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Optimization of the management of platelet concentrate stocks in the Basque Country using mathematical simulation

M. Á. Pérez Vaquero,[1] C. Gorria,[2] M. Lezaun,[2] F. J. López,[3] J. Monge,[1] C. Eguizabal[1] & M. A. Vesga[1]

[1]*Basque Centre for Transfusion and Human Tissues (CVTTH), Galdakao Bizkaia, Spain*
[2]*Department of Applied Mathematics, Statistics and Operations Research, University of the Basque Country - UPV/EHU, Leioa, Bizkaia, Spain*
[3]*Department of Statistical Methods, Institute for Biocomputation and Physics of Complex Systems (BIFI), University of Zaragoza, Zaragoza, Spain*

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Background and Objectives The management of platelet concentrate (PC) stocks is not simple given their short shelf life and variable demand. In general, managers decide on PC production based on personal experience. The objective of this study was to provide a tool to help decide how many PC units to produce each day in a more rational and objective way.

Materials and Methods From the historical data on PCs produced, transfused and discarded in the Basque Country in 2012, a mathematical model was built, based on the normality of the time series of the transfusions performed on each day of the week throughout the year. This model was implemented in an easy-to-use Excel spreadsheet and validated using real production data from 2013.

Results Comparing with real 2013 data, in the best scenario, the number of PC units that expired was 87·7% lower, PC production, 14·3% lower and the age of the PCs transfused nearly 1-day younger in the simulation. If we want to ensure a minimum stock at the end of each day, the outdating rate and average age of the transfused PCs progressively increase.

Conclusion The practical application of the designed tool can facilitate decision-making about how many PC units to produce each day, resulting in very significant reductions in PC production and wastage and corresponding cost savings, together with an almost 1 day decrease in the mean age of PCs transfused.

Key words: mathematical simulation, optimization, platelet concentrate stocks.

Introduction

Optimization of the platelet concentrate (PC) production process is important for achieving a better use of healthcare resources. The management of PC inventories is difficult given the short shelf life of this product and the fact that patients requiring platelet transfusion cannot wait. This means that there is generally excess production, which in turn leads to high rates of wastage due to outdating, and higher economic costs. Further, given that PCs are obtained from voluntary non-remunerated donations, wastage of this type of product is ethically unacceptable. Although the ultimate goal of the producers of blood products and the users (blood transfusion services) are the same, their requirements are different in terms of production and management of the inventory: the former focus on logistic and organizational issues and the latter on clinical factors. In this context, we need to search for a balance between production and demand that is satisfactory from both perspectives.

Platelet component preparation processes vary not only between but also within countries. In particular, there are differences in production methods (apheresis, buffy coat or platelet-rich plasma), the use of pathogen inactivation procedures and/or additive solutions, and the shelf life of the product (5 or 7 days), as well as transfusion policies themselves. Further, the level of co-ordination between hospital transfusion services and producers of blood components differs between regions. Given all this, rates of

Correspondence: Miguel Ángel Pérez Vaquero, Basque Centre for Transfusion and Human Tissues (CVTTH), Barrio Labeaga s/n, Galdakao, Bizkaia 48960, Spain
Email: miguelangel.perezvaquero@osakidetza.eus

wastage vary widely. In Spain, these rates range from 0 to 38·7% in hospitals and in production units are around 3·49 and 1·62% for products with shelf lives of 5 or 7 days, respectively [1]. A study carried out in 10 European countries found a mean discard rate of 14% [2].

In contrast, an outdating rate of just 1% was found when using an information technology (IT) tool for optimizing production (the thrombocyte inventory management optimizer), but such tools are rarely used to guide inventory management [3]. In general, decisions are made on the basis of the personal experience of the people in charge of the production, and situations of uncertainty tend to result in overproduction. Given this, having reviewed the literature on the use of mathematical tools for optimizing PC inventory management [4–8], the Basque Centre for Human Tissue and Transfusions (CVTTH) contacted mathematicians at the University of the Basque Country to undertake a collaborative project. The aim of this project was to develop an IT tool that would support decision-making on how many PC units to produce each day in the CVTTH on the basis of objective criteria.

