***Thawing Time Difference between Fresh Frozen Plasma Using***

***Ziplock Plastic and non-Ziplock Plastic in Blood Transfusion Unit***

 ***Hasan Sadikin Hospital Bandung***

*Rima Rinanty1, Leni Lismayanti 2, Raja Iqbal Mulya Harahap2*

*1Clinical Pathology Resident, Medical Faculty of Padjajaran University;*

*2Clinical Pathology Department Medical Faculty of Padjajaran University*

*rimarinanty@gmail.com*

***ABSTRACT***

***Background****: In cases of bleeding that require FFP transfusion, the readiness of FFP depends on thawing time. Waterbath is often used in blood transfusion units because it is easy to perform, affordable and, easy to look for. To reduce the risk of contamination, protective plastics (Ziplock and non-Ziplock) are used. This study aims to determine whether there is a difference in thawing time between FFP using Ziplock plastic and non-Ziplock plastic.*

***Method****: This was an experimental design, conducted in the Blood Bank Unit of Hasan Sadikin Hospital from June-August 2021. Samples was divided into two groups: thawing using Ziplock and non-Ziplock, each group consists of volume 160-200 ml and 201-240 ml.*

***Results****: Total samples were 24 FFP bags. Blood group O+ was the most commonly ordered by the clinician followed by A+, B+, and AB+. In group 160-200 ml, median thawing time using Ziplock plastic was 8 minutes, non-Ziplock was 7 minutes with p value 0,111.While in group 201-240 ml, median thawing time using Ziplock was 15 minutes, non-Ziplock was 20 minutes with p value 0,332. Although there was a time difference in both groups, the difference was non-significant.*

***Conclusions****: There was no significant difference of thawing time between the two group. It is because the thawing time is affected by the volume, not the type of plastics. The more volume, the more heat transfer needed, the time will be longer. Although there was no significance different time, Ziplock plastic can be used to reduce the risk of contamination.*

***Keywords****: FFP, waterbath, thawing time, Ziplock plastic, and non-Ziplock plastic*

***Thawing Time Difference between Fresh Frozen Plasma Using***

***Ziplock Plastic and non-Ziplock Plastic in Blood Transfusion Unit***

 ***Hasan Sadikin Hospital Bandung***

Rima Rinanty1, Leni Lismayanti 2, Raja Iqbal Mulya Harahap2

1PPDS Patologi Klinik, Fakultas Kedokteran Universitas Padjadjaran;

2Departemen Patologi Klinik, Fakultas Kedokteran Universitas Padjadjaran.

rimarinanty@gmail.com

1. **INTRODUCTION**

Fresh Frozen Plasma (FFP) is a single unit of blood component, containing 250-500 mL of plasma which is frozen at a temperature of -30°C, at a predetermined time, which is 8 hours after phlebotomy.1 Fresh Frozen Plasma contains albumin, fibrinogen, protein C, protein S, antithrombin, and tissue pathway inhibitor.2 FFP transfusion is used to replace some coagulation factors and is indicated in patients who experience bleeding with a history of routine use of warfarin who will undergo invasive procedures, Thrombotic Thrombocytopenia Purpura (TTP), Hemolytic Uremic Syndrome (HUS), deficiency of coagulation factors, massive transfusion in hypocoagulable and hypovolemic patients. After FFP transfusion, coagulation factors will increase by as much as 20%.1,34

 In the case of bleeding requiring FFP transfusion, the readiness to administer FFP depends on the rate at which FFP is thawed.5 There are several tools that can be used to defrost FFP, namely a dry oven (incubator with temperature control) which requires a fast defrosted time of 10 minutes and is able to reduce the risk of contamination by bacteria.6 The second tool is a microwave oven, the advantage of this tool is that it has the fastest defrosting ability compared to other methods, which is ± 2-3 minutes, the disadvantages are that it is expensive and has limited capacity. The third tool is a waterbath, the advantage of this tool is that it is easy to use, by placing the FFP into a waterbath whose temperature has been set between 30-37°C for 20-30 minutes and the price is relatively affordable and easy to obtain, the disadvantage is that there is a risk of contamination when defrosting if the FFP is not covered with protective plastic when defrosting in the waterbath. Among the three FFP liquefaction tools, the waterbath is the most frequently used.7,8 A good quality FFP bag must meet several requirements such as being resistant to cold and hot temperatures, mechanically resistant, not releasing harmful substances into blood components, and having no color (transparent). Materials that meet these requirements are polyvinyl chloride (PVC).9,10 The use of plastic bags is highly recommended for thawing FFP in waterbath to avoid contamination by bacteria. Diluting FFP in waterbath without using a protective bag will increase the risk of septicemia as reported in a study conducted by Keller-Stanislawski B in Germany in 2009, found cases of septicemia caused by *Pseudomonas aeruginosa* due to thawing of FFP in waterbath that were not coated with plastic. Further research shows that a liquid volume of 0.025 ml on thawing without using plastic is capable of causing infection.7 Therefore, the plastic bags used in the FFP liquefaction process must be resistant to chemicals, water vapor, have a high melting point (115-135°C), easy to obtain and inexpensive.11,12 The best plastic material for this purpose is polyethylene which consists of High-Density Polyethylene (HDPE) and Low-Density Polyethylene (LDPE).9

