

Utilization of Cryoprecipitate-A Retrospective Record Based Study

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Abstract: Cryoprecipitate is a product rich in clotting factors and is obtained from freezing and thawing of the plasma. It is originally developed as a therapy mainly for patients with anti-hemophilic factor deficiency, or hemophilia A which is a genetic disorder, cryoprecipitate has been in use for more than 60 years. However, cryoprecipitate is no longer administered according to its original purpose, and is now the usage has been shifted to replenish fibrinogen levels in patients with acquired coagulopathy, such as in clinical settings with hemorrhage including cardiac surgery, trauma, liver transplantation (LT), or obstetric hemorrhage. The main aim of this study was to know about the usage of cryoprecipitate in our institute. This is a retrospective record based audit carried out from January 2017 to March 2018. The requisition forms and the patients who received cryoprecipitate during this time were reviewed by using their medical records (including recipient age, sex, clinical diagnosis, and related management) and clinical laboratory. The number of concentrates of cryoprecipitate used and the number of transfusions (pools of concentrates) used were noted. Each requisition form was evaluated and the indication mentioned in the request form was labeled as appropriate or inappropriate. When the clinical condition matched with the absolute indications of cryoprecipitate usage then the usage was labeled as appropriate. Total 746 cryoprecipitate issues were done. 69.5 % were Females and 30.5 % Males. Most of the cases were in the age group 41 years to 55 years. Most of the cryoprecipitate units were utilized by medical oncology department and least units were used by plastic surgery, rheumatology, surgical oncology, cardiology and emergency medicine. Most common clinical diagnosis for which most of the cryoprecipitate units were used was multiple myeloma and least units were used for mitral valve replacement surgery. In this study, the majority of the utilization was appropriate as they were trained about the usage of blood and blood components and also they were under the supervision of the most experienced clinicians and nursing staff.

Keywords: cryoprecipitate, von willebrand factor, fibrinogen, hemophilia, multiple myeloma, coagulopathy. Factor xiii.

INTRODUCTION

Cryoprecipitate, commonly known as cryo is a frozen concentrate of high-molecular weight plasma proteins. Cryoprecipitate is a plasma product rich in factor VIII, von Willebrand factor (vWF); fibrinogen, factor XIII, and a few other minor cryoprecipitable proteins, including fibronectin [1]. Appropriate indications for cryoprecipitate use are very limited. The indications for transfusion acceptable at our institution are hypofibrinogenemia of various etiology, Tissue Plasminogen Activator (TPA) related life threatening hemorrhage, massive transfusion, uremic bleeding and von wille brand disease. These are the main indications for cryoprecipitate usage published in various blood transfusion practice guidelines [2, 3]. Each unit of

cryoprecipitate is commonly prepared from 1 unit of fresh frozen plasma. Plasma is obtained after centrifugation of whole blood unit within 6 hours of collection. After separation, plasma is stored at -30 degrees for 24 hours and later for cryoprecipitate preparation FFP is transferred to -80 degrees refrigerator for 2 hours. These units are thawed at for 30-45 minutes at 4 degrees temperature so as to bring the frozen plasma to liquid state and this plasma unit is centrifuged at 4 degrees centigrade at 3200 RPM for 10 minutes. A thick slushy like material is obtained at the bottom which is called cryoprecipitate and the supernatant fluid is called as cryo-poor plasma. Cryoprecipitate can be stored at -30 degrees centigrade for a period of one year. The process of deep freezing

and thawing of plasma (obtained from one unit of blood) during the preparation process generates platelet membrane microparticles, which are concentrated by cryoprecipitation; the microparticle concentration of cryoprecipitate is 265 times greater than that of the source plasma or frozen plasma [4]. These microparticles have been found to contain glycoproteins which are able to interact with fibrinogen, platelets, von Willebrand factor, and other proteins, and this interaction may be enhanced by cryoprecipitation [5].