The mathematical model developed, which is relatively easy to understand, assumes a normal distribution of demand on each day of the week throughout the year, as observed in the 2012 time series of transfusions. The result is an easy-to-use Excel spreadsheet that provides an estimate of the daily production of PCs required across the planning horizon. To validate the model, we compared the production level recommended by the model with the real production in 2013.

Materials and methods

Basque blood transfusion network

The Basque transfusion network is composed of a production centre (CVTTH), 12 public hospitals and nine private clinics, although PCs are only kept in stock in five public hospitals. When hospitals or clinics that do not hold stock need to perform a transfusion, CVTTH provides them directly and immediately with the units required. There is a corporate information system covering all the aforementioned organizations, except five of the private clinics, and this documents the entire chain from donation to transfusion. In this way, there is direct centralized management of all donations and 94% of transfusions in the Basque Country. The shelf life of the PCs is set at 5 days, even though it is tested for bacteria, and each unit contains a minimum of 3×10^{11} platelets, resuspended in an additive solution. In 2013, The CVTTH produces and provides 10 300 units of PC; 47% of the PC units were produced by apheresis (Terumo BCT, Denver, CO, USA) and 53% by pooling five interim platelet units obtained with a platelet-rich plasma method using the REVEOS automated blood processing system (Terumo BCT).

Mathematical model and data used: statistical analysis

The model designed for the management of PCs in the Basque Country assumes a single stock held by the CVTTH, without considering the stock held at hospitals. The CVTTH provided an Excel spreadsheet with daily historical data on PCs produced, including units in stock, discarded and transfused from 9 January 2012 to 29 December 2013. These data for the 103 complete weeks were split into two sets: data for the first 51 weeks, which were used to build the mathematical model; and those for the 52 weeks of 2013, which were used to validate the model, by comparing these real data for 2013 with the model's predictions.

Regarding the days of PC production, we have not included Saturdays (little production) or Sundays (no production), to simplify the model. The PC units produced on Monday, Tuesday, Wednesday and Thursday are placed in stock the following morning, with an age of 1 day, while PCs produced on Friday become part of the stock the following Monday morning, with an age of 3 days, reflecting the real process. At the end of each day, once all transfusions have been given, outdated PC units are discarded. The stock is updated daily in the mornings, after both discarding outdated PCs and including the most recent production. We have applied the first-in, first-out (FIFO) blood management policy for transfusions. The modelling is based on units of PCs transfused without distinguishing between ABO/Rh groups or the source of the PCs (apheresis or platelet pools). We have excluded PCs produced but discarded for various reasons other than outdating (e.g. breaks, and positive serological or nucleic acid test results), and imported PCs, this representing very few units.

In contrast to the case of non-perishable items, for which optimal solutions are known in a variety of settings, the problem of inventory management of perishable items is much more complicated and optimal solutions are known only in very specific situations [9, 10]. In practice, most blood banks use simple heuristic order-up-to rules for platelet production scheduling [11]. Recently, there have been some interesting studies based on discrete-event computer simulations, allowing different policies to be compared [12, 13]. Another interesting approach is the use of dynamic programming[3–5]; since the mathematical problem has a high number of dimensions, it cannot be exactly solved in real time and approximate solutions have been found.

As we do not include set-up costs or an upper bound for daily platelet production in our model, we believed that an order-up-to rule would work well. Note, however, that the problem is not simple, since demand is not stationary (rather it depends on the day of the week), production is only possible 5 days out of seven, and lead time is positive and varies (being one day for Monday, Tuesday, Wednesday and Thursday and three for Friday). While, in many blood banks, the parameters of the order-up-to rule are decided empirically [11], we fix them using a statistical analysis of demand.