 Factors that can affect the thawing time of FFP are volume, number of bags of FFP being defrosted simultaneously, thawing temperature, and the type of protective plastic. According to research conducted by Platton S in London (2019), the larger the volume of disbursed FFP, the longer it will take to melt.13,14 Another study conducted by Rhame et al, stated that the melting time of FFP without the use of plastic at 37°C takes 17 minutes and the melting process using plastic at the same temperature takes 28 minutes. Although faster, thawing of FFP without the use of plastic can pose a risk of septicemia.15–17 Dry ovens and microwave ovens are rarely available and are more expensive than waterbath, therefore the use of waterbath can help hospitals or blood care units to choose which method has the fastest thawing time without risking contamination.

1. **RESEARCH PURPOSES**

 This study aims to analyze the difference in the thawing time of FFP using Ziplock and non-Ziplock plastics.

1. **RESEARCH METHODS**

 This study used an experimental method with a total sample of 24 FFP bags, which were determined based on the Federer formula.18 The study was conducted at the Blood Service Unit of Hasan Sadikin General Hospital starting from June until August 2021. This study used an FFP bag that was ordered by a clinician and met the predetermined volume groups, namely 160-200 ml and 201-240 ml. Apart from volume, the FFP groups were divided into two groups of defrosting, using Ziplock and non-Ziplock plastic bags. Before thawing, pre-warming waterbath was performed at 37°C for ± 10 minutes in the Ziplock and non-Ziplock groups. The chi-square test was carried out to determine the characteristics of the data, the normality test of the data using Shapiro-Wilk followed by a different test using Mann Whitney for the analysis of time differences with p value <0.05 is significant. This study protocol was approved by the Ethical Committee of Dr. Hasan Sadikin General Hospital Bandung.

1. **RESULT**

 During the study, 24 samples were obtained, with a description of the characteristics listed in Table 1.

**Table 1 Data Characteristics of FFP Samples**

|  |  |  |
| --- | --- | --- |
| Sample characteristics | Ziplock n (%) | Non-Ziplock n (%) |
| Blood type |  |  |
| A+ | 3 (25,0) | 2 (16,7) |
| B+ | 1 (8,3) | 3 (23,0) |
| AB+ | 0 (0,0) | 1 (8,3) |
| O+ | 8 (66,7) | 6 (50,0) |

From table 1, it is found that the highest demand for FFP is in the O+ blood group, both from the Ziplock and non-Ziplock groups, and the least demand is in the AB+ blood group both from the Ziplock and non-Ziplock groups.

**Table 2 Comparison of Volumes Using Zip Lock and non-Zip Lock Plastics**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Ziplock plastic****(n=12)** | **Non-Ziplock plastic** **(n=12)** | ***p-value*** |
| Median (Min-Max) | Median (Min-Max) |
| **Volume (ml)** | 201(180-220) | 208 (183-239) | 0.524 |

 Table 2 shows that the volume in the Ziplock group is less than the volume in the non-Ziplock group, but the difference is not significant. The data normality test was carried out using Shapiro Wilk and the data was not normally distributed, followed by the Mann-Whitney test to analyze the difference in thawing time between FFP using Ziplock and non-Ziplock plastic, the results were as shown in Table 3.

**Table 3 Comparison of FFP Thawing Time Using Ziplock Plastic and non-Ziplock Plastic**

|  |  |  |  |
| --- | --- | --- | --- |
| **FFP BagVolume** | **Thawing time (minute)** | **Median difference****(95% CI)** | ***p value*** |
| **Ziplock plastic bag****(n=12)** | **Non-Ziplock plastic****bag (n=12)** |
| Median (Min-Max) | Median (Min-Max) |
| 160-200 ml | 8 (8-16) | 15 (8-16) |  -7 (-8 – 0) | 0,11 |
| 201-240 ml | 15 (8-28) | 20 (14-30) |  -5 (-15 – 8) | 0,33 |

 From the results of the analysis above, there is non-significant time difference between thawing using Ziplock and non-Ziplock plastics.

