World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(RESEARCH ARTICLE)

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A retrospective study of Quality Control of Fresh Frozen Plasma (FFP) using Factor VIII levels in Central Blood Transfusion Services Indonesian Red Cross

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World Journal of Biology Pharmacy and Health Sciences, 2024, 20(01), 109–112

Publication history: Received on 26 August 2024; revised on 02 October 2024; accepted on 04 October 2024

Article DOI: https://doi.org/10.30574/wjbphs.2024.20.1.0719

Abstract

Background: According to a report from the Ministry of Health of the Republic of Indonesia, there are 470 blood transfusion units in Indonesia (235 units managed by PMI, 220 units managed by the government, four units of health services provinces, nine units of vertical hospital BTUs, two unit's Indonesian police and army hospital) distributed in 38 provinces. With so many BTUs spread throughout Indonesia, each BTU must have the same quality standards to maintain and improve blood services. Therefore, it is necessary to carry out Quality Control of the blood component products produced. Quality control is critical in safely and effectively processing blood and other components. A quality concept comprises quality control, assurance, and management. The laboratory service should have a quality control system. Quality testing and monitoring of blood components for transfusion have led to manufacturing or development. Factor VIII levels are internal quality control parameters required for quality analysis of Fresh Frozen plasma (FFP). As per international standard guidelines and government national regulations (PMK 91/2015) for quality assurance of FFP, 1% of all the units prepared, or four units per month, are tested for stable coagulation factors, including Factor VIII levels.

Objective: This study aims to evaluate factor VIII levels in each units FFP to ensure the availability of high-quality products with maximum therapeutic and minimal risk to recipients.

Methods: The retrospective data were collected from Research and Development CBTS Indonesian Red Cross archives from 1 January 2019 to 30 April 2023. Out of total 284 units FFP collected from Blood Transfusion Unit Indonesian Red Cross from Sumatera Island (Lampung Province, Palembang City, Pekanbaru City), DKI Jakarta Province (CBTS IRC), Jawa Barat Province (Depok City, District of Bekasi City, District of Bogor City), Banten Province (Tangerang City, District South of Tangerang City), Government Hospital (Fatmawati Hospital BTU), Army Hospital (RSPAD Gatot Soebroto BTU) were tested Quality Control with semi-automated Sysmex CA50 and automated Sysmex CA620 to determine of factor VIII levels in each unit FFP.

Results: A total of 284 units of FFP were tested, and mean factor VIII levels were 1,2 IU/mL with a range of 0,3 IU/mL-5,3 IU/mL, the normal range measure being > 0,7 IU/mL. Only 4,9 % (14/284) FFP units were inappropriate from the standard, while 95,1 % (270/284) FFP units could be accepted criteria standard.

Conclusion: We conclude that there are still those below-standard Quality FFP products from blood transfusion units; it is necessary to increase the processing of blood components so that the coagulation factors are maintained. From

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taking blood collecting, transporting, and shipping, it is required to carry out quality control to produce products that meet national and international standards.

Keywords: Quality Control; Blood Component Production; Fresh Frozen Plasma; Factor VIII

1. Introduction

Based on data reports from the Ministry of Health of the Republic of Indonesia from the registration application for health facilities, 265 registered Blood Transfusion Units (BTU) in Indonesia are organized by the government, local government, and the Indonesian Red Cross (PMI) in 2021[1]. While in 2023, there will be about 470 BTUs in Indonesia (235 units managed by the Indonesian Red Cross, 220 units managed by the government, four units of health services provinces, nine units of vertical hospital BTUs, two units of Indonesian police and army hospital) distributed in 38 provinces[2]. With so many BTUs spread throughout Indonesia, each BTU must have the same quality standards to maintain and improve blood services. Therefore, it is necessary to control the quality of blood component product. Quality control is critical in safely and effectively processing blood and other components. A quality concept comprises quality control, assurance, and management. The laboratory service should have a quality control system. Quality testing and monitoring of blood components for transfusion is carried out during the manufacturing or production development process. Factor VIII levels are internal quality control parameters required for quality analysis of Fresh Frozen plasma (FFP)[3]. According to international standard guidelines and national government regulations (PMK 91/2015), coagulation factors are tested to ensure the quality of FFP products, including factor VIII levels as much as 1% of all units produced, or four units of blood per month[5]. Based on the background above, researchers want to research the quality control production of FFP blood components to evaluate factor VIII levels in each FFP unit to ensure the availability of a standard quality product with maximum therapeutic effects and minimum risks for recipients.

2. Methods

The retrospective data were collected from Research and Development CBTS Indonesian Red Cross archives from 1 January 2019 to 30 April 2023. Out of total 272 units FFP collected from Blood Transfusion Unit (BTU) Indonesian Red Cross from Sumatera Island (Lampung Province, Palembang City, Pekanbaru City), DKI Jakarta Province (CBTS IRC), Jawa Barat Province (Depok City, District of Bekasi City, District of Bogor City), Banten Province (Tangerang City, District South of Tangerang City), Government Hospital (Fatmawati Hospital BTU), Army Hospital (RSPAD Gatot Soebroto BTU) were tested quality control with semi-automated Sysmex CA50 and automated Sysmex CA620 to determine of factor VIII levels in each unit FFP.

