FACTORS INFLUENCING PLATELET APHERESIS YIELD AND EFFECTS OF DONATION AMONG PLATELET APHERESIS DONORS

BY

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Dissertation Submitted In Partial Fulfilment Of The Requirements For The Degree Of Masters Of Pathology (Haematology)

UNIVERSITI SAINS MALAYSIA
2016

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ACKNOWLEDGEMENT

In the name of ALLAH, the Most Merciful and Compassionate. All praises and gratitude are due to Allah. May peace and blessing be upon Prophet Muhammad s.a.w, his family and companions.

First and foremost, I would like to take this opportunity to thank my supervisor Dr Marini Ramli for her sincere infinite dedication, support, patience, guidance and encouragement that she has embraced in me throughout the study and an excellent positive criticism that she has given as a feedback during the writing of this dissertation.

Besides that, I would like to offer my special gratitude to Puan Salamah and all the respected staff nurses who were involved in helping out and guiding me throughout many aspect of my laboratory work carried out during this study.

Apart from that, I would like to thank Associate Prof Dr Suhair Abbas, my co-supervisor and Haematologist of HUSM for her great support and helpful advices. A great word of appreciation goes also to the haematological laboratory technician of transfusion unit and to the medical officer of transfusion unit Dr

Salfarina for her great contribution of ideas and opinions on the procedure aspect of my study. This study was supported by USM Grant No: 304/PPSP/61313134.

Last but not least, I would like to dedicate this academic endeavour to my beloved wife, Dr Faizah bt Mohamed Sikandar, my children: Najihah, Nabilah and Faris for their love, support and motivation in making this study successful.

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List of Abbreviations

AABB	American Association Blood Bank
ACD-A	Anti-coagulant citrate dextrose adenine.
CFC	Continous flow centrifugation.
FBC	Full Blood Count
EDTA	Disodium Ethylene Diamine Tetra Acetic Acid
Hb.	Haemoglobin.
HPA	Human Platelet Antigen
IFC	Intermittent flow centrifugation.
HUSM	Hospital Universiti Sains Malaysia.
PTP	Post Transfusion Purpura.
RBC'S	Red Blood Cells
SD	Standard Deviation.
WBC'S	White Blood Cells

ABSTRACT

FACTORS INFLUENCING PLATELET APHERESIS YIELD AND EFFECT OF DONATION AMONG DONORS.

The development in transfusion practice with discovery of advanced cell separators have defined platelet therapy in terms of quality and productivity. Previous studies have shown that transfusion of high yield platelet products could reduce the requirement of transfusion among thrombocytopenic patients

The aim of this study was to investigate the factors that influence the platelet apheresis yield among apheresis donors by studying the donor variables and machine variables . Differences in donors peripheral count pre and post apheresis procedure were also studied. Correlation of serum ferritin level with platelet apheresis yield was also determined in this study.

A prospective study was conducted from September 2015 to August 2016 at Hospital Universiti Sains Malaysia (HUSM) , Kubang Kerian, Kelantan. Thirty five male subjects were recruited for this study

Full blood count (FBC) and serum ferritin were taken prior to the donation. Post donation, another sample of FBC was taken. FBC and serum ferritin was run by Diagnostic Stago haematology analyser Sysmex XE 5000 and Bio-Architect respectively. FBC was analysed pre and post donation for haemoglobin level, haematocrit and platelet count. Other donors demographic data which included age, height, weight, frequency of donation and ABO blood group were taken from the donor apheresis registry book. Data regarding machine variables (anticoagulation infusion rate, processing time and plasma volume

collected) were retrieved from the apheresis machine. The apheresis machine used in this study was Trima Accel cell separator.

Height, pre donation platelet count and machine variables revealed significant positive correlations with platelet apheresis yield. There were also significant differences in donor peripheral counts pre and post apheresis procedure. Positive correlation of serum ferritin level with platelet yield was seen. No significant IDA was detected among the apheresis donors.

In conclusion, some of the donors' and all machine related variables showed significant relationship with platelet apheresis yield. There were also significant changes pre and post donation peripheral counts. Donors with high pre platelet count with adequate optimisation of machine variables can potentially produce a higher platelet apheresis yield collection.

ABSTRAK

FAKTOR YANG MEMPENGARUHI KEPEKATAN AFERESIS PLATELET DAN KESAN PENDERMAAN KEPADA PENDERMA.