1. **DISCUSSION**

From the data characteristics in table 1, it is found that the most blood type is O+ and the least is AB+. This is in accordance with research by Amit Agrawal et al in India, that out of a total of 10,000 donors, blood type O+ is the most common (37.1%) followed by B+ (32.3%), A+ (22.8%), and AB+. (7.7%).11 The distribution of this blood group corresponds to the percentage in the world, which is the most O+ blood group.19,20

 In table 3, the volume group is 160-200 ml, the median time to defrost Ziplock vs non-Ziplock plastic bags is 8 minutes vs 15 minutes; p=0.11. In the 201-240 ml volume group, the median time for thawing of FFP using a Ziplock VS non-Ziplock plastic bag was 15 vs 20 minutes; p = 0.33. There was no significant difference in thawing time using Ziplock and non-Ziplock plastic.

The difference in thawing time was not significant because the thawing time was mainly influenced by the volume of FFP, not by the type of plastic.21 In table 3, the more volume, the longer the thawing time. The theoretical basis of this statement is that the more volume, the greater the heat transfer required for thawing, this is in accordance with research conducted by Virtanen et al who carried out the thawing process using a microwave assisted thawing apparatus on a food system model with thick and homogeneous consistency. There was no significant volume change during the freezing and thawing process, the models were divided into two treatment groups, namely samples with a thickness of 3.6 cm and 5.5 cm. From this study, it was found that volume is the most significant factor affecting the thawing time, a sample with a thickness of 5.5 cm takes three times longer than a sample with a thickness of 3.6 cm. From this research, it was found that volume is the most influencing factor in thawing time.19,21

 Ziplock plastic base material is LDPE which has a thickness of ± 0.5 mm, thinner than non-Ziplock plastic with HDPE base material, which is thicker (10-30 mm). In addition, Ziplock plastic has a plastic tip that is tight, so that there is no air coming in and out during the defrosting process, the temperature during defrosting is stable. In contrast to non-Ziplock plastic which does not have a tight end, causing air to enter and exit during defrosting so that the temperature during defrosting is unstable, this also causes non-Ziplock plastic to not be completely submerged during defrosting, in contrast to Ziplock plastic which is completely submerged.19,21

 Although not significantly different, defrosting using Ziplock plastic can be an option in daily practice, because the melting temperature is stable and can reduce the risk of contamination, because LDPE plastic has resistance to temperatures up to 90°C.

1. **CONCLUSION**

 There was no significant difference in the duration of FFP thawing using Ziplock and non-Ziplock plastic. However, Ziplock plastic can be an option to reduce the risk of contamination.

**REFERENCES**

1. Duguid J, O’Shaughnessy DF, Atterbury C, Maggs PB, Murphy M, Thomas D, et al. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. British Journal of Haematology [Internet]. 2004 Jul 1 [cited 2021Apr05];126(1):1128.Availablefrom:https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-2141.2004.0.

2. Khawar H, Kelley W, Stevens JB, Guzman N. Fresh Frozen Plasma (FFP). StatPearls [Internet]. 2021 Sep 24 [cited 2021 Apr 11]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK513347/

3. Veera RRL, Schneider D, Pickens P v. Fresh Frozen Plasma (FFP) Usage and Appropriateness in Adult Medical in-Patients: A Retrospective Audit. Blood [Internet]. 2012 Nov 16 [cited 2021 Apr 11];120(21):4375–4375. Availablefrom:https://ashpublications.org/blood/article/120/21/4375/86602/Fresh-Frozen-Plasma-FFP-Usage-and-Appropriateness

4. Cardigan R, Green L. Thawed and liquid plasma – what do we know? Vox Sanguinis [Internet]. 2015 Jul 1 [cited 2021 Apr 15];109(1):1–10. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/vox.12251

5. Meledeo MA, Peltier GC, McIntosh CS, Corley JB, Bynum JA, Cap AP. Field-expedient thawing of fresh-frozen plasma. Transfusion (Paris) [Internet]. 2020 Jun 1 [cited 2021 Apr 15];60(S3):S87–95. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/trf.15652

6. Churchill WH, Schmidt B, Lindsey J, Greenberg M, Boudrow S, Brugnara C. Thawing fresh frozen plasma in a microwave oven. A comparison with thawing in a 37 °C waterbath. American Journal of Clinical Pathology. 1992;97(2):227–32.

