Review Article

Prolonged Platelet Storage – a solution to the increased demand?

ABSTRACT

Platelets are small, anuclear blood cells derived from megakaryocytes in the bone marrow. Their role is to stop bleeding (haemostasis) during haemorrhage and are also used as part of cancer treatment. Hence, the importance and demand for platelet concentrates (PCs) should never be underestimated. The short shelf-life of PCs poses a problem in terms of availability and a costly waste of resources, equipment, and time management. Increasing the shelf-life from the current 5-day storage period to 7 days is one way of managing this problem. A 7-day storage shelf-life is already implemented by various Blood Banks worldwide. However, many Blood Establishments still struggle with their decision to prolong the shelf-life of this product. This review highlights some important factors which should be considered for introducing a longer storage shelf-life.

Keywords: Platelet Concentrates, prolonged shelf-life, quality, safety

1. INTRODUCTION

Prolonging the shelf-life of platelets is becoming an essential turning stone as this leads to the prevention of cancelling or postponing interventions due to the lack of platelet concentrate (PC) availability. In addition, it avoids situations where due to the limited supply, this product is not readily available to treat patients. The production of platelets is a costly endeavour and having a very brief 5-day shelf-life proves to be very expensive. Many studies have shown the possibility of prolonging their shelf-life and nowadays some institutes, such as Canadian Blood Services(1) and Australian Red Cross Life Blood(2) are opting for this solution for meeting the continuous increase in demand of the product. Nonetheless, other establishments have yet to determine whether such an option would satisfy their needs.

2. PLATELETS AND THEIR ROLE IN CLINICAL TRANSFUSION

Platelets are small fragmented cells, which together with red blood cells and white blood cells make up 45% of blood(3). They are formed from megakaryocytes in the bone marrow. Platelets play a very important role in haemostasis where they help stop bleeding when activated due to the clotting factors they secrete and their ability to morph into a compact sphere with dendritic extensions to facilitate adhesion(4). The most discernible clinical applications of platelets in transfusion include prophylaxis for low platelet counts or to help arrest a major bleed. PCs are also used as prophylaxis before certain operative procedures where the patients have a higher risk of bleeding due to other health conditions or thrombocyte disorders they might have. However, their major role is in supporting haematological

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cancer treatment. Oncology patients depend on platelet transfusions to maintain an adequate count for treatment to be effective as well as to top-up their platelet counts which might plummet as a result of the chemotherapy received.

3. STORAGE OF PLATELETS

A common practice is to preserve PCs in Platelet Additive Solution (PAS) for 5 days, in bags that allow the gaseous exchange of oxygen and carbon dioxide. PCs are stored at 22℃±2℃ with constant, gentle agitation, which guarantees oxygen availability and prevents platelet storage lesions (PSLs) that affect the structure, function, and metabolic activity of the platelets(5). Storing platelets at room temperature makes them more susceptible to bacterial contamination, hence the short shelf-life.

3.1. Alternative approaches to storage of platelets

To minimise the risks associated with storage of platelets at room temperature, alternative methods of storage are being looked into, such as storing platelets at colder temperatures and even cryopreserving them. These methods minimise the risk of bacterial growth as well as PSLs, making it easier to increase PC shelf-life and in turn make the product more accessible and available to patients, thus reducing waste(6).

Cold storage of platelets (4℃) is technically not a new approach as this was common practice in the 1960s. However, cold storage conditions were abolished in the 1970s as new findings suggested that even though cold-stored platelets resulted to be superior to platelets stored at room temperature in vitro, this was not the case in vivo(7). Recently, though, cold storage of platelets is again being explored by several research projects.

Another alternative method of cold-storing platelets is cryopreservation. This involves the use of cryoprotective agents such as dimethyl sulfoxide (DMSO), dextran, glycerol or hydroxyethyl starch to store PCs at -80℃(6). Bohoněk(8), concluded that cryopreserved platelets have the potential to last for approximately 2 years maximum; however, documentation shows that such extreme storage conditions tend to cause platelets to lose glycoprotein essential for activation as a consequence of what is known as cryo-damage(9).

4. INCREASE IN PLATELET DEMANDS

The availability of PCs depends solely on voluntary blood donations, but unfortunately, blood shortages are a common occurrence due to several factors. Starting with stringent regulations to counteract the current lifestyle of the population in order to safeguard the safety of the blood supply and the fact that there is an age limit to donate blood which combined with the ever-increasing demand for blood products, limits their availability. Greinacher& Hoffmann(10), noted that as a consequence of a general increase in population numbers and a longer life expectancy, the demand for platelets has been on increase in industrialised countries.

Having larger populations also results in an increased prevalence of haematological malignancies, critical accidents, traumas or simply child-birthing complications, all of which may all require platelet transfusions. Locally, the influx of migrants who for various reasons are unable to donate blood but on the other hand might require it, maybe another contributing factor to the lack of platelets availability. Another factor that led to an increase in demand for platelets is a change in the management and treatment of patients with haematological malignancies. Ongoing studies focusing on platelets and their functions in the human body(11,12) and how these can be employed as part of treatments for various diseases and conditions, will most likely also increase the demand for this blood product.