Kemajuan dalam bidang transfusi telah dikenal pasti dengan penemuan mesin yang bernama " Mesin apheresis " atau " sel pemisah " yang dapat menghasilkan platelet yang effisien dari segi kualiti dan produktiviti. . Kajian telah membuktikan bahawa pemindahan komponenen platelet aferesis yang berkepekatan tinggi boleh membantu mengurangkan keperluan pemindahan platelet dalam kuantiti yang banyak kepada pesakit yang mengalami masalah kekurangan platelet.

Tujuan kajian ini adalah untuk mengkaji faktor-faktor yang mempengaruhi hasil platelet aferesis di kalangan penderma aferesis tetap dengan mengkaji pembolehubah penderma dan mesin aferesis. Perbezaan kiraan penderma periferal pra dan selepas prosedur juga di kaji. Perhubungan di antara tahap serum ferritin dengan hasil pekatan platelet aferesis juga elah diselidk dalam kajian ini.

Satu kajian telah dilakukan dari bulan September 2015 hingga Ogos 2016 (selama tempoh 11 bulan) di HUSM, Kubang Kerian, Kelantan. Seramai 35 penderma apheresis di ambil sebagai subjek kajian dimana kesemua penderma tersebut terdiri daripada kaum lelaki.

Ujian kiraan sample darah sel darah penuh dan tahap serum ferritin di ambil sebelum pendermaan. Selepas pendermaan, cuma ujian kiraan sel darah penuh sahaja telah di ambil. . Ujian tersebut dikendalikan oleh mesin Diagnostik Stago penganalisa hematologi Sysmex XE 5000 dan mesin Bio-architect. Ujjian

kiraan sel darah penuh di analisa untuk mengenal pasti bacaan sel daha haemoglobin, hematokrrit and skiraan sel darah platelet sebelum dan selepas pendermaan. Sebahagian pembolehubah data demografik penderma seperti, umur, ketinggia, berat, kekerapan menderma dan kumpulan darah ABO penderma di ambil dari buku pendaftaran apheresis penderma. Bagi data untuk parameter mesin seperti kadar anti-koagulasi, masa pemprosesan dan bilangan plasma terkumpul telah di ambil dari mesin aferesis. Jenis mesin aferess yang di gunakan dalam kajian ini ialah Trima Accel sel pemisah

Kajian membuktikan bahawa ketinggian dan bilangan sel darah platelet pra penderma serta kesemua pembolehubah mesin menunjukkan hubungan secara langsung dengan kepekatan hasil platelet. Kajian juga membuktikan terdapat pengurangan ketara dalam bilangan sel darah sebelum dan selepas . Hubungan secara langsung dapat dilihat di antara tahap serum ferritin dengan kepekatan hasil platelet serta kesemua subjek kajian kami memiliki tahap serum feritin yang normal.

Kesimpulannya, sebilangan pembolehubah penderma serta kesemua bolehubah mesin hubungan yang berkait rapat dengan hasil platelet apheresis. Terdapat juga perubahan ketara ujian sel darah penderma sebelum dan selepas pendermaan.

CHAPTER 1

INTRODUCTION

1.0 GENERAL INTRODUCTION

Platelet transfusion has been one of the most important supportive therapies for thrombocytopenic patients. This is clearly evidenced by persistent increase in the number of platelet transfusion over the past few decades. However, platelet transfusion have also evoked dilemma which was mostly due to non-judicious usage and request of platelet transfusion. As far as platelet component is concerned, platelets were collected from whole blood donation where they prepared the components via a soft spin centrifugation before separating them into platelet rich plasma component (Jefffrey McCulogh, Transfusion Medicine, Second Edition, 2005)

However, the advent of new technologies and rising in medical as well as surgical indications have forced the blood transfusion services to increase the new method in preparation of platelet component which was known as single donor platelet or also named as apheresis platelet (Shukla, *et al*., 2005). The new generation of cell separators have made possible to obtain a high quality platelets with minimum donor manipulation. Anyway, the transfusion specialist was very concerned about the collection of platelets that could able to generate an optimum level of yield in order to balance the pre and post donation hematological counts in the donors (Goodnough *et al.,* 1999). As a result, this cause the arise of research to demonstrate the possible associative factors that would determine the platelet apheresis yield and effect of donation among apheresis donors.

Previous study done by Goodnough *et al*., (1999) had shown the direct relationship of pre donation platelet count with the platelet apheresis yield.

