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Human Platelet Concentrates and Derivatives Preparation Issues Pretransfusion

Badlou BA*

Bbadvies and Research, Research and Development Dept, Zeist, The Netherlands

Introduction

In this paper is tried to put forward the important differences in preparation condition of platelets(PLTs) concentrates (PCs) as pharmaceutics- therapeutically products. Although it looks like a very simple task but the 'knowledge' behind human PLTs and derivatives transfusion is more than only isolation, preparation and storage of a blood product. Moreover, the PLTs are very fragile blood cells, and the related Transfusion Medicine procedures are complex basic Medical Sciences. Worldwide, there is 'limited published standard' procedure for appropriate PCs and derivatives preparation (product quality issues). After all, prepared PCs should be transfused to a random (unknown) matched recipients with bleeding disorders, and PLTs function defect (unknown recipient issues). Nonetheless, One might expect that the most Clinics and Blood banking centra work on the standard procedures that previously written, and which they might produced PCs according to the different International establishments. Because these kind of selection and arrangements have major impact on patients' safety, and affect morbidity and mortality rate of transfused recipients, however. The room temperature (RT)-stored PCs are currently used for either therapeutic or prophylactic applications in the Hospitals. On the other hand, the metabolic suppressed PCs (MSPs) are better haemostatic products, and they might be safer in that aspect that they are less prone to bacterial growth and multiplication. Indeed Clinical tests needed to warrant usage of this novel product, in vivo.

Based on recent research and developments published up to 2015 could be said that maybe an "one-size-fits-all" standard strategy for PCs preparation should be implemented in 'the Jungle of transfusion'. Otherwise, preventative measure should be implemented both in the Quality Control (QC) department of the Blood collection centra, and in the Surgery and the ICU/CCU departments to perform QCs, again.

Blood transfusion and cell therapies are life saving procedures. Human whole blood contains three kinds of cells viz. Red Blood Cells (RBCs), White Blood Cells (WBCs) and platelets (PLTs). In the blood collection centers is routinely PLT concentrates (PCs) isolated from voluntary blood donors, and in clinics used as cosmetic and/or therapeutic products. The main issues over the human PCs preparation are transfusion transmitted diseases, immunogenic-, hemostatically ineffective-, and non-feasible PCs [1,2]. Although it's look like a simple procedure, but the 'Knowledge' behind transfusion and transplantation is more than only isolation, preparation and storage of human blood cells as a product [3-6] Moreover, the PCs transfusion knowledge is still very premature and complex to be standardized. The basic Medical Science mixed up with the Biotechnology and Material Sciences [1,2,4] Furthermore which factors underlie the decisions that shaped global PCs usage policy pretransfusion (ordering issue). Worldwide, there are no consistency in standard procedure for appropriate human PCs isolation and preparation that result in no side effects, posttransfusion (product quality issue). After all, prepared PCs should be transfuse to a random patient with bleeding disorders, and PLTs function defect (unmatched and unknown recipient issues) [4]. Nonetheless, the most Blood banks and Transfusion centra work on the appointments and previous set of rules, which they have made during different symposia with each others. These kind of selection and arrangements have major impact on patients safety, and affect morbidity and mortality rate of transfused patients. In addition, there is limited insight about the appropriate PCs preparation- storage to transfuse to any arbitrary hematooncologic (infant and/or elderly) patients (male/female) suffering from active bleeding, who have got PLTs function defect, at random severity. The most transfusion episodes are still occurring with the best hopes, and yet there is no warranty for cure and care, after all. The likelihood of success mainly depends on the recipient immune response, posttransfusion.

Recall, prior to 1950 the human isolated PCs stored under cold condition based on their intuition between 1-10 °C.(7) Subsequently, 70 years basic research of the different laboratories have resulted in a new alternative method, which consequently recommended to produce and store 'the human isolated PCs' under room temperature (RT) condition [6,7]. It is now obvious for whole world that the RT-stored PCs are less haemostatically active, potentially contain unknown proliferated microorganisms, in some extent immunogenic, and could result in septic reactions [2,3,5,8].

In last decade our group have established that (fresh or old) human isolated PCs should be stored not only under metabolically suppressed but also kept under cold condition (MSP4), pretransfusion [5]. In this way quality, quantity, function and viability of (un-) pooled PCs as product could be preserved for more than 18 days [1]. The risk and benefits of cold storage is already established by Pidcoke HF and colleagues but for the MSP4 (Novel product) needed indeed more Clinical tests to monitor adverse events and efficacy to provide verifications for the Clinics and the Regulatory Affairs approval.

Although, there are different reports that have shown the RT-stored PCs could be better stored up to 7 days but the FDA limited these kind production procedures up to 5days due to their high risk of potential (un-) known proliferation of the microorganism, and consecutively septic reactions in the recipients, posttransfusion [4,12].

