



Review

Storage and handling of blood components – perspectives

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ARTICLE INFO

Keywords

Storage conditions
red cell concentrates
platelet concentrates
FFP

ABSTRACT

The storage and handling conditions of cellular blood components and plasma are often rigorous, which is causing extensive discard of components that may be of acceptable quality as the rules for “out of optimal storage conditions” seem to be based more on tradition than scientific investigations. This short review summarizes some of the key papers indicating that it should be time for reconsideration of these rules, and some new suggestions are carefully indicated. Red cell concentrates, platelet concentrates and FFP are considered; lyophilized plasma and never-frozen liquid plasma are not included in this paper.

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Contents

1. Red cell concentrates	104
2. Platelet concentrates	104
3. Plasma	104
4. Out-of-blood bank handling of blood components	105
5. Conclusions	105
References	105

When blood banking emerged, blood was stored cold for a short time only. After improvements of storage solutions, the storage time was extended to up to 4 weeks. During whole blood storage, the quality of the blood components; red cells, platelets and plasma deteriorated at different speeds. This fact, and as patient treatment improved – only a minority of patients need all components of whole blood, led to the development of component therapy. Red cell concentrates were stored at 2–6 °C, plasma was frozen to a temperature below – 20 °C and many plasma factors were isolated and concentrated through fractionation.

Based on laboratory studies, platelet quality may be best conserved at low temperatures, but unfortunately – a cold platelet storage lesion leads to a clustering of GPIb on the platelet surface [1]. In vivo, this change provides an early removal of the platelets from the circulation. Correspondingly, 20–24 °C was chosen as the optimal storage temperature for platelet concentrates [2]. Later, it became available that also agitation during platelet storage was highly preferable [3], and agitation during storage was later implemented as a general routine.

During the last decades, a necessary focus has been given on Good Manufacturing Practice (GMP), including quality control of the blood components.

It is obvious that optimal quality is not only desirable when the components are stored in the blood bank, but also during transportation and in the wards and operating theaters before the actual transfusion to the patients. This again

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led to extremely strict rules and guidelines for handling of the components – not at least rules for how long the components were allowed to stay out of the blood bank before discarding instead of returning the not transfused units to the blood bank.

For red cell concentrates, “the 30-minute rule” was predominant. If red cell concentrates were kept more than 30 minutes at ambient temperature it had to be discarded. In countries such as Norway, some local regulations allowed only 10–15 minutes. The justification of this rule was fear of risk of bacterial growth in the concentrate in addition to the possible reduction in quality.

For platelet concentrates, a major concern was the time without agitation during transportation – in addition to the fear of the influence from changing temperature. Concerning plasma, similar concerns were raised. For special plasma preparations, as solvent–detergent plasma, the manufacturer allowed only 4 hours interval between thawing and transfusion. For regular plasma, in Sweden, unfrozen, refrigerated plasma was – and is – stored for up to 7 days for use in emergency situations, whereas in other locations, the thawed plasma was discarded after only 4 hours.

The idea behind all these strict rules was always good – to ensure optimal quality of the components transfused. However, the rules led to substantial blood component destruction. In Norway, during the last 10 years, around 15,000 of a total of 200,000 red cell concentrates yearly were discarded. Obviously, this is not the intention neither by the blood donors providing their gift for the benefit of the patients nor by the blood banks struggling to achieve sufficient blood supply for the patients’ needs.

The purpose of this short review paper is to point to newer research that indicate that more attention must be given to storage and handling of blood components – to suggest ways to clarify what is needed to establish practical and safe routines – ensuring that patients are transfused with low-risk, high-quality blood components without a parallel high blood component discard rate.

1. Red cell concentrates

The European Committee on Blood Transfusion guidelines for red cell concentrates state that storage conditions must be between 2 and 6 °C and that validated transport systems must ensure that at no time during a maximum transit time of 24 hours did the temperature exceed 10 °C [4]. The UK guidelines say that transportation should take place under conditions as close as possible to the specific storage requirements and that the quality must comply with the general quality specifications [5]. Similar approach is indicated by the AABB Technical Manual [6], whereas the Australian guidelines stress the “30 minute rule” [7].

In 2011, Hancock et al. [8] conducted a study where they exposed red cell concentrates for a temperature of 10 °C for 12 h for two periods of 5 h and 12 h each. No significant loss of quality was detected. The same group has published later papers concerning effects of storage at different temperatures. In one study, it was shown that multiple short-term storage episodes to 22 °C to –2 °C did not affect red cell quality, opposing a marked decline in quality when the red cell concentrates were exposed to 25 °C for a storage time

of 24–48 h [9]. The group showed that exposure to 30 °C for three periods of 30 min each did not affect red cell quality [10]. Although they stressed that bacterial contamination studies were not included [9], a 60-minute rule could be more appropriate than the 30-minute rule [10].