AIM OF THE STUDY

To know the utilization of Cryoprecipitate in this Institute

MATERIALS AND METHODS

This is a retrospective record based audit carried out from January 2017 to March 2018, in the Department of Transfusion Medicine, Nizam’s Institute of Medical Sciences (NIMS), and Hyderabad. The requisition forms and the patients who received cryoprecipitate during this time were reviewed by using their medical records (including recipient age, sex,

clinical diagnosis, and related management) and clinical laboratory. The number of concentrates of cryoprecipitate used and the number of transfusions (pools of concentrates) used were noted. Each requisition form was evaluated and the indication mentioned in the request form was labeled as appropriate or inappropriate. When the clinical condition matched with the absolute indications of cryoprecipitate usage then the usage was labeled as appropriate.

RESULTS

Total of 107 cases from various departments of Nizam’s Institute of Medical sciences were included in this study between January 2017 and March 2018. Total 746 cryoprecipitate issues were done. 69.5 % were Females and 30.5 % Males. Most of the cases were in the age group 41years to 55 years and most number of cryoprecipitate units were utilized by the same age group; least cases belonged to age group 10 to 25 years and least number of cryoprecipitate units were utilized by them (TABLE 1).

Table-1: age wise distribution of cryoprecipitate issues

Age Group	Number Of Cases	Number Of Units Received
10 To 25 Years	16	109
26 To 40 Years	19	133
41 To 55 Years	43	316
> 56 Years	29	188
Total	107	746

In this study, most of the cryoprecipitate units were utilized by medical oncology department and least units were used by plastic surgery, rheumatology,

surgical oncology, cardiology and emergency medicine (TABLE 2).

Table-2: Department-wise cryoprecipitate utilization

Department	Number Of Issues
Medical Oncology	359
Ct Surgery	133
General Medicine	69
Hematology	65
Surgical Gastroenterology	54
Neurology	25
Orthopedics	15
Nephrology	6
Plastic Surgery, Rhuematology, Surgical Oncology,Cardiology And Emergency Medicine	4 Each
Total	746

Most common clinical diagnosis for which most of the cryoprecipitate units were used was

multiple myeloma and least units were used for mitral valve replacement surgery (TABLE 3).

Table-3: Clinical diagnosis of the cases

Clinical Diagnosis	Number Of Units Transfused
Multiple Myeloma	335
Liver Failure	137
Acute Promyelocytic Leukemia	74
Aortic Dissection Repair	52
Post Cabg	41
Polytrauma & Amputations	34
Chronic Kidney Disease	27
Liver Transplant Cases	16
Mitral Valve Replacement	07
Others	23

Number Of Cases	Number Of Units	Number Of Episodes
18	2	1
19	2	2
11	3	2
09	3	3
27	4	2
11	5	3
5	3	4
4	3	5
3	2	7
Total = 107		

In this study, number of cryoprecipitate transfusions ranged from 1 to 7 (TABLE 4)

DISCUSSION

Cryoprecipitate is a frozen product of plasma and can be obtained by deep freezing and thawing of the plasma at a specific temperature and centrifugation speed. It contains Factor VIII, von Willebrand Factor, Fibrinogen, Factor XIII, fibronectin and platelet micro-particles [1]. Indications for giving cryoprecipitate include Hemophilia, von Willebrand disease, Hypofibrinogenemia of various etiologies, Afibrinogenemia, Massive hemorrhage, disseminated intravascular coagulation and uremic bleeding tendency [6].

Fibrinogen is one of the essential factors for aggregation of platelets and also participates in secondary hemostasis. Fibrinogen deficiency could be congenital or acquired/ secondary. The congenital abnormalities of fibrinogen classified as rare disorders. Acquired hypofibrinogenemia may be secondary to consumptive coagulopathies such as disseminated intravascular coagulation (DIC), or post-partum hemorrhage. Other causes include underlying disease states that limit fibrinogen synthesis (hepatic dysfunction, hematological malignancies), or dilutional in massive blood transfusion, or from increased fibrinolysis [7]. Fibrinogen levels greater than 100 mg/dL generally are considered adequate for homeostasis [8].

