Perspectives on the six pillars of quality in multi-component apheresis: The Lisbon regional blood centre experience

Abstract

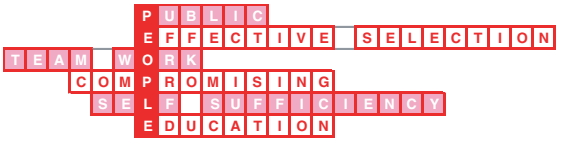
Quality in apheresis technology, whether single or multi-component collections, is synonymous with safety from beginning to end, or from needle to needle. The essential pillars of a good apheresis programme (GAP) are therefore based on, at least six interrelated P's:

1. The right People, including both motivated donors and skilled personnel.
2. The multitask, validated, interactive, automated Process designed for production of purer and safer Products, having optimal yields and minimal side effects.
3. The evidence-based efficient and safe transfusion practice for targeted Patients.

The three others, physically less apparent, which are conceptually accepted to contribute to safety of supply, include: Periodicity, Priority and Price. The best practice, however, must be evidence based, with no harm to donor, operator or recipient. This must be proven with combined laboratory and clinical observations; surveillance and hemovigilance from donors to recipients as well as a review of the lessons learned for continual improvement.

This manuscript highlights the views of the Lisbon Regional Blood Centre apheresis unit on the GAP essential six pillars of quality, bearing in mind that "there are more than six P's that cross everyone's head"... just like a "big crossword" as indicated below.

1. People



When considering the six pillars of the best practice in GAP the very first focus point in everyone's mind is people: how to inform the public, educate, motivate and increase consciousness about self-sufficiency. Donor availability depends on the promotion, recruitment/retention and commitment of healthy and highly motivated people, capable of creating an effective and excellent panel of donors [1,2].

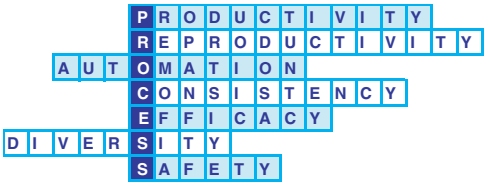
Portugal is a small country with approximately 10 million inhabitants (data related to the 2001 census), more women than men, and has grown 5%, mainly because of the migratory flows from Africa, Brazil and the Eastern countries. This new population introduces some new emergent diseases as far as transfusion safety is concerned.

In the Portuguese age pyramid, we can see that the number of individuals younger than 15 has decreased whereas the number of individuals older than 60 has increased: we are perhaps getting old and more in need of transfusion therapy.

Regarding the number of Transfusion Medicine specialists (named Immunohemotherapy) and considering the data of the National Health Service (2002), overall 157 are spread over regions with a feeble relationship to the number of inhabitants (1.5/100,000 inhabitants). Clearly, developing the right communication skills both horizontally and vertically is now becoming a fundamental asset in organisational structures, and externally.

This is of particular relevance to recruitment/retention of suitable donors as a citizen's availability for donation depends on the donation's acceptability level (i.e. solidarity, religious, social and cultural motivations) but also the trust level that the citizen has in the country's transfusion system (hence there is an absolute need for positive communication made by the specialised communication operators). In Lisbon, at the Regional Blood Center (LRBC) the mobilization of donors to the Apheresis Collection Program was made through a professional and personalized campaign using a brochure called a "different way of giving blood".

2. Process



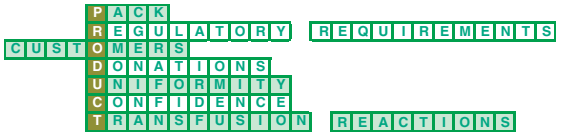
The capacity to develop and implement automated processes not only increases productivity and efficiency with consistency but also improves safety [1,3]. Currently, automated multicomponent collection by an apheresis process has transformed blood component production into a highly automated controlled process with adherence to Good Manufacturing Practice and other regulatory requirements. In this context, the apheresis processes are based on a methodological consistency assured by the fulfilling of operational procedures that describe, in detail, the objectives and final specifications of the product. The divergence from the set specifications, allow us to investigate the short-comings and put in place remedial actions, as exemplified below.

We compared the results obtained by two cell separators at the LRBC apheresis unit (Trima 4 and Trima Accel), in terms of efficiency and donor safety. We have observed that besides increasing donor safety (reduction of the percentage of moderate and light reactions), the efficiency of the process is considerably increased (up to 13%) and in some cases it becomes possible to convert the donors of simple donations of platelets (SDP) into double donations (DDP). Moreover the reproducibility of the results was not at 100% with Trima 4, as this model of cell separator could poorly fulfil the final quality specifications of the desired product. We have observed that there may be at least two types of donors: good responders (ratio programmed profitability/profitability obtained >1) and poor responder donors (programmed profitability/obtained profitability <1). To address the possible cause and effect relationship in the poor-responders we have compared the characteristic of platelets present in the LRS chamber with those at the end of donation and to donor hematological parameters (de Sousa et al., in press).