Ramirez-Arcos and collaborators have investigated the effect of extended storage at room temperature of bacterial growth by inoculating red cell concentrates by several bacteria, including *Yersinia enterocolitica*, *Staphylococcus epidermidis*, *Escherichia coli* and *Serratia* species [11,12]. They concluded that at least 3 hours in room temperature was safe, but multiplex exposures to room temperature did slightly promote bacterial growth in contaminated units, although the RBC quality was not affected.

Several devices and packing methods are available to ensure optimal storage conditions during transportation. Use of this equipment may significantly reduce the risk of red cell deterioration [13,14].

2. Platelet concentrates

Concerning platelet concentrates, the UK, AABB and Australian regulations do not indicate specific detail instructions for transportation, but a storage temperature of 20–24 °C is mandatory as well as agitation during storage. Also, the European Committee on Blood components use general terms to describe storage conditions.

In a review paper, van der Meer and de Korte underlined the importance of storage container, temperature and agitation during storage. However, as transportation without agitation is unavoidable, this is acceptable although local hypoxia may lead to some reduction in platelet function [15]. This conclusion was in part based on studies by Wagner et al. that demonstrated that the quality of apheresis platelets was maintained for 5 days of storage, opposing documented loss in platelet function after 7 days of storage [16]. Vassallo et al. have published a study showing similar results for interruption of agitation for 24 h of whole-blood derived platelets [17].

Skripchenko et al. published in 2012 that a rest period before agitation could be preferential for platelet quality [18]. In 2013, the group performed a study indicating that use of platelet additive solution as storage medium may lead to significantly more damage to platelet function under storage without agitation compared with platelets stored in plasma [19].

3. Plasma

Concerning plasma, the European guidelines are clear: Thawed plasma must be used as soon as possible and must not be refrozen. Other guidelines reflect similar opinions – and for pooled, pathogen reduced plasma specific instructions are provided.

There are many publications indicating that these guidelines are too strict and lead to unjustified discard of plasma. Several studies report no significant loss of coagulation factor activities on thawed plasma during a holding period of up to 7 days in the refrigerator. This also seems to be valid for SD-treated pooled plasma. Storage of liquid plasma for emer-

gency transfusions may be advantageous even over fresh-frozen plasma.

4. Out-of-blood bank handling of blood components

The published papers strongly indicate that the current guidelines are too strict concerning re-inclusion of issued blood components. Thus, the discard rate of “the gift of the donors” is beyond what is reasonable. However, if the guidelines or recommendations should be prepared only to protect the blood stock, this could easily cause serious concerns for patient safety.

For red cell concentrates, it seems well reasoned to allow at least a “60-minute out of blood bank refrigerator rule” [8–11,13,14,17]. This is documented by several studies, and based on hemovigilance data, bacterial contamination of red cell concentrates are extremely seldomly reported as cause of clinical detectable infection [20–23]. However, as documented in an excellent overview of red cell research and research opportunities, more information is needed to evaluate the red cell storage lesion and its clinical relevance [24].

Since many quality assured temperature surveillance systems now are available, it should be possible to establish good local regulations for inclusion of red cell concentrates into the stock, as detailed information of “the storage and transport history” can be documented by these systems.

Concerning platelet concentrates, storage conditions without agitation for 24 h seem safe, also based on earlier publications [25]. The temperature issue is less clear. Cold storage may improve the in vitro quality of the platelets [26], but the “cold storage lesion” may significantly reduce the platelet life span in non-bleeding patients receiving prophylactic platelet transfusions [2]. The publication indicating a negative effect of platelet additive solution [19] definitely needs attention as this storage medium becomes more widespread and the content more and more sophisticated – to reduce the residual plasma content.

Several articles and extensive clinical experience should allow thawed plasma to be kept in the blood bank refrigerator for at least 7 days. Concerning commercially produced pathogen reduced plasma, similar results are reported as for thawed regular fresh-frozen plasma, but formal and legal issues could hamper liquid storage of this component – as pharmaceutical principles may apply [27–30].

5. Conclusions

Storage and handling of blood components is a delicate balance – between the need to optimize the gift of the blood donors and to ensure optimal quality of the blood components transfused to the patients. Further research is definitely needed, but based on available information it should be safe to indicate that

- Red cell concentrates may be re-included in the blood bank stock if it has been kept up to 60 minutes out of standard storage conditions.
- Platelet concentrates may be transfused after 24 h out of standard storage condition.

- Thawed fresh frozen plasma may be stored in a refrigerator for 7 days before transfusion.

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