Besides that, different trials showed gender had a significant influence on the platelet apheresis yield. Women had higher yield compared to males donor, as reported by Kalish *et al.,* (1987). Those are the variables investigated by the previous studies and was categorized as donor predicting variables. They have found that those variables have significance influence on the platelet apheresis yield.

On the other hand, additional studies that was done have cause the discovery of other variables that could influence the platelet apheresis yield. Studies was proven by researchers that found a direct correlation between the machine related variables like anticoagulation infusion rate, processing time and plasma volume collected with platelet apheresis yield collection (Enein, *et al* 2006).

A higher platelet apheresis yield collection could help to produce a greater increment of platelet count after transfusion specifically among patients with various medical conditions. This group patients have the vulnerability to get exposed to many blood and plasma product of transfusion in order to optimise their blood counts (Parash A., *et al* 2009). Single donor platelet transfusion with good yield collection could ultimately increase the platelet count post transfusion and also prolonged the duration of platelet free transfusion period. The longer the period of platelet transfusion free period, the less likelihood for the patients to be exposed to various complication due to platelet transfusion therapy (Despotis., *et al* 1999).

Therefore, a study was done in order to justify these possible factors that would influence the yield which could be a good predictive value in future to obtain a product with good platelet apheresis yield.(M. and A., 1998)

CHAPTER 2

LITERATURE REVIEW

2.1 BACKGROUND

The first successful transfusion ever done before was on a woman who had recovered from severe post partum haemorrhage after receiving eight ounces of blood from Dr James Blundell's assistant during the course of three hours. (Leonard, 2006). It was more than 150 years after the discovery of human blood circulatory system by Sir William Harvey in 1628. However in the era of 20th century, the discovery of Dr Karl Landsteiner of four main groups of blood A, B, AB, O has led blood transfusion evolve into a new era of saving lives (Learoyd, 2006)

The first record of blood donation was performed by the British Red Cross in year 1921 and in return, the first voluntary blood service had been recorded. Blood donation had become well known long before time, and by year 1937, both America and Britain had their first set up of blood bank . Currently, the noble service of blood donation and apheresis donation is provided by various health care institutional and blood bank centres (Enein *et al.*, 2007a). Despite of having said that all donation processes are non-remunerated, the safety issues in that procedures had become an issues to be discussed and ascertained. However, based on previous published articles, many authors concluded that whole blood donation and apheresis donation are safe (Winters, 2006)

These reviews are partly agreed upon by many health care providers as due to the very minimal and mild form of complications caused by transfusion. Rarely, very serious complications are encountered during or after the procedures of transfusion, thus precautions need to be taken in order to provide the best care management for the recipients. However, despite of having a safe image on

donations, not many study articles or feedback reviews had been done on the safety values of the aspect donations especially for platelet apheresis donations (Winters, 2006).

In addition, with increasing use of single donor platelet, the need for potential platelet apheresis donors also increases. Although the collection of quality single donor platelet was more efficient by the discovery of cell separator but anyhow, by identifying the possible related factors that influence the platelet yield like via donor and machine related variables could determine a potential apheresis donors to produce a good platelet yield (Das *et al.*, 2005).

Thus, it is important to study all these factors and to apply these related parameters as predictive values in order to get a good quality platelet products (Guerrero-Rivera *et al.*, 2003).

2.2 BLOOD DONATIONS.

Blood donation are divided into two categories, these are whole blood donation (whole blood is collected from the donor) and automated apheresis donation (only selected blood component is collected). The frequently collected blood donation is whole blood donation, although there is no absolute indication for routine use except on few circumstances where whole blood is applicable in exchange transfusion and replacement of massive blood loss where fresh whole blood is recommended (Harmening, 2012).

In addition, the major function of whole blood is that it serves as source of material for blood component preparation. As far as whole blood is concerned, it contains red blood cells, white blood cells, platelets, plasma and few other components (Hoffbrand, Postgraduate of Haematology, 2008). In order to depart it into component preparation, a manual processing and separating procedures are essential in the blood bank.

A series of laboratory work processing is required to separate the whole blood proportion into several other components such as: centrifugation, freezing and thawing, adhering to a standardized established guideline system (Harmening, Modern blood banking, 2010).

However, with evolutions of current modern technology have actually given us the privilege to extract the whole blood component into a plasma component by using automated apheresis machine (R. Chaudhary et al, 2006)).

