

State of affairs: the US platelet supply and the role of whole blood-derived platelets

US platelet supply and WB-derived platelets

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Abstract

Purpose – The US platelet supply is almost exclusively dependent on apheresis donors who are “aging out.” As a result, blood centers and hospitals have been experiencing spot shortages and have resorted to transfusing low-dose platelets. This paper explores using whole blood-derived platelets (WB-PLTs) to supplement the apheresis platelet (APH-PLT) supply.

Design/methodology/approach – This paper reviews the history leading to the current state of the US platelet supply and includes the impact of recent events such as the COVID-19 pandemic and the implementation of the US Food and Drug Administration (FDA)-mandated bacterial mitigation strategies.

Findings – WB-PLTs represent a viable source of platelets that can be used to supplement the APH-PLT supply. Whole blood automation represents a new methodology to more easily prepare WB-PLTs. Advances in donor testing and screening as well as pre-storage leukoreduction have improved the safety of WB-PLTs to the same level as APH-PLTs. Blood services in the US and abroad transfuse WB-PLTs interchangeably in all patient populations.

Originality/value – This paper highlights how the US blood industry is essentially “sole-sourced” in terms of APH-PLTs. In this post-COVID-19 period, when most industries are building redundancies in their supply chains, blood centers should consider WB-PLTs as an additional source of platelets to bolster the US platelet supply.

Keywords US platelet supply, Whole blood-derived platelets, Apheresis platelet donors

Paper type General review

Introduction

According to the most recent National Blood Collection and Utilization Survey, 2.5M platelets were distributed in the US in 2021, of which 96% were collected by apheresis (Free *et al.*, 2023). For years, blood centers have been warning that apheresis donors are “aging out,” meaning that at some point in time these dedicated apheresis donors will no longer be able or eligible to donate (Pandey *et al.*, 2021; Sayers, 2022, US Department of Health and Human Services, 2020). With age, these individuals may become platelet users rather than platelet donors (Pandey *et al.*, 2021; Sayers, 2022). At the same time, blood centers have been struggling to recruit younger donors, especially for apheresis (Stubbs, Shaz, Vassallo, & Roback, 2022; Sayers, 2022). Even blood centers that have successfully recruited younger donors into their apheresis programs still rely on older donors to contribute the largest volume of apheresis platelet units (Lasky, Singh, & Young, 2023). US blood centers are producing fewer apheresis platelets after implementation of the US Food and Drug Administration (FDA)-mandated bacterial mitigation strategies (Garcia & Razatos, 2021; Pandey *et al.*, 2021; US Food and Drug Administration, 2020). Mitigation strategies require either larger volumes to be sampled for



bacterial screening or pathogen reduction, both of which result in fewer platelets available for transfusion (Garcia & Razatos, 2021; Benjamin, Katz, Gammon, Stramer, & Quinley, 2019). Blood centers and hospitals have resorted to transfusing platelets containing less than the standard dose of 3.0×10^{11} to meet patient needs (Pandey *et al.*, 2021).

This complete dependence on apheresis donors puts the US platelet supply at risk. With the exception of China and Japan, countries outside of the US rely on a balance of apheresis platelets (APH-PLT) and whole blood-derived platelets (WB-PLT) to meet transfusion needs (World Health Organization, 2021). For example, the Canadian platelet supply consists of 30% APH-PLTs, the UK consists of 54% APH-PLTs and Germany consists of 59% APH-PLTs.

A recent survey of chief medical officers at US blood centers reported that the primary barrier to WB-PLTs in the US has been logistics/inventory management (Yazer, Razatos, & Sayers, 2023). Whole blood intended to manufacture platelets should not be stored at temperatures less than 20°C; cold storage reduces the ability to isolate the platelets from the whole blood (Acker, Razatos, & Marks, 2023). Outside of the US, whole blood can be held at room temperature (20–24°C) for up to 24 hours to be processed into components (European Committee on Blood Transfusion, 2023). In the US, current regulations limit the time whole blood can be stored at 20–24°C for processing into platelets to eight hours (Gammon *et al.*, 2021). Getting whole blood back to the blood center to be processed within the 8-h time frame is a logistical challenge, which limits the number of WB-PLTs that can be manufactured (Stubbs *et al.*, 2022). The purpose of this review is to highlight the current state of the US platelet supply and to propose WB-PLTs as a secondary source to supplement the apheresis platelet supply.

