



Original article

Clinical effects of different types of red cell concentrates in patients with thalassemia and sickle cell disease

Effets cliniques de différents types de concentrés érythrocytaires dans les hémoglobinopathies

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Abstract

The treatment of thalassemia is still essentially based on continuous transfusion supporting using red cell concentrates (RCC) prepared in different ways. For patients with sickle-cell disorders, either urgent or chronic red blood cell transfusion therapy, is widely used in the management of sickle cell disease (SCD) because it reduces HbS level and generally prevents recurrent vaso-occlusive disease (VOD). Recently, the introduction of prestorage filtration to remove leukocytes and the use of techniques for multicomponent donation have increased the types of blood components available for transfusion purposes. The clinical effects of different types of blood components in thalassaemic and sickle-cell patients have not been extensively studied so far. We evaluated the impact of the various different blood components currently available on transfusion needs, transfusion intervals and adverse reactions in order to determine which is the most advantageous for transfusion-dependent thalassaemic and sickle-cell patients followed in our centre. We believe that the optimal characteristics of the RCC are aged less than 10 days from time of collection; Hb content greater than 56 g per unit; Hct: 55–60%; volume (including additive) 300 mL $\pm$ 20%; leucodepleted to less than 200,000 leukocytes per unit; low cytokine content (achievable by prestorage filtration carried out between two and 24 hours after the collection); lack of microaggregates (achievable by prestorage filtration or filtration in the laboratory) and protein content less than 0.5 g per unit for patients allergic to plasma proteins (achievable with manual or automated washing).

It is still recommended that the blood transfused should be as fresh as possible, compatible with the centre's product availability and the centre's organisation should be continuously adapted to this aim. We always transfuse blood within 10 days of its collection, respecting Rh and Kell system phenotypes. Prestorage filtration is strongly recommended, both in order to prevent adverse reactions through the marked leucodepletion (less than 200,000 leukocytes per unit) and for a better standardisation of the final product, including the certainty that the product does not contain clots, an assurance that bed-side filtration cannot give. The RCC should be produced using a method causing as little as possible stress to the red cell membrane. The use of RCC with a high content of Hb (less than 56 g per unit) is strongly recommended, because our study clearly shows that this reduces the number of exposures to donors and the number of accesses to hospital, thus improving the patient's quality of life.

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Résumé

Le traitement de la thalassémie reste essentiellement basé sur la transfusion de concentrés de culots globulaires (CGR) préparés de diverses manières. Dans les désordres drépanocytaires, la transfusion chronique ou en urgence de CGR est largement utilisée dans la gestion de la maladie, car elle permet de réduire le taux de HbS et prévient généralement les accidents vaso-occlusifs récurrents. Récemment, l'introduction de la déleucocytation avant conservation et l'utilisation de techniques multidons ont permis d'augmenter le nombre de composants sanguins transfusionnels disponibles. L'efficacité clinique de ces divers composants sanguins chez les sujets thalassémiques et drépanocytaires n'a pas été examinée jusqu'à présent. Nous avons évalué l'impact des composants actuellement disponibles sur les besoins transfusionnels, l'intervalle entre les transfusions et les réactions secondaires afin de déterminer lequel est le plus avantageux pour les malades transfusion-dépendants de notre centre. Nous pensons que les caractéristiques optimales des CGR sont âge inférieur à dix jours après prélèvement ; contenu Hb supérieur à 56 g par unité ; Htc: 55–60 % ; volume

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(avec additif): 300 ml $\pm$ 20 % ; leucodéplétion: supérieur à 20 000 leucocytes par unité ; faible contenu en chimiokines (réalisable par filtration deux à 24 heures après prélèvement) ; absence de microaggrégats (réalisable par préfiltration ou filtration au laboratoire) ; contenu en protéines inférieur à 0.5 g par unité pour les maladies allergiques aux protéines plasmatiques (réalisable par lavage manuel ou automatique).