Daily PC production

The mathematical model is based on the observed normality of the distribution of the 2012 data on transfusions carried out on each day of the week, from Monday to Friday, combining Monday and Tuesday, Tuesday and Wednesday, Wednesday and Thursday, Thursday to Sunday, and Friday to Monday. Specifically, the normality of data were confirmed in all cases with Shapiro–Wilk and Kolmogorov–Smirnov tests, using IBM SPSS (Armonk, NY, USA) Statistics for Windows, each data set fitting a normal distribution with corresponding mean and standard deviation. The same analysis was performed on 2013 data with similar results in terms of normality and producing similar statistics to those of 2012.

For each day of the week, we set the order-up-to value for the production of PC to keep a safety margin, that is we set it to the mean plus three times the standard deviation of corresponding distribution of 2012 transfusion data. We selected these values as 99·7% of the data lie between $\mu - 3\sigma$ and $\mu + 3\sigma$ in normal distribution with mean μ and standard deviation σ.

The subscripts $i = 1, 2, \ldots, 7$ indicate the day of the week from Monday to Sunday and j the week of the year. The decision regarding how many units of PCs $p_{i,j}$ to produce on day i of week j is based on the current stock $s_{i,j}$ and the estimate of the units that will be transfused over the days to be covered. The decision depends on the day of the week, given that the number of units placed into stock varies through the week. Below, we briefly outline the model for Monday of week j. The production of the following day, Tuesday, is not placed in stock until Wednesday. Hence, regardless of the units ordered on Tuesday, the demand for Monday and Tuesday should be covered by $p_{1,j}$ from Monday and stock $s_{1,j}$. Keeping a safety margin, the order-up-to value is set at $d_1 = \mu_{12} + 3\sigma_{12}$, where μ_{12} is the mean and σ_{12} The standard deviation of the total number of units transfused on Mondays and Tuesdays in 2012. Hence, according to the model, the production $p_{1,j}$ on this Monday is

$$p_{1,j} = d_1 - s_{1,j} \quad (1)$$

or 0 in the event that this quantity is negative. For a more detailed description of the modelling process, see Supporting Information.

Simulations performed

Table 1 shows the number of transfusions that should be covered by each day of production keeping a safety margin, that is, the order-up-to values. We fixed these values for all the calculations of the 2013 simulation. The model allows different parameters to be used for different periods of the year. Experience indicates that there are fewer transfusions during the summer, specifically, from the last week of July to the first week of September. To account for this, we can adjust the safety margins during the summer, using the corresponding means for these 6 weeks from the 2012 data.

To run the simulation, we developed an Excel spreadsheet that calculates what would have been the daily production in 2013 to meet the real demand, using the model based on 2012 data.

The data used for the calculation are the total units of PCs in stock broken down by age, the safe demands and units that expire. More precisely, once the stock $s_{i,j,k}$ of day (i,j) has been updated in the morning, we consider that a total of $p_{i,j}$ units of PCs are produced according to eqn (1), equivalent equations for Tuesday or Wednesday, eqn (2) or eqn (3) (in Appendix S1), depending on the day of the week, i. The number of units transfused is taken from the real data for 2013, in line with a FIFO policy, and outdated units are discarded. The following morning, the stock is updated by including the most recently produced PCs and subtracting units that expired the previous day. This process is repeated day after day, assuming no production on Saturdays and Sundays. Table 2 illustrates the steps of this process.

Results

This section shows the results obtained by applying the Excel spreadsheet to the real transfusion activity in 2013. Table 3 summarizes the comparison of the main results of the simulation with real 2013 data. It can be seen that, using the mathematical model, demand would have been met with 14·42% fewer units of PC and without having

Table 1 Order-up-to values based on keeping a safety margin for each day of the week

Monday	Tuesday	Wednesday	Thursday	Friday
$d_1 = 81$	$d_2 = 81$	$d_3 = 80$	$d_4 = 124$	$d_5 = 127$