Preparation of platelets for transfusion

Platelets can either be extracted manually from a unit of whole blood or collected directly from the donor by apheresis (Acker *et al.*, 2023; European Committee on Blood Transfusion, 2023). Blood is collected as whole blood, which is later processed in a laboratory. Methods to derive platelets from whole blood consist of either the platelet-rich-plasma (PRP) method or the buffy coat (BC) method (Acker *et al.*, 2023; European Committee on Blood Transfusion, 2023). Both methods are manual and involve two centrifugations and two expression steps when preparing three components: red blood cells, plasma and platelets (Acker *et al.*, 2023; European Committee on Blood Transfusion, 2023). Apheresis devices separate blood into the desired components while the donor is connected to the device; blood that is not collected is returned to the donor (Acker *et al.*, 2023). Apheresis allows for the collection of platelets with concurrent plasma and/or red blood cells from an individual donor (Acker *et al.*, 2023). The advantage of apheresis is that one donor can potentially donate up to three transfusable platelet doses, whereas platelets extracted from a single unit of whole blood represent only a fraction of a dose, such that intermediate platelet units from four or six donors must be pooled into one transfusable dose (Acker *et al.*, 2023). Advances in automation have introduced a third fully automated method to process whole blood into red blood cells, plasma and platelets (Acker *et al.*, 2023; Malvaux *et al.*, 2021; Perez *et al.*, 2021). First introduced in Europe and now available in the US, it is referred to as a “single centrifugation method” by European regulators because it involves a single centrifugation step followed by a single expression step (Acker *et al.*, 2023; European Committee on Blood Transfusion, 2023).

Clinical considerations

Apheresis platelets, also known as single-donor platelets, gained popularity in the 1980s during the AIDS epidemic. At the time, poor donor screening and viral testing drove the

industry to minimize donor exposure by preferentially transfusing apheresis single-donor platelets instead of pooled platelets prepared from multiple whole blood donors (Zeger, Williams, & Shulman, 1997). However, advances in donor screening and viral testing available since the early 2000s have increased the safety profile of WB-derived platelets. For example, the German National Blood Donor Surveillance System reported that the residual risks for pooled and apheresis platelets were comparable for HIV, HCV and HBV during the period 2006–2012 (An der Heiden, Ritter, Hamouda, & Offergeld, 2015). According to Seheult, Triulzi and Yazer (2016), “in the era of nucleic acid testing and rigorous donor screening, the difference in donor exposures of 4–6 vs 1 has minimal clinical relevance.” In addition to donor screening and testing, the transition from bed-side leukoreduction to pre-storage leukoreduction of WB-derived platelets decreased adverse transfusion reactions, further improving the safety profile of WB-derived platelets (Andreu *et al.*, 2002; Hebert *et al.*, 2003). Removing white blood cells before storage reduces the accumulation of cytokines that can cause adverse transfusion reactions (Wang, Triulzi, & Qu, 2012). A review of published literature also indicates that WB-PTLs have the same hemostatic efficacy and the same alloimmunization risk compared to APH-PLTs (Mowla *et al.*, 2021; TRAP Study Group, 1997; Triulzi *et al.*, 2012). There are patient populations for which APH-PLTs are indicated. APH-PLTs are preferred in the treatment of high-risk populations such as patients with immune-based platelet refractoriness who require crossmatch-compatible or human leukocyte antigen (HLA)-matched platelet units (Alcaina, 2020; Cohn, 2020; Kekomäki, 1998; Messerschmidt *et al.*, 1988).

Current US platelet supply issues

Several authors describe the increasing reliance of US blood collectors on older donors to contribute the majority of the platelet supply (Sayers, 2022; Lasky *et al.*, 2023). For example, one US blood collector published that “in 2001, 34% of the apheresis platelet annual inventory came from individuals between the ages of 36 and 45 but this percentage contribution had dwindled to 12% in 2020” (Sayers, 2022). The US platelet supply has also been strained by the implementation of the US FDA-mandated bacterial mitigation strategies that went into effect in October 2021 (US Food and Drug Administration, 2020). Modeling predicted a 4% decrease in APH-PLT productivity with the adoption of large volume sampling and a 10% decrease in productivity with the adoption of pathogen reduction compared to the previous small volume bacterial sampling methodology (Garcia & Razatos, 2021). Challenges to maintain an adequate blood supply were exacerbated during the COVID-19 pandemic due to canceled blood drives, hesitation among blood donors to present and challenges with the supply of medical devices (Kracalik *et al.*, 2021; Riley, Love, & McCullough, 2021). These compounding challenges to the US platelet supply have resulted in delays in surgeries, delays in outpatient transfusions and transfusions of low-dose platelets (Pandey *et al.*, 2021).

