Platelet therapy is always changing

Physicians have been dealing with the question of what constitutes the best platelet (PLT) therapy ever since PLTs in any form became readily available in the 1960s. Although the goal of identifying the best therapy has remained the same, the answer continues to evolve with the passage of time.

Whole blood–derived PLTs (WBDPs) constituted essentially all PLT therapy in the 1970s and controversies involved such topics as warm versus cold storage, the choice of the anticoagulant solution, the best plastic for CO_2 exchange and pH maintenance, and the design of storage agitators. These and other issues were worked out with carefully designed studies which pointed the way to the high-quality PLT products available to patients today.

Single-donor PLTs (SDPs) produced on automated platforms made their appearance in the 1980s; besides increasing the supply of PLTs, SDPs had the advantage of decreasing the number of donor infectious disease exposures at about the time the HIV pandemic spread around the world. HLA-matched or cross-match–compatible SDPs could also be collected in sufficient quantity to effectively treat refractory, immunized patients.

The substitution of WBDPs by SDPs was also abetted by the steady improvement in the design of apheresis equipment. Not only could SDPs be routinely leukoreduced, but a single donor with an adequate PLT count could safely donate a sufficient number of PLTs to make up more than one adult therapeutic dose. Splitting of donations into multiple doses had the amazing financial effect of doubling or tripling blood center income from a single apheresis donation without a material increase in the cost of the collection. The income generated from splitting apheresis donations helped to keep down the cost of other blood components but directly led to equipment manufacturers and blood centers making an enormous investment in the technology of producing SDPs. The use of apheresis PLTs grew dramatically and replaced WBDPs in many parts of the country.

In 2004, AABB's Standard 5.1.5.1 required the bacterial testing of all PLT products before transfusion, further emphasizing the advantages of SDPs over WBDPs. Many hospitals and blood centers were unable or unwilling to perform bacterial testing on WBDPs, and their use became problematic without some form of scientifically valid bacterial quality control (QC). FDA rules require that pooled WBDPs (pWBDPs) be transfused within 4 hours of pooling, making it logistically impossible for blood centers to supply pWBDPs to hospitals before transfusion.[1,2]

With all of these factors in mind, it is not surprising that in 2004, the most recent year for which data are available and immediately after the implementation of AABB Standard 5.1.5.1, of a total of approximately 1.7 million adult therapeutic doses of PLTs given to patients, 1,390,000 were provided as SDPs and 256,000 as pWBDPs. The shift away from WBDPs to SDPs could not be more dramatic.

But time has a way of changing reality and the assumptions supporting the heavy use of SDPs as opposed to WBDPs may not stand up to critical analysis in today's environment. Improved production technologies and greatly reduced infectious disease transmission risks have combined to make pWBDPs once again a viable choice for clinicians.

The efficiency of blood bank component centrifuges and gas transport through plastic PLT containers improved over time. Yields on WBDPs improved from the 50 percent levels seen in the 1960s to 90 percent with currently available equipment. Four to five WBDP units now constitute an adult therapeutic dose of 3.0×10^{11} whereas 10 or more units were needed to obtain the same dose in the 1970s and 1980s.

Methods for bacterial QC of pWBDPs have recently been licensed by the FDA which will probably reduce the risk of bacterial contamination to that of similarly cultured SDPs. These same systems efficiently leukoreduce PLT concentrates eliminating the concerns associated with white cell contamination and interaction in pWBDPs.[3]

Improvements in infectious disease testing significantly reduced the risk of transfusion transmitted diseases making the argument that an SDP transfusion is safer than pWBDPs and more difficult to support. Testing improvements combined with pooling 4 to 5 WBDP units instead of 10 units to make up an adult therapeutic dose has further reduced the infectious disease risk of pooled PLTs. It needs to be remembered also that patients receiving PLT therapy are likely to be receiving many other blood products as well, further weakening the argument that the use of SDPs reduces the chances for disease transmission by blood products.

The TRAP study published in 1997 found leukoreduction rather than limiting donor exposures by use of SDPs reduced the risk of immunologic refractoriness in multiply transfused PLT recipients. This multicenter controlled

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study directly compared the efficacy of both products.[4] Both SDPs and pWBDPs were leukoreduced in the TRAP trial. There was no difference in patient outcomes comparing the two products.

In a telling commentary, current supporters of the use of either SDPs or pWBDPs are both able to produce studies supporting their positions, a circumstance that alerts one to the fact that there may be less to the issue of which product is better for patients than meets the eye.[5,6] Regardless of which is the better product, blood centers and some hospitals as well as equipment manufacturers are heavily invested in the technology of SDPs. Some blood centers do not even produce WBDPs, preferring to meet patients' needs entirely with SDPs. The financial implications must be considered in light of the fact that millions of potential WBDP units may not be produced if SDPs are the only form of PLT therapy given to patients. The marginal cost of producing a unit of WBDPs is just a few dollars. The potential availability of inexpensive WBDPs for pooling is probably quite high, and the existing pooling systems may result in the production of appropriately sized pools at a cost that is competitive with SDPs.

The process of pooling WBDPs is not without its problems. There are at least three times the number of chances for bacterial contamination of the pools during manufacturing as opposed to SDPs and the number of pWBDPs with positive bacterial cultures is at least two times that of SDPs (Morris P, Community Blood Centers of Southern Florida, Lauderhill, FL, personal communication, 2006). The great majority of the organisms found in both components are skin contaminants. The finding of bacterial contamination in a pool of WBDPs, however, might dictate that all the RBCs and plasma products made from those whole-blood donations must be discarded, reducing the value and increasing the cost of pWBDPs. Logistical issues involving the production of WBDPs and subsequent pooling of similarly dated WBDP units are formidable even in a large blood center. As with all new products, these and other issues will need to be worked out over time.

It is too soon to say if pWBDPs will begin to reverse the national trend in favor of SDPs. The low cost of production, equivalent efficacy, and the potential abundance of raw material may make a compelling case for the expanded use of pWBDPs. As more manufacturers come to market with licensed pooling algorithms, the cost of production is bound to decrease.

So the answer as to what constitutes the best PLT product for patients has become more complicated. If pWBDPs thought to be of therapeutic equivalence become widely available and are priced below that of SDPs, hospitals and physicians may rethink which PLT product to order.

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