Table 2 Excel spreadsheet illustrating the 2013 simulation

		Daily stock								Number of daily transfusions						
Date	Day	$s_{i,j,1}$	$s_{i,j,2}$	$s_{i,j,3}$	$s_{ij,4}$	$s_{i,j,5}$	$s_{i,j}$	d_i	$p_{i,j}$	$x_{i,j}$	$x_{i,j}$	$x_{i,j,2}$	$x_{i,j,3}$	$x_{i,j,4}$	$x_{i,j,5}$	e_{ij}
12/31/2012	1, 1	0	0	34	41	2	77	81	4	29	0	0	0	27	2	0
01/01/2013	2, 1	4	0	0	34	14	52	81	29	10	0	0	0	0	10	4
01/02/2013	3, 1	29	4	0	0	34	67	80	13	31	0	0	0	0	31	3
01/03/2013	4, 1	13	29	4	0	0	46	124	78	16	0	12	4	0	0	0
01/04/2013	5, 1	78	13	17	0	0	108	127	19	27	0	10	17	0	0	0
01/05/2013	6, 1	0	78	3	0	0	81	0	0	13	0	10	3	0	0	0
01/06/2013	7, 1	0	0	68	0	0	68	0	0	9	0	0	9	0	0	0
01/07/2013	1, 2	0	0	19	59	0	78	81	3	34	0	0	0	34	0	0
01/08/2013	2, 2	3	0	0	19	25	47	81	34	23	0	0	0	0	23	2
01/09/2013	3, 2	34	3	0	0	19	56	80	24	24	2	3	0	0	19	0
01/10/2013	4, 2	24	32	0	0	0	56	124	68	31	0	31	0	0	0	0
01/11/2013	5, 2	68	24	1	0	0	93	127	34	26	1	24	1	0	0	0
01/12/2013	6, 2	0	67	0	0	0	67	0	0	16	0	16	0	0	0	0
01/13/2013	7, 2	0	0	51	0	0	51	0	0	14	0	0	14	0	0	0
01/14/2013	1, 3	0	0	34	37	0	71	81	10	35	0	0	0	35	0	0

With subscripts i = 1, 2,. . ., 7 indicating the day of the week from Monday to Sunday and j the week of the year, $x_{i,j}$ are real units transfused in 2013, $p_{i,j}$ and $e_{i,j}$ are units needed to be ordered and discarded each day due to expiry as calculated by the model, and $s_{i,j,k}$ and $x_{i,j,k}$ with k = 1, 2,. . ., 7 are the stock and transfusions of units k days old, respectively. Platelet concentrate was supplied according to a first-in, first-out policy.

Table 3 Results of the simulation and real data from 2013

	Estimate	Real data
Units of platelet concentrate produced	8735	10 207
Units of platelet concentrate expiring	159	1619
% Units expiring	1·82	15·86
Shortfall in units of platelet concentrate	0	0
Average age of units transfused (days)	2·96	3·89
Units transfused at 5 days old	1142	3269
% Units transfused at 5 days old	13·30%	38·06%

to import PC. This would have led directly to a very significant reduction (90·18%) in the quantity of PCs expiring, compared to the real figure. As a secondary effect, we would have reduced the mean age of PCs transfused by almost 1 day, there being a 65·07% reduction in the transfusion of 5 day-old PC.

Further, discarding would have been concentrated in a few days, as can been seen in Fig. 1. Analysing these peaks in wastage, we found that they arose from excess production due to having considered Thursday and Friday in 2 weeks as working days when they were in fact holidays, one in Holy Week and the other in December, and not taking into account the fall in demand for transfusions in the summer. In particular, 36 units expired on the Tuesday after Holy Week, the largest number of units expiring on a single day. Given this, we modified the model, using a value to keep a suitable safety margin over the aforementioned holidays, namely $\mu_1 + 3\sigma_1$ in place of $\mu_4 + 3\sigma_4$ and $\mu_5 + 3\sigma_5$, and adjusting the calculations for the summer as indicated earlier. The result was the production of 8643 units of PCs (92 fewer) and 67 units expiring (92 fewer), just 0·78% of those produced. This demonstrates that in practice stock does need to be managed differently around such days.

