

Blood Products Advisory Committee
March 15, 2002

Review of Data Supporting Extension of Dating Period for Platelets

Issue: Extension of platelet storage time

Bacterial contamination of platelet products continues to be a problem with a contamination rate estimated at 1/2000 units. Storage of platelets at room temperature for up to 5 days allows for proliferation of bacteria in platelet units, and "older" platelets have been associated with increased incidence of septic transfusion reactions. Various approaches are being developed that would either screen or chemically decontaminate platelet units prior to transfusion. If such methods are shown to decrease bacterial contamination of platelet products, storage of platelets out to 7 days may become practical. At this presentation, we will discuss current thinking on the criteria that will be needed for acceptance of 7 day old platelets.

Background

Platelet transfusion products include pooled random donor platelets and single donor apheresis platelets. Random donor platelets are produced from whole blood collections and stored individually for up to 5 days at room temperature. They are pooled (4-6 units) prior to transfusion and transfused within 4 hours of pooling. Single donor apheresis platelets are stored for up to 5 days at room temperature and do not require pooling. In 1981, platelet storage was extended from 3 days to 5 days at room temperature due to improved platelet storage bags that allowed more efficient gas exchange. In 1984 this was further extended to 7 days. However, with the extended storage at room temperature, bacterial proliferation became a significant problem and an increased number of platelet transfusion-associated sepsis reactions were reported. In 1986, on the advice of the BPAC committee, the storage time for platelets was changed back to 5 days.

FDA approach to evaluating 7 day old platelets stored under current conditions

In 1984, a majority of platelets for transfusion were non-leukoreduced, random donor platelets. Today, platelet products are leukoreduced, include apheresis platelets, and are stored in plastic bags with gas permeability properties different from earlier bags. Thus, current storage conditions are vastly different from what was used in 1984-1986 and it is not clear whether the current conditions will adequately support platelets stored up to 7 days.

Evidence that storage conditions have changed in at least one parameter over time comes from studies the FDA has carried out on platelet products received from collection centers around the country in support of licensure. These products are tested for pH, volume, and platelet count at the end of the storage period. The data presented in Figure 1 are pH values of platelet products submitted to the FDA in the years 1995-1999 (2). During these years the pH has risen steadily from 7.0 to 7.33. Figure 2 shows the

percent of the products submitted that had pH values greater than 7.4 for each year. In 1995, the percentage was 2%, but by 1999 it increased to 45%. These changes correlate well with the change from non-leukoreduced to leukoreduced products shown in Figure 3. In 1999 leukoreduced products accounted for only 2.5% of the submitted products, but this changed to 95% by 1999.

This change in pH may affect the quality of the final platelet product. The AABB recommends that platelets with pH <6.2 not be used for transfusion, and in Europe the recommendation also extends to platelets with a pH >7.6. A pH of <6.2 or >7.6 is known to be a good indicator that the circulation of transfused platelets will be poor (1,2).

To evaluate the quality of platelet products, the Agency relies on a battery of in vitro measurements, and on an in vivo test. In vitro testing only identifies severely damaged platelets and does not predict clinical performance. In vivo testing consists of following the recovery and circulation time of radiolabeled, autologous platelets re-infused into human volunteers. The in vivo radiolabeled test is the current "gold standard" for evaluation of platelets. In most cases it is a surrogate for the ability of platelets to perform adequately in preventing and stopping bleeding episodes. The ability of each marketed platelet storage bag to support platelet viability out to 7 days will need to be demonstrated by these test methods.

Presentations

Drs. Slichter and AuBuchon will present their assessment of the quality of platelets stored out to 7 days.

- 1) Murphy S, Gardner FH. Platelet storage at 22 C: Role of gas transport across plastic containers in maintenance of viability. *Blood*; 46(2):209-218, 1975
- 2) Poindexter, B.J., Shafer, B.C., Mondoro, T. and Vostal, J.G. Increase in the pH and mean platelet volume of Platelets, Pheresis Products submitted to the FDA for quality control testing. *Transfusion* Vol 39 Suppl; S76-P. 1999

Discussion points:

What should be the minimal standard of in vivo "efficacy" that 7 day old platelets will need to meet? For example, would initial recovery of 40% and a 5 day lifespan be sufficient?

If the 7 day old platelets are approved, should there be a surveillance study to monitor any unexpected transfusion reactions?