Treatment of fibrinogen deficiency underlying the cause of the coagulopathy, but when bleeding

occurs or invasive procedures are planned, then replacement therapy using virally inactivated fibrinogen concentrate is the treatment of choice[7]. This offers rapid restoration of fibrinogen levels with a small volume infusion, minimal preparation time and lower potential risk of transfusion transmitted viral infections [9].

Cryoprecipitate and FFP are alternative treatments that should be used only when fibrinogen concentrate is not available [10]. Cryoprecipitate has been used successfully for the supplementation of fibrinogen in patients with acquired [11] hypofibrinogenemia. Although the fibrinogen content of cryoprecipitate may be variable [12], current standards require that all tested individual units of cryoprecipitate contain a minimum of 150 mg (4.4 μ mol) of fibrinogen. Commercially available factor concentrate are the product of choice for treatment of congenital or acquired specific deficiency [11]. They have far lower risks of blood-borne viral infection, particularly HIV, and are preferred to blood component therapy [10]. Von Willebrand's disease (VWD) is the most common inherited bleeding disorder [11]. The aim of therapy in VWD is to increase both, vWF and factor VIII levels. Cryoprecipitate has the full range of vWF multimers [9, 13] and provides a higher concentration of high-molecular-weight vWF than FFP [1]. Congenital factor XIII (FXIII) deficiency is a very rare form of hemophilia (one in 5 million) [14].

Acquired causes include disseminated intravascular coagulation, liver disease, L-asparaginase or fibrinolytic therapy. The bleeding manifestation is

characterized by umbilical stump bleeding in up to 80% [14], spontaneous abortion, mucosal bleeding and a high rate of spontaneous intracranial hemorrhage [15,16]. One to ten percent. Factor XIII activities in plasma is adequate for hemostasis [17]. Plasma-derived (PD) pasteurized FXIII concentrates or recombinant FXIII-A2 are used for prophylaxis [18].

Abnormal coagulation screen in conjunction with ongoing bleeding or oozing from puncture sites, mucous surfaces, or wounds usually calls for a blood product of component therapy. Despite the introduction of several guidelines, transfusion criteria still vary widely between clinicians [19]. A multidisciplinary team of obstetrician, anesthetists and hematologist is needed for the best management of PPH [20, 21].

Massive transfusion is arbitrarily defined as the replacement of a patient's total blood volume in less than 24 hrs [22]. Patients who receive massive transfusions may develop a dilution coagulopathy or DIC with thrombocytopenia and hypofibrinogenemia [23]. Most often, bleeding in such patients is related to thrombocytopenia, but there is evidence to suggest a possible advantage for using cryoprecipitate in these cases. It is generally considered appropriate to transfuse cryoprecipitate to correct prolongation of PT/APTT (> 1.5 x mean normal value) correlated with an increased microvascular bleeding, and to maintain Fibrinogen >1.0 g/l If not corrected by FFP.

Uremic bleeding syndrome is a well-recognized consequence of renal failure for more than 100 years [24]. The bleeding disorder of CRF is primarily an acquired defect of primary hemostasis leading to mucocutaneous type bleeding [25]. Platelet dysfunction and abnormal platelet-endothelial interaction are the main determinations of uremic Bleeding [26, 27].

Cryoprecipitate does not contain sufficient quantities of clotting factors: II, VII, IX and X. Therefore, it should not be used as a replacement therapy in patients with global coagulation factor deficiencies, like warfarin reversal or hepatic coagulopathy. In such cases FFP is used instead of cryoprecipitate.

In our study, 746 units were issued to patients with various department of this institute and all the usage was appropriate; our study is in correlation with the studies conducted by Pantanowitz *et al.* [28] and Nascimento *et al.* [29].

CONCLUSION

Cryoprecipitate transfusion is an integral part of management of bleeding and a good knowledge about the product use and adherence to appropriate indications will give desired results in patients with various absolute indications. In this study, the majority

of the utilization was appropriate as they were trained about the usage of blood and blood components and also they were under the supervision of the most experienced clinicians and nursing staff.

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