In brief, we found a higher level of platelet aggregates, with a small MPV, which translates into a greater degree of platelet activation/microvesiculation in certain donor populations. Since the comparative study of the content of the two LRS chambers (Tr4 and Tr Accel) showed a similar pattern we concluded that either some donors may have a greater susceptibility to platelet activation (i.e. donors with factors associated with tobacco, physical exercise and some medications such as contraceptive, etc.) or this is related to poor performance of the LRS chamber in the cell separator in Tr4 which is not large enough for complete retention of aggregated platelets and leukocytes, when a greater level of activated platelets are present. This finding is in line with the UK experience with the Spectra, reported by one of us in this symposium [4].

In short, the implementation of automated collection by Tr Accel allows us to obtain more consistent, uniform products in accordance with the specifications previously established, regardless of the hematological variability of the donor. Moreover, the lower incidence of transfusion reactions leads to the satisfaction of our clients [5].

3. Product

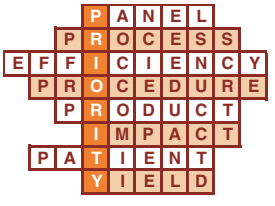


The concepts of product quality and safety/efficacy have evolved through time: in the seventies and at the beginning of the eighties the perception of the risk as related to the product was very small (fewer informatics, equipment, regulation and documentation). The emergence of transmissible infectious agents through transfusion led not only to a more comprehensive donor selection/screening and universal leukoreduction but also to growing involvement of the authorities

that regulate the blood sector and stringent adherence to the principles of quality and GMP production (as a sub-industry focused on the quality of the product) [1,6]. Furthermore, blood bank activity in every European Union member state is regulated by Directives, namely 2002/98/CE, that will become mandatory in February 2005.

In Portugal the Council of Europe and European Union guidelines has been adopted for apheresis [7]. Adherence to this standard of practice helps in the harmonisation program and in quality improvement. The minimum requirements for platelet quality are based on the cellular content, on platelet function and metabolic activity indicators such as pH (optimal range: 6.8–7.4). The higher pH facilitates platelet aggregate formation and microvesiculation, while the lower pH leads to cellular damage and necrosis. Using EU guidelines, we find two deviations: with the concentration and the pH. First, we found about 15% of platelets collected by apheresis presented with concentrations higher than 1.500 plt/uL. This deviation was resolved after changing the cell separator program. Secondly, we observed that the pH value on the fifth day of storage, at 22°, remained higher than the acceptable limit. An investigation has been undertaken to assess the impact of different periods of the post-collection resting period (1, 3 and 8 h) on the maintenance of pH in the optimal range (6.8–7.4). Even though the results were, on average, better with the eight hour resting period, according to the manufacturing recommendation, we adopted the three hour resting period.

4. Priority



The excessive focus on the regulation of the product's quality can lead to the omission of other important circles of dependence of quality, for instance, the creation of a faithful and healthy donor panel, the revision of the use of blood, the regulations for monitoring patients to transfuse and the evaluation of the transfusion efficacy. The optimization of transfusion practice leads to an increased Quality Assurance of the whole transfusion chain, from donor to recipient. This represents a priority, which changes in line with scientific evolution and other scenarios related to continual quality improvement, that are in constant change.

The top priority for the LRBC apheresis unit is to create a healthy and faithful donor panel, allowing an increase in the efficiency of the process. Nevertheless the increase in productivity (efficiency) will depend on the donor's hematological characteristics. In other words, the conversion of single to double dose apheresis donors depends on the previous counting of platelets, and as far as the active apheresis donor panel is concerned, it becomes less performable given the average counting of platelets in the Portuguese population.

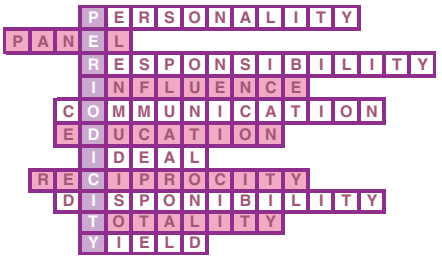
The fulfilment of the minimum requirements of the product's quality does not necessarily define the ideal product to transfuse which will have to consider the donor's profile and the transfusion protocols established in each institution.

It is therefore of vital importance that Apheresis Collection Centres receive information about the clinical situation (neoplasic, transplanted) of patients in need of a platelet transfusion, namely what platelet component transfusion protocols are in use, the kind of platelet component (low doses versus high dose), as well as the physician's expectations and the transfusion efficacy of transfused products, to be able to provide the right component in the right dose for the right patient [8].

Clearly, a safe therapeutic transfusion is a complex process that requires insertion and coordination of different hospital services (medicine, surgery, anaesthetics, nursing, pharmacology). In this context, it is important to refer to the part played by the Hospital Transfusion Committees and its articulation to the Regional Blood Centres.