Although, under the Blood banks' compatible condition is established that the metabolically suppressed (fresh and/or old) PCs stored under cold condition are better preserved [1] and might be less prone to macrophages *in vivo* (less immunogenic), still the RT-stored PCs transfused daily. Other study group claimed that the isolated and prepared cryopreserved PCs also have an enhanced haemostatic activity [11] Obviously, for the different providers, it does not matter which kind of preparation method is used to produce PCs. Additionally, [3] assessed that cold PCs have superior haemostatic functions compared to active RT-stored PCs that contain high glucose [3]. Nevertheless, the

*Corresponding author: Bahram Alamdary Badlou , BBAdvies and Research, Research and Development dept. Zeist, The Netherlands, Tel: +31302211328; Email: bbadlou@casema.nl

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most Blood collection centra are working on the so-called 'Standard Operating Procedures (SOPs), which they have previously prepared during different International meetings. Such agreements and arrangements in one hand, have major impact on the PCs preparation condition, and subsequently, on the recipients' safety [3,4,7,8]. In the other hand, the PCs usage have remarkably become 'out of control' and at random procedure, which eventually are resulting in so many (not-) reported adverse reactions.

From the limited published studies could be seen that in the developed countries, the final volume of PCs that are transfused to a random ICU-bleeding patients are not the same as in the developed countries [9,10]. Additionally, focused on different aspects of assessments on which such selection were made, One might intuitively say that the random system might result in deviation of ordered volume that being transfused.

The isolated PCs are prepared from either pooled random-donors, or single-donor aphaeresis and then transported to the ICU/CCU departments of Hospitals. There are still different unsolved issues in each step of isolation and preparation from donors toward the recipients (Figure 1).

When at random produced PCs being stored up to 7 days, all of these PCs are equally assumed to be efficacious [4] while in practice different patients are responding, dissimilarly. Where a recipient is cured, another might develop sepsis and transfusion allergic reactions.

There are raising evidences that under *in-vitro* preparation methods determined the quality, quantity, function and survival of produced PCs posttransfusion [4]. In last 10 years our group have shown that under diverse conditions the MSP4 either in the small laboratory plastic tubes (1-2 ml), or in the specific permeable plastic bags (500 mL and pooled) were better preserved compared to 'actively stored (cold or RT)' controls [1,5,12].Moreover, the same principle of metabolic resting was applicable for 'the old PCs' produced under RT-condition and continued agitation [2,5].

Although our MSP4 (novel product) offers so many advantages still different Blood banks do not use it, might be due to missing final *in-vivo* trials. In addition, the MSP4 could be adapted to any random extreme environmental condition and/or preparation's time, globally [3].

I assume when all available knowledge be gathered together, the Blood banks can prepare all kind of PCs, which are perfect product for requested demands in the clinics. In 21th Century One should not be confused in clinic during ordering desired PCs, and ask himself/herself , which kind of PCs I need to cure (and/or care) my patient? Whether I need functional PCs to prevent massive bleeding? or I should order PCs to support homeostasis prior to massive bleeding? Do I need to mention in my ordering forms that I need haemostatic active Cold PCs? Or RT-stored PCs? Which one is better in case that I need to use it therapeutically? Or prophylactic? And/or both?

In a perfect world a Surgeon in the ICU and/or CCU of Hospitals should order according to the SOPs and sort what he/she needs. When she/he needs, and knows how many she/he needs to cure and care her/his patient (Figure 2). Consequently, the recipients get the perfect matched PCs at the time that they need without side effects.

At last but not least, One might assume that misguidedly the most blood banks' obliged to produce and implement their final goal toward 'super PCs' that (should) possess both function and survival properties, at the same time. At this moment, neither the Companies

- storage condition	- Surgery department
- time and environment	- ICU/ CCU of Hospital
	 storage condition time and environment

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Preferred demand ~ preparation of PCs \rightarrow proper cure and care \rightarrow no side effects

Figure 2: Perfect situation is a balance between desired demands vs. desired PCs produced without side effects in patient post transfusion.

have succeeded to produce such 'super PCs' nor the governmental Research groups. Eventually, could be said that the "one-size-fits-all" concept did lead into different controversial results, which neither patients' nor the clinical society have had profit of it. Hence, I think that we have to go back to sketch, and highlight more about the SOPs, using 'all proper' Medical Scientific data, and not economicbased improper procedures. Taken together, the 'proper balance' between order-delivery-usage- efficacy and side effects is not optimally present yet. Generally, the appropriate bridge between demanding organizations (Hospitals) and providers (Blood banks) is still not properly formed, and however persistently there is misbalance in the communications, which finally affects patient's health and causes side effects, haemostatic. Misunderstandings' as are proposed evidencebasely by different research groups from bench to bed implicates that One in clinical setting still cannot order required PCs, which fulfill his desired therapeutic goals.

The future clinical studies could provide evidences whether the metabolic approaches can offer a base for widely available therapeutic products to cure and care different bleeding episodes.

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