On recommande d'utiliser des CGR aussi fraîchement prélevés que possible selon les disponibilités du centre de production et l'organisation des Centres devrait en permanence s'adapter à ce besoin. Nous transfusions toujours du sang prélevé dans les dix jours, en respectant les compatibilités Rh et Kell. La déleucocytation avant stockage est fortement recommandée à la fois pour éviter des réactions secondaires grâce à une diminution drastique du nombre de leucocytes (inférieur à 2 000 000 par CGR) et pour une meilleure standardisation du produit final, incluant la certitude que le produit ne contient pas de caillots, ce que ne peut pas garantir une filtration au lit du malade. Le CGR devrait être préparé à l'aide d'une méthode occasionnant le moins possible de stress à la membrane érythrocytaire. L'utilisation de CGR à contenu élevé en Hb (supérieur à 56 g par unité) est fortement recommandée, car notre étude indique clairement que cela réduit le nombre d'expositions à des donneurs et le nombre de séjours hospitaliers, améliorant ainsi la qualité de vie des malades.

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Keywords: Thalassemia; RBC transfusion; Adverse reaction; RBC quality control

Mots clés : Thalassémie ; Transfusion de globules rouges ; Réactions secondaires ; Contrôle de qualité

1. Introduction

Despite the great progress made in the treatment of thalassemia, in the vast majority of cases this treatment, which has become very standardised over the years, is still based on transfusions [1,2]. For those patients with severe sickle cell disease, three major therapeutic options are currently available: blood transfusion, hydroxyurea and bone marrow transplantation. Either urgent or chronic red blood cell transfusion therapy is widely used in the management of sickle cell disease (SCD) because it reduces HbS level and generally prevents recurrent vaso-occlusive disease (VOD) but simultaneously, determines a progressive increase of ferritin level that needs regular chelating therapy [3–7]. Transfusion therapy is also limited by the development of antibodies to red cell antigens [8–10] and potential exposure to transfusion-transmitted infectious disease. Recently, the introduction of prestorage filtration to remove leukocytes and the use of techniques for multicomponent donation [11,12] have increased the types of blood components available for transfusion purposes. Extensive studies on the clinical effects of the various types of red cell concentrates (RCC) used in thalassaemic and sickle cell disease patients have not, however, been conducted so far. In our centre, we follow 176 patients affected by haemoglobinopathies, of whom nine are free of transfusion treatment following bone marrow transplantation and 100 remain transfusion-dependent. In the two years from 1st July 2003 to 30th June 2005 the patients were transfused with RCC obtained from filtering whole blood prestorage or with RCC from apheresis filtered prestorage.

These products differed from those used in the preceding two years, during which the leucodepletion was obtained by bed-side filtration. The aim of our study was to evaluate the clinical effects of the different blood components in terms of annual transfusion needs and the intervals between transfusion, in order to determine which are more advantageous for our patients. Moreover, in sickle cell disease, we evaluated the efficacy of chronic red blood cell exchange (automatic with cell separator) in preventing SCD complications and limiting iron overload.

2. Materials and methods

2.1. Patients

Of the 176 patients treated in the microcythaemia centre of Ragusa Hospital, we selected 76 patients, affected by major thalassemia (Table 1) and 10 patients affected by sickle cell disease (Table 2), for fulfilling the following criteria:

- continuous treatment at the Centre for at least 48 months with no interruptions, even sporadic;
- absolute transfusion dependency.

2.2. Sickle cell disease patients characteristics

Chronic red blood cell exchange (automatic with cell separator) was introduced because of a high incidence of the

Table 1

Characteristics of the patients enrolled in the study, divided according to age range and compared with all Sicilians with thalassemia major

Stratification of the study patients			All Sicilian patients	
Age	Total study patients	Percentage (%)	Total Sicilian patients	Percentage (%)
0–10	3	3.94	108	10.01
11–20	15	19.73	347	32.18
21–30	34	44.73	459	42.57
31–40	16	21.05	148	13.72
> 41	8	10.52	16	1.4
TOTAL	76		1078	