In practical terms, it is very important to ensure a minimum stock at the end of each day. In the model described, the minimum stock is 3 units. Table 4 shows the results of the simulations when systematically increasing the production on Mondays, Tuesdays and Wednesdays by k_1 units, as defined by the corresponding eqn (1) and that on Thursdays and Fridays by k_2 units, as given by eqns (2) and (3). It becomes clear that increasing k_1 and k_2, the minimum stock increases, while keeping low percentages of outdating. Figure 2 illustrates the usual behaviour of the daily PC stock from the mathematical simulation with k_1 = 36 and k_2 = 18. Finally, to assess the stability of the model, we ran the model again using different plausible data for 2013, and the results obtained were similar.

Discussion

Given rising economic costs, it is of great interest to optimize PC production to ensure efficient use of healthcare resources. In the literature on blood management, various papers address this problem using simulation tools [3, 4], but few have actually been applied to daily practice [3]. On the other hand, there are multiple publications concerning wastage, although the sources are not always equivalent (hospital-based blood banks, blood transfusion

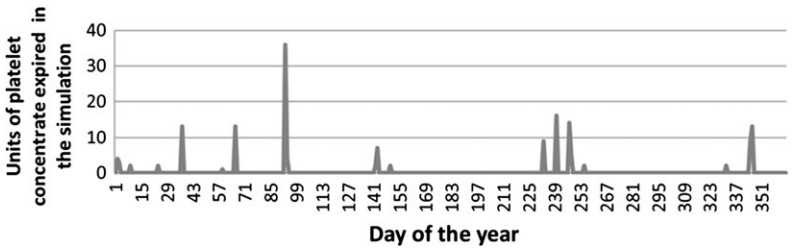

Fig. 1 Number of units of platelet concentrate expiring per day in the simulation of 2013.

Table 4 Results obtained from the model when systematically increasing the production on Mondays, Tuesdays and Wednesdays by k_1 units and that on Thursdays and Fridays by k_2 units

k_1	k_2	Minimum stock of platelet concentrate at the end of the day (units)	% Units expiring	Average age of units transfused (days)
0	0	3	1·82	2·96
4	2	7	2·26	3·06
12	6	13	3·16	3·24
20	10	17	4·15	3·42
28	14	21	5·33	3·58
36	18	25	6·56	3·73

centres) and there are differences in the definition of a PC dose, which makes benchmarking difficult. The Blood Stock Management Scheme in the United Kingdom and Republic of Ireland represents a similar situation to ours, being based on pooled data sets from blood services and hospitals. In 2010, in UK and North UK, where 7 day storage is permitted, wastage as a percentage of issues was 7·2%, while in UK and the Republic of Ireland, where storage is limited to 5 days, these rates were 14·1 and 14·2%, respectively [14].

In our opinion, the wastage of blood components and in particular PCs should be addressed together across the whole transfusion chain, not independently in production units and hospitals. For this, it is essential to have a good IT system that provides data on the production and transfusion of PCs across all the area covered. In the Basque Country, the operation of the transfusion system as a co-ordinated network is established by law and there is a single corporate information system, shared between the CVTTH and the great majority of transfusion centres. The wastage rate in the Basque Country is 15·86%, 14·2% of units being discarded in hospital transfusion centres. The low wastage of PCs in the CVTTH is attributable to the fact that units supplied, to hospitals that keep PCs in stock or for transfusions in health centres that do not hold stock, are always the oldest available (following the FIFO policy). The mean age of PCs supplied by the CVTTH is 3·5 days.