Increasing the shelf-life of platelet concentrates from the current 5-days to that of 7-days would alleviate stress on the healthcare system by making the supply of this precious blood product more accessible to the needs of the patient and ultimately reducing the overall expenditure which results from expired PCs.

5. PLATELETS AND THEIR QUALITY

Being considered a pharmaceutical product, platelet products are highly regulated by both international and local authorities. Both lay down the minimum requirements to ensure that the product is of high quality and fit for use.

pH - The pH of PAS has a direct impact on the metabolic activity of platelets. Over storage time, the pH level tends to shift to the acidic spectrum as a result of the production of lactic acid and carbon dioxide by platelet metabolisms. This can have grave consequences as platelets become irreversibly damaged and suffer a loss of their functions. It has been shown that at a pH below 6.8, platelets assume a spherical shape, a change that is irreversible if the pH goes below 6.2(13).

Platelet Count and Indices - Maintaining a sufficient platelet count is essential in ensuring an adequate product is being transfused. As a result of storage, storage lesions invariably occur and this causes the count to decrease.PSLs are one of the main reasons why platelets have such a short shelf-life and are defined as a significant loss of function of platelets *in vitro* which may result in functionality decrease when transfused to patients(14). Aggregation of platelets during storage is one such PSL that decreases platelet count due to platelets being activated. Centrifugation during component separation and agitation while in storage can also cause platelet lysis, further decreasing the count(15).

Sterility - Given that platelets are stored at 22°C±2°C, they are more susceptible to bacterial contamination, as this temperature is optimal for bacterial growth. This may cause septicaemia in patients. Contaminants are usually commensal flora which result from the donor's skin when an improper disinfection technique of the puncture site is employed; or else, in rare cases bacterial contamination may result from donors who are asymptomatic carriers(16).

5.1. Considering other parameters for quality monitoring

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The standard parameters mentioned above are the minimum requirements to endure the quality of the product. However, with tailored treatment it is now necessary to consider the quality of platelets also from a different point of view(17).

Cytokines - Platelets are carriers of cytokines or chemokines, which are vital in the platelets' haemostatic processes as well as in pro and anti-inflammatory processes. Platelets release cytokines upon activation. The primary function of platelet cytokines is the regulation of inflammatory processes such as leukocyte migration, phagocytosis and reactive oxygen species generation(17,18). Amongst the cytokines which are being followed, one may find PF4 which is the most abundant cytokine and is typically released during platelet aggregation(19). TGF-β plays a role in tissue repair(20), Il-6 stimulates the synthesis of megakaryocytes, thus increasing the number of platelets in circulation(21), while IL-8 triggers platelet activation(22).

Glucose & Lactate Dehydrogenase (LDH) levels - Glucose is metabolised into lactic acid during platelet storage and excessive metabolic activity results in a low pH(23). This is undesirable as a sharp fall in pH will lead to substantial loss of vital platelet functions, nulling storage viability. High levels of LDH also indicate extensive storage lesions.

6. GENERAL OUTCOMESOF PROLONGED STORAGE STUDIES

In general, most studies show healthy maintenance of platelet functionality and quality upon extended storage. For example, a study by Hornsey et al.(24)has shown that the in vitro quality of platelets stored in PAS media is superior to that of platelets stored in plasma, oftentimes maintained up to storage day 9. The study analysed platelet counts, gases, pH and cytokines and the results showed that all these parameters remained consistent throughout the storage time. Similarly, Gupta et al.(25), analysed the platelet count, platelet factor 3, lactate dehydrogenase (LDH), pH, glucose, and platelet aggregation of 30 random donor platelet samples. Once again, the results obtained demonstrate that platelets can have their shelf-life increased to 7 days without the risk of bacterial contamination and loss of functional quality. Another study additionally showed that platelet counts and indices, pH andcytokines remain stable in platelets stored in PAS for 10 days at room temperature(26).

However, Cardigan & Williamson(27), argue that as platelet storage time increases, there is likely to be a reduction in the therapeutic efficacy of PCs. Their study also refers to the difficulty to sustain their statement as there is no predictor test to confirm efficacy in vivo, whereas the in vitro quality of PCs with extended shelf-life can be assessed through various other analyses. It is suggested that internationally agreed standards for manufacturers and blood services could help provide the best possible products for transfusion to patients without compromising the quality and efficacy of PCs with extended shelf-life.

7. CONCLUSION

It is well known that there are certain risks in extending the shelf-life of this product. Being stored at a temperature of 22±℃ makes platelets an optimal medium for bacteria to flourish and may also subject them to what is known as platelet storage lesions which can compromise the safeness and quality of the product respectively. Blood Establishments must guarantee that extending the shelf-life of PCs will not impact the safety and quality of the product. Although many studies have proven that prolonged storage does not impair quality, it is not a risk-free approach. The concerned institute should determine the pros and cons in terms of their local setup and risk, and assess whether the benefits of electing for shelf-life extension outweigh the associated risks.

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CONSENT

Not applicable

ETHICAL APPROVAL

Not applicable

REFERENCES

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