COVID-19 was followed by staffing and work force issues known as the “great resignation” that continue to this day (Ferguson, 2023). Retention of skilled labor is particularly impactful for apheresis collections, as these devices require specialized training beyond basic phlebotomy and whole blood collection. Retention of skilled labor is also impactful for manual whole blood processing, which is tedious and manual. The single centrifugation method, which is fully automated, can help blood centers supplement apheresis platelets with a system that is easy to train and simple to use. Modeling has shown that even newly unexperienced lab technicians can run the single centrifugation method to make WB-PLTs during an acute spike in platelet demand (Brouard, Robidoux, Cayer, & Dussault, 2023).

Manufacturing limits to WB-PLTs in the US

As US blood collectors struggle to maintain an adequate apheresis platelet supply, the platelets available in whole blood are discarded. According to the National Blood Collection and Utilization Survey, a total of 9.8M units of whole blood were collected in the US in 2021 (Free *et al.*, 2023). Only 4% of platelets in the US were derived from whole blood (Free *et al.*, 2023). To make platelets, whole blood must be held at room temperature; refrigeration activates platelets, making them difficult to isolate (Acker *et al.*, 2023; Gammon *et al.*, 2021). One of the primary factors limiting the manufacture of WBDP in the US is that whole blood can only be held at room temperature (20–24°C) for up to eight hours post-collection (Gammon *et al.*, 2021). The vast majority of whole blood collected in the US is refrigerated soon after collection per the Code of Federal Regulations (21 CFR Part 640) and is processed into two components, red blood cells and plasma, while the platelets are discarded.

Outside of the US, whole blood can be stored at room temperature (20–24°C) for up to 24 h, known as overnight hold (European Committee on Blood Transfusion, 2023; Gammon *et al.*, 2021, Van der Meer *et al.*, 2011). This 24 h hold allows adequate time for blood centers to return whole blood collected at remote locations or mobile blood drives to central processing facilities to be manufactured into three components: red blood cells, plasma and platelets (Gammon *et al.*, 2021; Van der Meer *et al.*, 2011). Conversely, in the US, whole blood must be refrigerated (1–6°C) within eight hours post-collection, which limits the number of units that can be processed into WB-PLTs (Gammon *et al.*, 2021; Van der Meer *et al.*, 2011).

In 2021, of these whole blood collections, 23% (2.25M) were processed within eight hours to make cryoprecipitate, which, at the time of the survey, had to be manufactured within eight hours (Free *et al.*, 2023). Assuming the same number of whole blood units could be processed within eight hours to produce WB-PLTs and assuming that five intermediate platelet units are pooled to create one transfusable dose, the production of WB-PLTs could create an additional 450,000 platelet doses per year.

Whole blood automation

The new fully automated whole blood processing system, referred to as the single centrifugation method, has simplified the manufacturing of WB-PLTs. Malvaux *et al.* (2021) reported a 59 min decrease in processing 12 whole blood units into pooled platelets compared to the manual buffy coat method. Perez *et al.* (2021) reported a reduction in routine manufacturing by half a shift, releasing the work capacity of one full-time equivalent operator. The equipment footprint was also reduced from 16 to 5 devices (Perez *et al.*, 2021). As expected, automation improved operational efficiencies by replacing a historically manual process. Although the single centrifugation method in the US is still limited to the 8-h hold for processing whole blood into platelets, it will streamline the current method by automating manual steps that will improve blood center operations and hopefully operator satisfaction.

With the single centrifugation method, operators are able to load four whole blood bags into one device and then move on to load several other devices while the first device is running. One operator can operate four devices at a time. Each cycle is on average 25 min and assuming a 7.5-h working day and 250 working days per year, one operator running four devices during one shift can process up to 72,000 WB units per year. The single centrifugation method allows the pooling of 4–5 intermediate platelet units into one transfusable dose. Assuming the worst case of five units per pool, 72,000 WB units yield 14,400 platelet doses for transfusion. This calculation demonstrates the productivity blood centers may experience by implementing the single centrifugation method.

Conclusions

The US platelet supply is at risk due to its dependence on aging apheresis donors. Meanwhile, platelets in whole blood collections are being discarded. The US blood collectors should consider manufacturing WB-PLT to supplement the apheresis platelet inventory and strengthen in the US blood supply. Moreover, the introduction of a fully automated whole blood processing system based on a single centrifugation cycle has simplified the manufacturing of WB-PLTs to deliver high-quality, consistent products without taxing the staff (Malvaux *et al.*, 2021; Perez *et al.*, 2021). Building resilience in the supply chain involves introducing multiple sources of material; in this case, platelets should be prepared by two different methodologies from two different donor populations: whole blood and apheresis.

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