 units, which is subtherapeutic. FFP usage is inappropriate in hypoproteinemic states, anemia, bleeding without coagulation factor deficiency and volume depletion.

Fresh-frozen plasma

One unit of fresh frozen plasma (FFP) is taken from a unit of fresh whole blood. It contains all coagulation factors in normal concentrations as the whole blood does. A milliliter of FFP/kg increases the level of the majority of factors by 1% immediately after transfusion administered as a bolus. It is given in emergency when a deficiency of certain coagulation factors, coagulation inhibitors, and increased effect of certain anticoagulants are documented and no adequate substitutions are available. The deficiency can develop due to liver disease, warfarin and coumarin therapy, disseminated intravascular coagulation (DIC), acute bleeding, massive red blood cell transfusion, and infusion hemodilution. Plasma replacement is the-

rapeutically useful in thrombotic thrombocytopenic purpura (TTP) and adult hemolytic-uremic syndrome (HUS).

The average volume of a FFP unit is about 200 mL and it must be ABO compatible. On the other hand, Rh factor may or may not be compatible. As FFP does not contain any white blood cells, red blood cells, platelets, it does not carry a risk of developing cytomegalo virus (CMV) infection and graft-versus-host disease (GVHD). FFP

Table 1.

RECOMMENDATIONS FOR THE USE OF FRESH FROZEN PLASMA.

FRESH FROZEN PLASMA	
Use of fresh frozen plasma is likely to be appropriate:	
INDICATION	CONSIDERATION
Single factor deficiencies	Use specific factors or desmopressin if available.
Warfarin effect	In the presence of life-threatening bleeding. Use in addition to vitamin-K-dependent concentrates.
Acute disseminated intravascular coagulation (DIC)	Indicated where there is bleeding and abnormal coagulation. Not indicated for chronic DIC.
Thrombotic thrombocytopenic purpura (TTP)	Accepted treatment in conjunction with plasma exchange
Hemolytic uremic syndrome (HUS)	Accepted treatment
Coagulation inhibitor deficiencies	May be appropriate in patients undergoing high-risk procedures. Use specific factors if available.
Following massive transfusion or cardiac bypass	May be appropriate in the presence of bleeding and abnormal coagulation.
Liver disease	May be appropriate in the presence of bleeding and abnormal coagulation.
FRESH FROZEN PLASMA	
Situations in which transfusion of fresh frozen plasma is judged inappropriate	
Active bleeding or preparation for emergency surgery or invasive procedure in patient with PT or INR, APTT $\leq 1.5 \times$ normal (12-15 sec PT, INR 0.85-1.15, APTT 26-36 sec)	
Coagulopathy without clinical evidence of bleeding	
Active bleeding with normal coagulation profile	
Active bleeding without a coagulation profile	
Preparation for minor procedure in patient with liver disease and INR ≤ 2	
Reversal of oral anticoagulation with no clinical evidence of bleeding	

can transmit viral infections including human immunodeficiency virus (HIV), hepatitis viruses and other blood-borne infections. There is a risk of circulation overload, allergic, febrile and hemolytic transfusion reactions, and transfusion-related lung injury (TRALI). However, FFP is still used inappropriately (2). There are situations where its use is recommended although its efficacy has not been documented, or where alternative therapies may produce the same or even better results (8-11). To reduce warfarin- and coumarin-related anticoagulation effect, FFP is clinically indicated in patients with severe hemorrhage or in cases where the risk of developing hemorrhage is high (12). Otherwise, vitamin K is to be administered (13). Abrupt, life-threatening bleeding can be stopped with recombinant factor VIIa.

Vitamin K

Vitamin K enables carboxylation of factors II, VII, IX, X, and proteins C, S, Z. Oral administration of vitamin K (phytonadione) has a similar effect compared to the intravenous route. It is used in people with no food absorption problems, who have been overdosed with warfarin or whose coagulation factor levels are reduced (14). Treatment with vitamin K is more efficacious in warfarin overdose (Martefarin) than acenocumarol (Sintrom) or phenprocoumon (Marcoumar) (15).

Vitamin K, mainly in the form of vitamin K₁, is principally absorbed from the jejunum and ileum. The efficiency of absorption is variable and ranges from 10% to 80%. Vitamin K is delivered to the enterocytes in micelles formed from bile salts and other substances. Vitamin K is secreted by enterocytes into the lymphatics in the form of chylomicrons. It enters the circulation via the thoracic duct and is carried in the circulation to various tissues including hepatic, bone and spleen, in the form of chylomicron remnants. In the liver, some vitamin K is stored, some is oxidized to inactive end products and some secreted with very low-density lipoprotein (VLDL). Approximately 50% of vitamin K is carried in the plasma in the form of VLDL, about 25% in low-density lipoprotein (LDL) and about 25% in high-density lipoprotein (HDL). Vitamin K undergoes some oxidative metabolism. Excretion of vitamin K and its metabolites is mainly via the feces. Some urinary excretion of vitamin K also occurs.