3. Results

From a total of 13 BTUs tested for quality, 272 FFP units tested for factor VIII had an average factor VIII content of 1.2 IU/mL with a range of 0.5 - 5.3 IU/mL, which is a normal level that should be >0.7 IU/mL (Table 1). Only 0.73% (2/272) of FFP units that do not meet the reference standards of the BTU have yet to implement GMP. Meanwhile, 99.27% (270/272) of FFP units were according to reference standards from BTUs receiving Good Manufacturing Practices (GMP) certification (Table 2).

4. Discussion

Plasma is the liquid part of blood, the pale-yellow liquid of whole blood consisting of water and several dissolved molecules, including proteins (such as albumin, fibrinogen, and globulin), electrolytes (such as sodium and chloride), sugars (such as glucose), lipids (such as cholesterol, and triglycerides), metabolic waste products (such as urea), amino acids, hormones, and vitamins[5]. FFP is prepared from whole blood or plasmapheresis within 8 hours of blood donation and should be stored at -18 °C or cooler. FFP has a shelf life of 12 months. It can be stored for up to 7 years at -65 °C if you want longer[6]. FFP contains labile coagulation factors, such as factor VIII. Usually, this FFP is required in blood transfusions for various diseases, such as coagulation factor deficiency with abnormal coagulation tests in the presence of active bleeding, planned surgery, thrombotic thrombocytopenic purpura, and congenital factor deficiency[7]. Our study assessed factor VIII levels in FFP storage units under quality control at CBTS and found 0.73% (2/272) of FFP units did not meet the reference standard. Several possibilities of decreasing factor VIII levels may be due to improper handling during blood collection, storage and transportation. Various factors related to personnel, machinery, materials, and techniques can influence clot formation. Several things can cause the loss of factor VIII in the FFP product, including the rate of blood flow that is not smooth, which will cause the formation of thrombus and increase the occurrence of blood clots[8]. Older studies have shown that recovery of factor VIII activity in plasma derived from whole blood decreases over

time up to 15-18 hours but is more excellent with whole blood stored at ambient temperature compared to 4º C[9,10]. Therefore, BTUs must be able to maintain the quality of the component products it produces. So, various things that can cause a decrease in product quality can be eliminated. The best thing every BTUs can do is implement GMP in their daily activities. World Health Organization (WHO) has implemented requirements for the collection, processing and quality control of blood, blood components and plasma derivatives by establishing a quality assurance system based on the existence of a national structure independent of the manufacturer, the presence of adherence to the quality assurance process for biological products, namely by carrying out control of starting materials, production processes and final products and strict adherence to GMP principles[11].

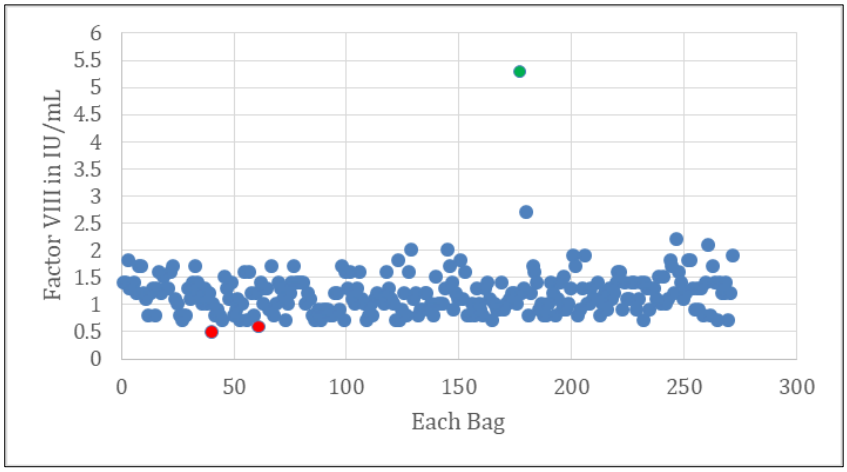

Figure 1 Factor VIII levels in IU/mL

Table 1 Quality control result of FFP units

Parameter	Mean	Range	The standard value of FVIII levels	Total of FFP Units
Factor VIII	1.2 IU/mL	0.5-5.3 IU/mL	>0.7 IU/mL	272

Table 2 Implementing GMP in BTUs

Description (BTUs)	Number of FFPs tested by QC	Number of FFPs that passed (%)	Number of FFPs that not passed (%)
Implementing GMP	221	100%	0%
Not yet implementing GMP	24	99.27% (270/272)	0.73% (2/272)
Not know	27	100%	0%
Total	272		

5. Conclusion

We conclude that there are still those below-standard quality FFP products from blood transfusion units; it is necessary to increase the processing of blood components to maintain the coagulation factors by implementing GMP by taking blood, collecting, transporting, and shipping. It is required to carry out quality control to produce products that meet national and international standards.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that none of them has any conflict of interest with any private, public or academic party related to the information contained in this manuscript.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study

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