In our region the first ones where created in 1996. This active and formal structure promotes hospital surveillance in terms of transfusion safety: they evaluate and establish new transfusion therapeutic protocols, assure the surveillance of the clinical benefits related to traditional therapeutics and are important strategies in the patient's safety and evaluation of the transfusion efficacy.

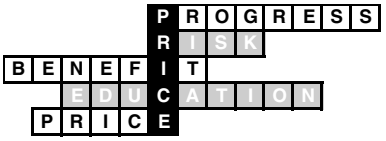
5. Periodicity



The donation's periodicity will depend very much on both the donor's and operator's personality and availability as well as the review and the statistic evaluation's periodicity with an indicator of quality and transfusion practice.

In the LRBC, we collected 880 apheresis concentrates, from 237 donors with a donation index by donor of 3.7. More than 50% of our donors are linked to the apheresis programme. Several factors reportedly can influence the donor's hematological parameters upon frequent and large double dose donations. Occasionally, in some donors, some leukocytes appear in the final products which appear to have limited adhesion property on the filters, indicating that they might be released from marginal pools or for some unknown reasons donors may take a longer time to generate the basal level of some hematological parameters [9,10]. Moreover, it is not known that long term repeated donations have any effect on leukocyte subpopulations. Clearly, more information on this topic is needed when switching to large scale multicomponent production.

6. Price



Quality in Transfusion Medicine is only complete if we discuss the cost in terms of the balance of clinical benefit, adverse effect and wastage (the best clinical management). Costs of good clinical management, through the implementation of automation and Information Technologies (IT) in the collection centres and hospital transfusion services are associated to the development of a correct medical practice and complemented with professional operators with transfusion medicine knowledge [1,11].

Nevertheless, an objective analysis of cost cannot be exclusively determined by the cost of the production process. It is fundamental to integrate the donor's parcel (with its hematological, biological and physical variability, its time and motivation, that determine the process's productivity) and the patient's parcel (what kind of thrombocytopenia, what complementary transfusion support and what dose to transfuse) along with the operator and the physician parcels.

The production and usage of new generation blood components play an essential role in contributing to the reduction of mortality and morbidity linked to transfusion; to reduce the hospital stay time and to increase life expectancy and quality and ultimately to increase health to the community in general.

To sum up, some of the essential pillars of GAP, which conceptually contribute to dual pillars of safety and supply are highlighted, simulating the crossword patterns. The good apheresis practice must be evidence-based and can only be achieved effectively by a close communication/collaboration, openness/transparency and trust between all parties involved (public, politicians, press, manufacturers, transfusionist/clinician and

regulatory agencies), in the benefit of patient's health care.

References

[1] Gail Rock, Seghatchian MJ. Quality assurance in transfusion medicine – conceptual, serological, and microbiological aspects (vol. I), and Methological advances and clinical aspects (vol. II); 1992.
[2] Chiavetta JA, Deeks S, Goldman M, Hannon J, Leach-Bennett J, Megânn H, et al. Proceedings of a consensus conference: blood-borne HIV and hepatitis – optimizing the donor selection process. Transf Med Rev 2003;17(1):1–30.
[3] Dzik WH, Corwin H, Goodnough LT, Higgins M, Kaplan H, Murphy M, et al. Patient safety and blood transfusion: new solutions. Transf Med Rev 2003;17(3):169–80.
[4] Seghatchian J. Platelet storage lesion: a comparative analysis of six leucoreduced processes in terms of biocompatibility, microvesiculation, retention of prion, and generation/removal of biological response modifiers. ABO 2004;(Suppl. 20).
[5] Sousa AP, Maurício R, Vasconcelos E, Seghatchian J, Negrão L, Xavier S, et al. The impact of Trima Accel on a blood transfusion center apheresis unit. Vox Sang 2004;87(Suppl. 3):S93–145.
[6] Farrugia Albert. The regulatory pendulum in Transfusion Medicine. Transf Med Rev 2002;16(4):273–82.
[7] Guide to the preparation, use and quality assurance of blood components. 10th ed. Council of Europe Publishing.
[8] Alan T. Tinmouth and John Freedman: Prophylactic platelet transfusions: Which dose is the best dose? A review of the literature. Transf Med Rev 2003;17(3): 181–93.
[9] Seghatchian J, Beard M, Kraladsiri P. A case of leucodepletion failure in Cobe Spectra plateletpheresis: further studies on the identification of the potential causes. Platelets 2001;12:302–8.
[10] Seghatchian J, Beard M, Krailadsiri P. Studies on the improvement of leucodepletion performance on the Haemonetics MCS plus for the production of leucodepleted platelet concentrate. Platelets 2001;12:298–301.
[11] Berman Keith E. Expensive blood safety technologies: understanding and managing cost and access-to-care issues. Transf Med Rev 2004;18(1):1–10.

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