Editorial

Single donor platelets versus whole blood derived platelets: are they the same?

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Twenty years ago, Dr. Ness co-authored a paper describing the advantages of single donor platelets (SDP) over pools of whole blood derived platelets (WBDP), at a time when he believed the evidence strongly favored the use of SDP (1). The potential advantages of SDP that were considered included the following:

(I) Reduction of infectious complications;
(II) Reduction of transfusion reactions;
(III) Ease of leukodepletion;
(IV) Reduction in transfusion frequency;
(V) Prevention of alloimmunization;
(VI) Treatment of alloimmunized recipients;
(VII) Enhancement of platelet quality;
(VIII) Elimination of the need to pool WBDP in transfusion service.

At the time of this earlier publication, it had already been clear from the Trial of Reduce Alloimmunization (TRAP Study) in adult leukemic patients that the goal of reducing alloimmunization by SDP was not achievable. Patients randomized to SDP or WBDP had similar rates of alloimmunization and platelet refractoriness (2); nonetheless, the other seven potential advantages listed above supported a recommendation for extensive or even exclusive use of SDP.

The most substantial advantage of SDP was the reduction of septic platelet transfusion reactions (SPTR) from bacterial contamination in platelets stored at room temperature. A 12-year study at Johns Hopkins demonstrated that SPTR were markedly reduced after switching to the exclusive use of SDP. As we moved from a starting point at which 50% of platelets were WBDP to a point where 100% were SDP, a significant drop in SPTR was noted over time (3). Based upon this data that SDP is critical to reduce SPTR, we took the initial step to exclusively use SDP. After this conversion to 100% SDP, however, we continued to track SPTR and noted only partial success, with the reduction but not elimination of significant reactions (4). In 2003, with the introduction of bacterial culture, these potentially lethal reactions were markedly reduced (5). Since then, the American Association of Blood Banks (AABB) started to require blood culture, and most of the platelet transfusions in the US moved to the provision of bacterially cultured SDP since reliable and cost-effective bacterial testing was not available for WBDP (6).

More recently, it became recognized that bacterial testing reduced the rate of SPTR by 60–70% so there continued to be room to further reduce these reactions. The United States Food and Drug Administration issued guidance to require enhanced bacterial testing later in platelet storage. The initial guidance was issued in 2016 and was finalized in 2019. Blood centers and hospitals could use larger volumes of platelets in the culture system, with delayed sampling (7), the use of a hospital based bacterial detection device later in storage (8), or pathogen inactivation (9) In addition, systems had become available to pool WBDP at the blood center and perform a single bacterial screening test of the pool (10). With the implementation of these enhanced techniques, the most important early advantage of SDP to reduce SPTR has become less relevant. Nonetheless, it remains true that emerging viral infections would be less of a concern with SDP as opposed to WBDP. In fact, pathogen inactivation technology is available only for SDP in the United States, rendering WBDP more susceptible to an emerging viral pathogen or even to a known transfusion transmitted viral pathogen that was missed by current testing methods. However, US blood centers have managed to respond

rapidly to new viruses such as West Nile Virus, so that the strongest argument for the exclusive use of SDP has become less persuasive.

Of the list of potential advantages of SDP, eliminating the need to pool platelets at the hospital was an important motivator for our move at Johns Hopkins to an exclusive SDP system. Nowadays, however, many countries have blood centers that are able to provide WBDP from pooled buffy coats, thereby eliminating the need for additional manipulation at the hospital transfusion service. In the US, where buffy coats are not yet licensed and available, blood centers can pool WBDP in evolving commercially available systems that enable pre-storage pooling and reduce the 4-hour outdating of post-storage pooled platelets (10).

Other potential advantages of SDP that were featured in the earlier list may still be valid, but they remain unproven. With respect to transfusion reactions, it is unclear whether Transfusion Related Acute Lung Injury (TRALI) risk is exacerbated by increasing the number of donor exposures in platelet pools or rather by exposure to the greater amount of plasma from an SDP donor capable of provoking TRALI. Likewise, SDP prepared with the use of platelet additive solutions (PAS) would seem to be less likely to provoke allergic transfusion reactions, but convincing evidence of the superiority of SDP is not abundant (11). Actually, as it pertains to out of group transfusions, SDP are commonly suspended in PAS and have a lower plasma content, which reduces the risk of hemolysis from high anti-A/anti-B titers. For patients requiring larger doses of platelets, it is probable that platelet pools with increases in donor exposure could cause more reactions. Nevertheless, in an attempt to avoid unneeded high doses in children and neonates, most blood centers now split apheresis platelet collections such that a patient requiring a larger dose of platelets provided by SDP may instead receive two or three products, each provided from a different single donor.

The indication for which SDP transfusion still has important advantages is bleeding prophylaxis during therapy for hematologic malignancies. Alloimmunization in these patients has been reduced but not eliminated by leukoreduction, so that a substantial subset will require either crossmatched or human leukocyte antigen (HLA) matched platelets which can only be obtained from SDP. These chronically transfused patients are also more commonly observed to have allergic transfusion reactions where SDP, particularly with PAS, can reduce these vexing reactions (12). As such, this population, which represents almost 50% of the platelet recipients in the US, should be supported with SDP. Similarly, HLA/human platelet antigen (HPA) matching is useful in cases of platelet refractoriness or neonatal alloimmune thrombocytopenia (NAIT), and single IgA deficient donors could prevent anaphylaxis in IgA deficient recipients.

For patients receiving platelets for trauma, surgical bleeding, and other indications, the platelet source is less critical. Although there is *in vitro* evidence that platelets collected by apheresis may have improved survival and less activation, enhanced activation in acute bleeding may actually be an undocumented advantage of WBDP (13). Relative to SDP, WBDP have comparable platelet content, quality and efficacy. Most intensivists and surgeons would not be concerned by the use of WBDP for these patients, suggesting that, in the US, a move backward towards increased use of WBDP would not be opposed. In most cases, clinicians ordering platelets are probably not aware of whether their patient is receiving SDP or WBDP. Since US hospitals pay a premium for SDP, this move away from the exclusive use of SDP would be helpful to reduce transfusion costs in our complicated medical system.

Another important consideration is the mismatch in platelet supply and demand. Although patient blood management programs have reduced red cell transfusions substantially in the US, platelet transfusions have remained stable or have grown. In turn, the main supply of apheresis platelets comes from older committed donors who have been difficult to replace with younger donors (14). In addition, platelets that undergo pathogen inactivation processes produce reduced post transfusion increments, necessitating a greater number of apheresis platelet transfusions. As a result of these stresses on the platelet donor supply, consideration is now being given to providing incentive financial payments to apheresis donors, while using pathogen inactivation of platelets collected from paid donors to address possibly higher infectious risks. Despite struggling to meet platelet demand for SDP, many blood centers are reluctant to move back to WBDP, and they continue permitting platelet wastage by discarding the platelet component of whole blood units.

Based upon these considerations, we believe that the principal advantages that drove many hospitals to the exclusive use of SDP have become less significant and, for the exception of oncology patients, moving backward to the increased use of WBDP could relieve the pressure on blood centers to collect SDP when alternatives exist. The solution may lie in maintaining a combined inventory of SDP for patients with hematologic malignancies and WBDP for

other patients, and it is expected to reduce blood center and hospital costs without compromising patient care.

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