The mathematical model proposed should be considered an approximation to the real situation, given its various limitations. These include the following: (i) neglecting the influence of outdating, this being relatively small; (ii) considering a single PC stock in the Basque Country, rather than including separately the main stock in the CVTTH and secondary stocks held in five hospitals, meaning that it does not take into account problems associated with distribution and cumulative ageing of PCs held in storage consecutively at two sites; (iii) assuming that the oldest PCs are always used first (FIFO policy); (iv) ignoring ABO/Rh group and other variables associated with PC processing (washing, radiation, preparation of aliquots for paediatric patients, etc.), while in routine practice clinicians always seek to achieve ABO-compatibility; (v) fixing the number of days of production at five, that is, excluding Saturdays; (vi) not taking into

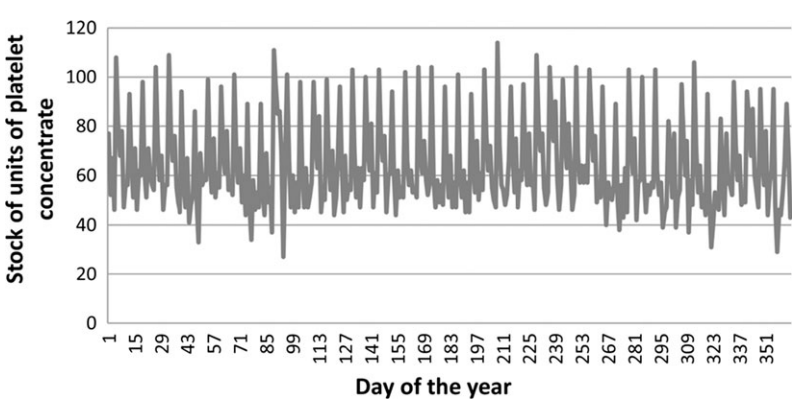

Fig. 2 Daily stock of platelet concentrate during 2013 given by the model taking $k_1 = 36$ and $k_2 = 18$.

account potential limitations in the daily production due to marked decreases in donations; (vii) excluding units produced that are not placed in stock, due to abnormal test results, bag ruptures, etc. (n = 40); (viii) disregarding apheresis platelets imported for refractory patients (n = 3); and (ix) not considering independently bank holidays and special occasions, such as Easter. On the other hand, we consider that the differences between the PC products (pooled and single-donor apheresis platelets) used in the Basque Country are not relevant to this analysis.

This work gives the CVTTH a new way of managing PC production, making the decision-making more rational and less empirical. The cornerstone of the approach is the demonstration that transfusions performed on each day of the week follow a normal distribution over time. Consequently, it can be assumed with a high level of certainty that to avoid a shortage of PC, we should produce up to the level of the mean usage plus three times the standard deviation for the corresponding days in the previous year. The tool designed calculates the quantity of PCs that the CVTHH should produce as a function of the available stock, without triggering excessive production. Its use makes it possible to reduce PC production by as much as 14·42% (1472 fewer units), without causing stock shortages.

All this undoubtedly has significant economic consequences. Considering the prices established for 2013 in the Basque Country, the potential savings associated with the proposed decrease in PC production would range from €420804·78 to €692704·02, depending on whether the PCs were obtained by pooling or apheresis, considering unit costs of €288·42 and €474·78, respectively. What is more, the mean age of PCs transfused would be reduced by almost 1 day, with the corresponding clinical benefits for patients [15].

Additionally, this study supports the FIFO policy for the use of PC, with exceptions and limitations as necessary in real practice. Our findings have encouraged the introduction of collaborative and logistic measures to facilitate transfers of PC, in particular, 4 and 5 day-old units, between the CVTTH and transfusion centres as described in previous studies [11].

To conclude, this study is useful to improve our understanding of the dynamics of production, distribution and transfusion of PCs in the Basque Country and makes it possible to establish some new guidelines. However, we consider that this model can only be used as a support tool in decision-making concerning platelet production, given its notable limitations We must now evaluate the aforementioned changes in procedures to assess the effectiveness of the measures adopted under real-world conditions, with the expectation that the results obtained will not be as optimal as those in the simulations. We should also note that, comparing 2012 and 2013 data, we observed a variation in the means and standard deviations of the quantities of PCs transfused each day of the week, underlining the need to regularly update the parameters of the model; in particular, this will ensure that the progressive increase in the demand for PCs is taken into account [16]. As a prerequisite for all this analysis, it is essential to have working methods and information systems that provide reliable and accurate information across the entire transfusion network in real time.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:
Appendix S1. Additional Information on Material and Methods.