Apheresis defined as ‘separate’ which was derived from a Greek word (Rudmann, 2005). This term refers to the process of removal of whole blood from a donor or patient, whereby a specific portion of the individual’s blood were removed and separated inside the apheresis machine eventually returning the remaining portions to donor or the patient himself (Figure 1.1). Apheresis has various purposes to fulfil which include harvesting specific component for transfusion, collecting plasma for further processing, or removing specific pathologic substances from a patients blood. Apheresis can be divided into three types like: cytapheresis, plasmapheresis, and therapeutic apheresis. (Prashant A et al, 2006)

Cytapheresis was preferably done for harvesting specific cellular components such as platelets (plateletpheresis) or granulocytes (leukapheresis). Each of the procedure shall remove the desired component and return the rest back to the donor. Plasmapheresis is a procedure of separation of plasma from the donor by using replacement solution like colloid or albumin and returning the rest to the donor. The purpose of replacement solution is to maintain an equilibrium balance of oncotic pressure. (Prashant A et al, 2009)

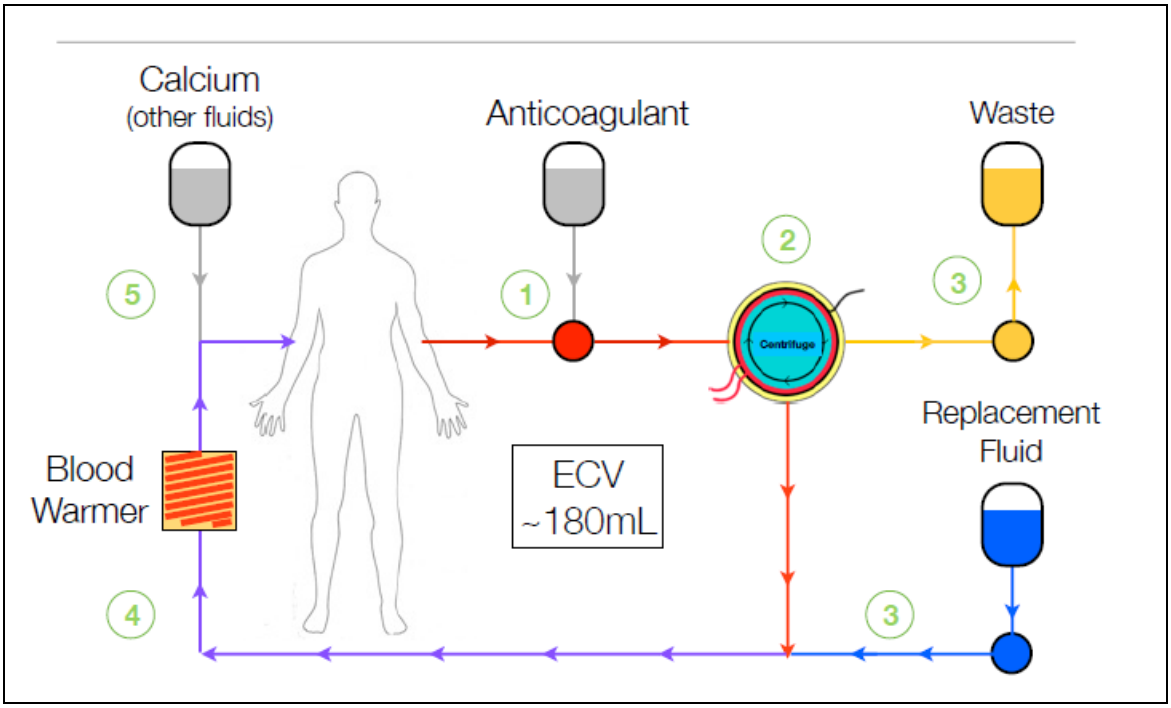

Figure 1.0 ; Schematic diagram of apheresis procedure (Adapted from apheresis programme British Columbia, 2013).

In the early 1900s, apheresis procedure was performed laboriously by manual techniques which resulted in limited success and acceptance. Automated apheresis was developed in year 1975 and since then a series of evolutions had taken place in terms of technical aspect, modification and established standardization in order to meet the inventory needs of transfusion services (Lazarus et al; 2001).