7. Pinki S, Mohan G, Rafi A, Innah S, Thomas T. Rapid dry plasma thawing system: An alternative to conventional thawing baths. Asian Journal of Transfusion Science [Internet]. 2017 Jul 1 [cited 2021 Apr 20];11(2):147. Available from: https://www.ajts.org/article.asp?issn=0973-6247;year=2017;volume=11;issue=2;spage=147;epage=150;aulast=Pinki

8. Heger A, Pock K, Römisch J. Thawing of Pooled, Solvent/Detergent-Treated Plasma octaplasLG®: Validation Studies Using Different Thawing Devices. Transfusion Medicine and Hemotherapy [Internet]. 2017 Apr 1 [cited 2021 Apr22];44(2):94Availablefrom:https://www.karger.com/Article/FullText/460

9. (PDF) Materials Selection Analysis: Bag for Viable Blood Storage [Internet]. [cited 2021 Apr 24].Available from: https://www.researchgate.net/publication/291766516\_Materials\_Selection\_Analysis\_Bag\_for\_Viable\_Blood\_Storage

10. Castillo B, Dasgupta A, Klein K, Tint H, Wahed A. Blood components: Processing, characteristics, and modifications. Transfusion Medicine for Pathologists. 2018;19–36.

11. (PDF) Materials Selection Analysis: Bag for Viable Blood Storage [Internet]. [cited 2021 May 1]. Available from: https://www.researchgate.net/publication/291766516\_Materials\_Selection\_Analysis\_Bag\_for\_Viable\_Blood\_Storage

12. Meutia Zahra N, Widiyanti P. The Role of Chitosan on Polyvinyl Chloride (PVC)-Glycerol Biocomposites for Blood Bag Application. 2018 [cited 2021 May 1]; Available from: www.scientific.net/JBBBE.37.94

13. Chavan SK. Determination of rate and analysis of reasons for discarding blood and blood components in a blood bank of tertiary care hospital:a retrospective study. International Journal of Research in Medical Sciences. 2017 Feb 20;5(3):1111.

14. Platton S, Elegbe O, Bower L, Cardigan R, Lancut J, McCullagh J, et al. Thawing times and hemostatic assessment of fresh frozen plasma thawed at 37°C and 45°C using water-bath methods. Transfusion (Paris) [Internet]. 2019 Nov 1 [cited 2021 May 5];59(11):3478–84. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/trf.15553

15. Green L, Bolton-Maggs P, Beattie C, Cardigan R, Kallis Y, Stanworth SJ, et al. British Society of Haematology Guidelines on the spectrum of fresh frozen plasma and cryoprecipitate products: their handling and use in various patient groups in the absence of major bleeding. British Journal of Haematology [Internet]. 2018 Apr 1 [cited 2021 May 5];181(1):54–67. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.15167

16. Plotz RD, Ciotola RT. Thawing of Fresh-Frozen Plasma at 45 °C versus 37 °C: Comparison Using Satellite Packs of the Same Donor Units. American Journal of Clinical Pathology [Internet]. 1988 Mar 1 [cited 2021 May 8];89(3):3814Availablefrom:https://academic.oup.com/ajcp/article/89/3/381/179082

17. Dhantole L, Dubey A, Sonker A. A study on factors influencing the hemostatic potential of fresh frozen plasma. Asian Journal of Transfusion Science [Internet]. 2019 Jan 1 [cited 2021 May 8];13(1):23. Available from: /pmc/articles/PMC6580834/

18. Ihwah A, Deoranto P, Wijana S, Dewi IA. Comparative study between Federer and Gomez method for number of replication in complete randomized design using simulation: study of Areca Palm (Areca catechu) as organic waste for producing handicraft paper. IOP Conference Series: Earth and Environmental Science [Internet]. 2018 Mar 1 [cited 2021 May 12];131(1):012049.Availablefrom:https://iopscience.iop.org/article/10.1088/1755-1315/131/1/012049

19. Agrawal A, Tiwari AK, Mehta N, Bhattacharya P, Wankhede R, Tulsiani S, et al. ABO and Rh (D) group distribution and gene frequency; the first multicentric study in India. Asian Journal of Transfusion Science [Internet]. 2014 [cited 2021 Jul 11];8(2):121. Available from: /pmc/articles/PMC4140055/

20. World Population By Percentage of Blood Types - WorldAtlas [Internet]. [cited2022May1].Availablefrom:https://www.worldatlas.com/articles/what-are-the-different-blood-types.html

21. Virtanen AJ, Goedeken DL, Tong CH. Microwave assisted thawing of model frozen foods using feed-back temperature control and surface cooling. Journal of Food Science. 1997;62(1):150–4.