MATERIAL AND METHODS

During five years, the Department of Transfusion Medicine was educating the Hospital staff in clinical indications for the appropriate use of FFP, with preference given to the administration of substitution therapy with vitamin K, ampoule à 10 mg i.v. The consumption of FFP units and vitamin K ampoules was retrospectively calculated according to the number of spent erythrocyte concentrate units and to the number of treated patients. Analysis was made when the FFP consumption curve sloping downward intersected the upward sloping curve of vitamin K consumption (Figure 1).

RESULTS

In the five years, the use of vitamin K ampoules increased by 137.5 %, while the FFP usage dropped by 39%. The number of patients decreased minimally, i.e. by 1.66%, and the number of spent erythrocyte concentrate units was re-

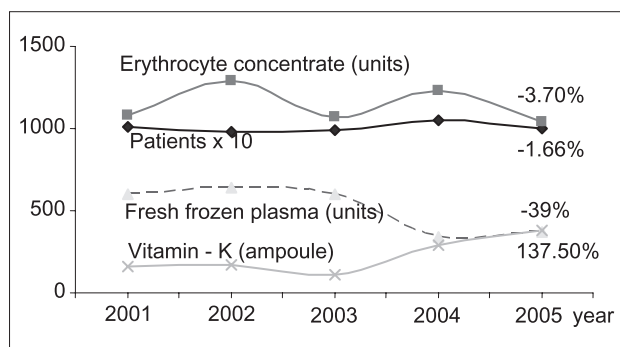


Figure 1. Use of erythrocyte concentrate, fresh frozen plasma and vitamin K in solid tumor patients over 5 years.

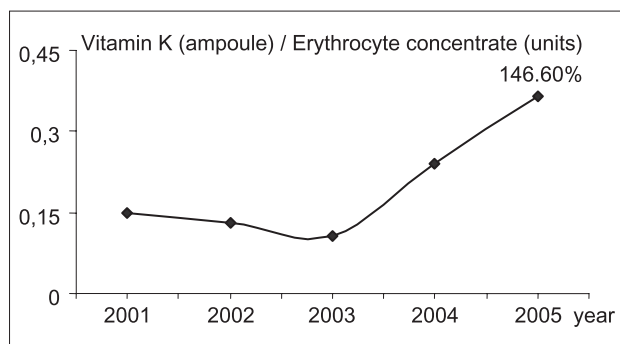


Figure 2. Increase in vitamin K usage compared to the use of erythrocyte concentrate in solid tumor patients over 5 years.

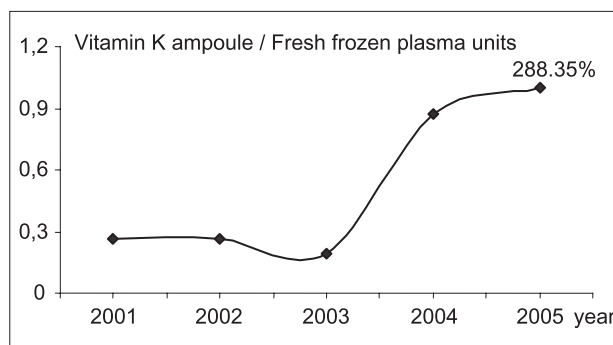


Figure 3. Increase in vitamin K usage compared to the use of fresh frozen plasma in solid tumor patients over 5 years.

duced by 3.7%. There were 30 unwanted effects reported to be caused by plasma therapy and none by vitamin K. The ratio of FFP and vitamin K price is 50:1.

DISCUSSION

Vitamin K has shown to be a cost-effective and beneficial replacement for FFP in the majority of coagulation disorders. With the administration of vitamin K there was no increase in patient bleeding requiring the increased use of erythrocyte concentrate units. However, it is not fully understood why FFP is frequently inappropriately used in both the developed and undeveloped world. Many medical professionals prescribe FFP, often without taking into account all aspects and the experience of transfusion medicine. Probably for inexperience, lack of knowledge and fear FFP is administered even when there is no clinical indication for its administration. Better education and communication between medical professionals are essential prerequisites for improving patient care and outcomes.

CONCLUSION

FFP should not be administered without documented coagulation disorder and appropriate clinical setting as this practice carries risks and is expensive. The rational use of FFP reduces treatment costs, risk of developing transfusion reactions, disease transmission, morbidity, mortality and the number of required plasma donors. The coagulation factor levels can be increased by oral or intravenous administration of vitamin K, which

carries less risk and cost than the administration of FFP. Adequate staff education and continuous monitoring assure adherence to norms and standards for FFP usage and improved quality of transfusion practice. The decreased use of FFP along with the increased use of vitamin K have reduced the incidence of unwanted effects to improve efficacy and cost effectiveness of treating patients with solid tumors.

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