As far as apheresis procedure is concerned, the desired apheresis procedure that were performed , varies according to the component of the blood to be harvested and the equipment to be used. The most commonly applied method was the centrifugation method of separation. This method can be divided into; (1)Intermittent flow centrifugation (IFC) and (2) continuous flow centrifugation (CFC) (Harmening, 2005).

Besides that, apheresis via membrane filtration is occasionally used. The recommended time for apheresis procedure can range from 45 to 120 minutes (Harmening, 2005).

The table 1 below showed the possible of advantages of centrifugation method compared to membrane separation method. (Adapted from apheresis programme British Columbia, 2013)

Table 1 : Comparison between two methods of cellular separation.

Centrifugation	**Membrane Separation**
Higher plasma extraction efficiency	Lower plasma extraction efficiency
Low blood flow rate (50-100mL/min)	High blood flow rate (400-600mL/min)
Peripheral (or central) venous access	Central venous access
Citrate (anticoagulant)	Heparin (anticoagulant)
Selective cell removal	Selective plasma protein removal
Specifically designed machines	Use on existing dialysis machines
Risk of cellular loss	Risk of haemolysis

In this study, the method applied was through centrifugation method of cellular separation by using the apheresis devices. The IFC is basically performed in a number of cycles. An anticoagulant should be added into the tubing system to prevent blood from clotting. After the venepuncture, the whole

blood would flow through the inlet port, causing the bowl to rotate at a fixed speed, separating the components to their specific gravities. The whole blood would be separated according to the desired components base on their mass value in which red cells were packed at the outer rim of the bowl, followed by white cells, platelets, and plasma. The apheresis machine used in this study was the Trima Accel cells separator machine. The separated desired components are diverted into the re-infusion bag and returned to the donor. The process of reinfusion would complete the first cycle process. It takes six to eight cycles to collect a therapeutic dose. IFC procedure can be done with only one venepuncture (Trudell and Harmening, 2005).

The most commonly utilized apheresis machines are the Haemonetics and Trima. In this study, Trima machines were used for the processing of plateet apheresis yield. These machines are portable, versatile and capable of efficient component collection. CFC procedures allow withdraw, process and returning of blood back to the individual simultaneouslyutilizes the method of continuous flow cell separator. CFC procedures allow withdraw, process, and returning of blood back to the individual simultaneously (Roback *et al.*, 2008).

Since, the process of withdrawing and returning of the blood was done continuously, two venepuncture sites were absolutely necessary. In occasional basis, a dual lumen central venous catheter was used. The components are separated via centrifugation, and the specific component required was diverted into a satellite collection bag. The remaining of the blood was reinserted back into the donor via second venepuncture. As a result, the process of phelobotomy, separation, and re infusion was not interrupted. This was totally in contrast with

IFC procedures, in which a one cycle of complete process need to be accomplished before beginning the next one. Examples of machine employing this concept are the Fenwal CS-3000, The Amicus, COBE Spectra and Fresenius AS-104 (Harmening 2005) and (Roback *et al.*, 2008)

The process of component collection in apheresis was done to obtain a specific blood component known as platelet apheresis product. During this procedure named, the donor losses only a specific cellular component, while the remaining composition of blood which were the red cells and plasma component was returned back to the donor. As for this reason, apheresis donation can be allowed for more frequent donations compared to whole blood donations .The red cell loss, should not exceed more than 25 ml per week, or 24 times in year. This was because donors who loses large number of red cells would cause them to have significant reduction in their haemoglobin level, which can lead to anaemia (Rudmann, 2005).

A s for the plasma loss, a maximum of 500 ml volume could be retained during the procedure or the volume described in the labelling for the automated blood cell separator device (Roback *et al.*, 2008)

More stringent regulations was expected for donors who participated in a serial apheresis program (more than once in 4 weeks) (Harmening, 2005). As this group of regular donors, a proper assessment and careful monitoring of height, weight, pre donation platelet count, pre donation haemoglobin level and haematocrit level was essential in term of determining the positive predicting variables that could contributed a good platelet yield collection (S. S. Das, R. K. Chaudry et al, 2005). Study done by Chaudhary D, 2005 had demonstrated

that there was a direct correlation observed between the pre donation platelet count and platelet apheresis yield. Other than that, Guerrero- Rivera, 2003 had also proven that there was an inverse relationship seen between pre donation haemoglobin level and platelet apheresis yield. But Ogata, 1981 observed no correlation seen between the pre donation haemoglobin level with platelet apheresis yield. This contradicting findings, could be a good space for this study to be conducted in order to determine the correlation between pre donation haemoglobin level and platelet apheresis yield.

Besides that, studying the machine predicting variables could also be helpful in producing a good efficient number of platelet yield collection which includes, the processing time, duration of the procedure, anticoagulation infusion, plasma volume collected. (Enein, 2006). As been done previously in studies by the same author, he demonstrated a direct positive correlation between the machine related variables with the platelet apheresis yield collection.

However, not many studies have been done in Malaysia to determine the specific factors that could influence the quality of platelet apheresis yield. Apart from that, research papers on the aspect of complications due to platelet apheresis procedure were still small in number. Therefore, more studies related to factors influencing the platelet apheresis yield and effect of donation among apheresis donors should be done in future (Enein *et al.*, 2007a)

2.3 PLATELET APHERESIS PREPARATION AND ADVANTAGES.

Emerging phenomena of increasing demand in blood utilization which was not parallel with increasing number of donor population pool, leads to maximum utilization of blood donation for each donor.

The platelet products were derived by two methods which is whole blood derived platelets (platelet-rich plasma (PRP) or buffy coat intermediate steps), or apheresis derived platelets. However, choices of producing platelet was mainly dependant on local supply, physician's preferences, or economic considerations. Single donor platelet or also knows as apheresis platelets have more advantages to patients who developed refractoriness to the random donor platelet as a result of frequent transfusion. These groups of patients requires a Human Platelet Antigen (HPA) or Human Leukocyte Antigen (HLA) matched platelet products that would benefit them by having less complications of transfusion and better increments in platelet counts after receiving an apheresis platelet product (Vassallo and Murphy, 2006).

Whole blood derived platelets was prepared directly from a whole blood donations via a process of centrifugation whereas apheresis derived platelets were prepared by connecting a donor to an apheresis machine set with double venepuncture site. In apheresis, the donors whole blood was anticoagulated as it passed through the instrument in which the blood was separated into red cells, plasma and leucocyte platelet fraction. Then the desired fraction or components were removed, and the remainder of the blood were recombined and returned back to the donor. Several litres of blood was processed simultaneously during the procedure and therefore a larger amount of desired component could be

obtained from one unit (450 ml) of blood (Petz, 1989). The prepared quality control of platelet yield or the concentration is equivalent to 6 - 10 random of platelet concentrate (Harmening, 2005). In regards to that, the minimum acceptable yield of platelet apheresis product should contained 2.5 - 3 x 1011/L of platelet yield concentration (Roback *et al.*, 2008).

All blood components that were collected should be stored at an appropriate temperature. Platelet concentrate or apheresis platelet are stored at room temperature within a range of 20- 24^{0}C in a platelet agitator to ensure their viability and to avoid platelet clumping. A gentle agitation is essential to permit adequate gas exchange and hence, prolong the shelf life of the platelets (Yasmin Ayob, 2008).

According to the standard AABB guideline and BCSH guideline, the allowable storage time of the platelet is 5 days. The longer the days of storage can augment the possible of bacterial growth in the product (Harmening, 2012).

Besides that, there were also progressive decline in platelet viability throughout the storage time. In addition, there were reflective changes that could occur in platelet morphology, activation state, metabolic capacity and physiological responsiveness as the platelets shelf life prolongs (Fijhneer, 1989 and Kamath (Kamath *et al.*, 2001).

The apheresis platelet preparation have their own advantages and disadvantages as compared to other type of platelet preparation which was illustrated in table 2.0. This was supported by study that showed different preparation method exhibited different properties of platelet at the beginning of storage (Rinder and Ault, 1998).

Table 2.0 : Advantages of various type of platelet preparations

.

Apheresis platelets

Lower donor exposure

Greater percentage of repeat donors

Compatible with cost effective, sensitive bacterial detection methods and promising new pathogen reduction technologies.

Less hospital preparation (pooling, point of care bacterial esting)

Rapid blood bank issue.

Decreased transfusion service paperwork.

Reduced wastage (compared with post storage pools).

Fewer febrile, non haemolytic reactions.

Lower level of platelet activation by in vitro assays.

Platelet rich plasma, whole blood derived platelets.

Cost effective than apheresis derived platelets.

Better dosing flexibility.

Less single donor plasma exposure.

Greater availability during holidays and bad weather.

Greater use of gift of whole blood donors without and additionall risk on apheresis associated risk.

Buffy coat, whole blood derived platelets

Provide all the benefits of platelet rich plasma derived platelets, including pre storage pooling. Adapted from (Vassallo and Murphy, 2006)

The core advantage of apheresis platelet is to minimise the number of donor exposure and hence can reduced the risk of transmission in viral infection. In addition, febrile non haemolytic transfusion reaction had been reported to be less common in apheresis platelet. These could be due to the less leucocyte contamination and as well as less non-specific proteins present in the apheresis product (Chambers *et al.*, 1990). Platelet alloimmunisation had also been reported to be less severe among patients who received apheresis platelet transfusion (Bajpai *et al.*, 2005)

Besides the benefit to patients or the recipients, apheresis platelet donation can also benefit the donors. The apheresis donors could be able to donate several time like 24 times per year (Rudman, 1995)

Apart from that, apheresis platelets have additional advantages which includes less hospital preparation (pooling, point of care bacterial testing) and more rapid blood bank issue. However, the drawback of apheresis platelet procedure was the technique of preparation and handling the set of the device which had remain expensive (Chambers and Herman, 1999).

2.3 COMPLICATIONS OF PLATELET APHERESIS PROCEDURES.

Apheresis technology has been said to be safe and efficient procedure, however no procedures are 100% safe. They still carry some additional risk to the donors. Apheresis technique shares the same risk in term of reactions and injuries found in whole blood donations. In addition, they could have a unique complications that may have resulted from frequency of donations and methods of collection. (Winters, 2006). Essentially, the overall reactions that occur pertaining to the apheresis procedure were less than the reactions seen in whole blood donation. However, the risk of severe reaction, requiring hospitalization were also greater (Despotis *et al.*, 1999).

Table 3.0 illustrates the possible reaction rates among apheresis donors. Few studies had shown the most frequent immediate adverse effects associated with apheresis donation were the venepuncture related complications like (haematoma, pain) (McLeod *et al.*, 1998).

Table 3.0 : Reactions rate among apheresis donors.

Reaction in apheresis donations	(%)
Haematoma or pain	1.15
Citrate toxicity	0.4
Mild vasovagal	0.05
Vasovagal with syncope	0.08

Adapted from (Mc Leod *et al*., 1998).

The primary anticoagulant used in the collection of platelet or platelet apheresis is citrate. Citrate had the ability to chelate calcium ions which can result in hypocalcaemia. In the apheresis instrument, the plasma citrate concentration should reach to 15 – 24 mmol/L, to lower the calcium level which is essential for clotting mechanism to take place. This requires the infusion of anticoagulant called as Acid- Citrate Dextrose Adenine) solution. However, in-vivo formation of citrate from the red cells metabolism and other tissue metabolism can also occur but various compensatory mechanisms that are generated by the body can balance these homeostasis changes. Parathyroid hormone can increase in response to hypocalcaemia due to citrate chelation effect and subsequently causing mobilization of ionized calcium bound to serum albumin) as well as diluting the existing citrate present in the blood by total extracellular fluid, not just the intravascular space. Besides that, other organs like liver and kidneys will also rapidly metabolize citrate, and release the bound calcium (Strauss, 1994).

Despite of harbouring an efficient compensatory mechanism, citrate infusion that occur during the apheresis procedure can ultimately decrease the ionized calcium levels to a point where symptoms can develop in donor. Donors may manifest signs and symptoms of hypocalcaemia like: tingling and numbness sensation or paraesthesia around perioral or acral, shivering, light headedness, twitching and tremors. Apart from that, some donors may also experience nausea and vomiting. A further drop in ionized calcium level may provoke further clinical manifestations like carpopedal spasm,, tetany, and seizure (Strauss, 1996). The ultimate treatment is by slowing the reinfusion rate in order to allow for dilution and metabolism of the citrate. Besides that, slowing the reinfusion rate

can also reduce the proportion of citrate to donor ratio and eventually decreased the amount of citrate infused. Administration of oral calcium simultaneously to the donor who did manifest sign and symptom of hypocalcaemia is the mainstay of immediate treatment (Harmening, 2012). In addition, effect of citrate can also include reducing the level of magnesium, increasing in blood pH and a fall in serum potassium levels (Bolan *et al.*, 2001).

Apart from that, hypotension can also develop during apheresis collection and it is mostly multifactorial due to intravascular depletion, vasovagal reactions, citrate reactions, severe allergic reactions, and air embolism. Hypovolemic and vasovagal reactions are treated similarly. In case of hypotensive episodes were to occur, the procedure should be stopped temporarily and a fluid bolus should be infused and if the insult is due to hypovolemia, the blood pressure should increase and the pulse rate should decrease in response to this intervention (Bolan., *et al* 2001).

As far as allergic reactions is concerned, donors who are undergoing collections like platelets, plasma and granulocytes, may also experience such similar reactions. Besides that, reactions to ethylene oxide that is used to sterilize the disposable sets have been described among platelet and plasma donors. It is commonly seen among regular donors (Susan F., *et al* 1986). Any donors who experiences such reactions, should alarm the managing team to abort the procedures that is being carried out and the subsequent mode of treatment to be administered is dependent on the severity of the manifestations. For simple allergic reactions like: pruritus, rashes, or chills and rigor, a simple oral antihistamines would alleviate the symptoms (Winters, 2006).

However, for more vigorous manifestations, like: intense itchiness accompanied by shortness of breath, choking sensation, bronchospasm with hypotension, which is named as anaphylactic reaction then, probably a more prompt treatment is indicated like: adrenalin infusion or aminophylline and IV line access maintained patent with saline infusion (Kaplan *et al*., 2012).

In addition, a significant fall or drop in platelet counts after an apheresis donation is a documented complications in many previous studies (Akay *et al.*, 2007) and (Kalish *et al.*, 1987). According to some studies, it takes 4 days for a platelet count to return back to a normal state for a male donor while as for female donor, the established thrombopoietin levels is slightly lower on day 4 post donation compared to males, hence there will be a slight delay in returning of the platelet count back to the baseline level (Dettke *et al*., 1998).

Apart from the transient decreases in platelet count after a single and a serial short term platelet apheresis collection, there were previous studies to demonstrate the possibility of significant and sustained decreased in platelet count in a long term regular platelet apheresis donors (Lazarus *et al.*, 2001).

Early platelet apheresis instrument utilization can also cause a significant loss of donor lymphocytes (5 to 10 x 10^9/procedure), hence this may evoke the possible concern of immunosuppression on donors post procedure. As a result, apheresis donation had been limited to maximum of 24 per year, in view of a potential warning for the platelet apheresis donors to develop lymphocyte depletion and hence, implicating a possible of deferral need to be carried out for apheresis donors who have lymphocyte counts below 1.2 x 10^9/L (Strauss, 1994). However a newer generation apheresis instruments showed no significant

differences in lymphocyte counts and lymphocyte subsets when compared to non-donors and whole blood donors (Lewis *et al*., 1997).

In addition, there is also some evidence to suggest that apheresis donation may produce adverse long term effects such as bone demineralization and cataract formation (Winters, 2006).

There have also been isolated case reports to suggest possible of long term effects of apheresis donations that could alter the haemostatic function among donors (Beyan *et al*., 2005)

2.4 FACTORS INFLUENCING PLATELET APHERESIS AND EFFECTS OF DONATION AMONG DONORS.

Overview on Factors Influencing platelet apheresis yield

Platelet apheresis procedure has emerged as a one of the important procedures in determining the outcome of a platelet product quality. Based on previous studies, this method of platelet collection was able to produce a better platelet yield in terms of volume as well as concentration (Goodnough *et al.*, 1998). Studies illustrated the possible variations involved in contributions to the outcome of the platelet apheresis yield collection. They have encountered the possible donor related factors and machine related parameters could influence the outcome of the platelet yield collection (Das *et al.*, 2005). There were many factors involved like the donor related factors which comprises of donor' s age, gender, height, weight, pre donation haemoglobin level and pre donation platelet count and blood group system. Previous studies demonstrated that the pre-donation platelet count had significant influence towards the platelet yield. Apheresis donors with pre-donation platelet count of > 250 x 109 /L have been determined to provide a desired haemostatic platelet dose for the recipient. Therefore, platelet yield for the apheresis product was predominantly dependant on the donor pre-platelet count (Ogata *et al.*, 1981) and (Goodnough *et al.*, 1999).

Other studies had also showed a positive correlation between the body mass index (BMI) and donors age with the platelet yield collection (Arun *et al.*, 2013). They suggested that increasing of body mass index and donors age would give a higher platelet yield collection. There was another study that demonstrated no significant correlation between weight and platelet yield