Table 2
Sickle cell disease Patients data prescheduled treatment

Paz	Age	B.W.kg	Diagnosis	ABO Rh	Clinical	Transfusion therapy	Ferritin level	Dat/Iat	Hbv/Hcv/Hiv
1 G.G.	29	54	HbSS	A+	Sepsis	PTP	1000	Neg/Neg	Neg/Pos/Neg
2 D.G.	34	72	HbSS	CcDee K-	Acute Vaso-occlusive (pain) crises	PTP	900	Neg/Neg	Hcv Rna Neg
3 P.G.	42	87	HbSS	A-	Sepsis, Infarction of heads of femur	PTP	300	Neg/Neg	Neg/Neg/Neg
4 A.G.	22	50	HbSS	Ccdee K-0+	Acute Vaso-occlusive (pain) crises	PTP	2800	Neg/Neg	Neg/Pos/Neg
5 B.V.	63	75	HbS β Thal	CcDee K-0+	Infarction of heads of femur	PTP	3500	Neg/Neg	Hcv Rna Neg
6 Pe.G.	35	74	HbS β Thal	CCDee K-	Acute Chest Syndrome	PTP	600	Neg/Neg	Neg/Pos/Neg
7 S.A.	17	66	HbS β Thal	Sepsis, Priapism	PTP	300	Neg/Neg	Neg/Pos/Neg	Hcv Rna Pos
8 L.F.	32	60	HbSS	Acute Vaso-occlusive (pain) crises	PTP	390	Neg/Neg	Neg/Pos/Neg	Hcv Rna Pos
9 T.A.	37	64	HbSS	A+	Sepsis	PTP	240	Neg/Neg	Neg/Pos/Neg
10 B.F.	28	70	HbS β Thal	CcDee K-0+	Acute Vaso-occlusive (pain) crises	PTP	1650	Neg/Neg	Neg/Pos/Neg
				CcDee K-	Infarction of heads of femur	PTP			
				A-	Priapism	PTP			
				ccddee K+	Acute Vaso-occlusive (pain) crises	PTP			
				A+	Sepsis	PTP			
				CcDee K-	Acute Vaso-occlusive (pain) crises	PTP			
					Acute Chest Syndrome	PTP			
				A+	Skin Ulcers	PTP			
				CcDee K-	Acute Vaso-occlusive (pain) crises	PTP			
				A-	Sepsis	PTP			
				ccddee K-	Acute Vaso-occlusive (pain) crises	PTP			

B.W.: body weight; PTP: previously treated patients; PUP: previously untreated patients; Y: yes; N: no; Dat: direct antiglobulin test; Iat: indirect antiglobulin test; Neg: negative, Pos: positive.

episodes of tissue infarction caused by microvascular obstruction. Only patients who had been hospitalized more than two times per year were included.

2.3. Follow-up

All 86 patients were evaluated for a period of four years, during which two different systems of producing RCC were used:

- first and second years (first two years): from 1st July 2001 to 30th June 2003 the separation system used was Top and Bottom bags (Optipress II system, Baxter Healthcare Corporation, Vienna, Austria) programmed for the production of buffy coat-deprived RCC, subsequently filtered at the bed-side or in the laboratory;
- third and fourth years (second two years): from 1st July 2003 to 30th June 2005 a Compomat separation system was used (Fresenius HemoCare GmbH, Bad Homburg, Germany), employing its related standard bags with in-line filters for prestorage leucoreduction of whole blood. The new system of producing RCC was implemented completely on July 1st, 2003, providing the ideal conditions for evaluating and comparing numerous parameters, since all the patients were transfused in the first two years with RCC from whole blood or from apheresis filtered at the bedside and all were transfused in the second two years with RCC from whole blood or apheresis, filtered prestorage. Since the transfusion regime in the two periods studied was not changed and the same 86 patients were treated in both periods, it is reasonable

to hypothesise that the only variable that differed was the quality of the blood components used in the second two years, compared to those in the first two years.

The data were collected separately for the two periods (each of 24 months), in order to be able to show any correlations between clinical effects and quality of the blood components.

2.4. Blood components used

The following blood components were used during the study period:

- RCC deprived of the buffy coat, leucodepleted at the patient's bedside or in the laboratory;
- RCC from whole blood, leucodepleted prestorage by in line filters;
- RCC from a multicomponent collection (MCC) (RBC plasma), leucodepleted at the patient's bedside;
- RCC from MCC apheresis (RBC-plasma) with in-line filtration, leucodepleted prestorage;
- RCC from MCC apheresis (RBC-RBC) with in-line filtration, leucodepleted prestorage;
- RCC filtered prestorage and washed manually;
- RCC filtered prestorage and washed with an automated technique (ACP215).

The blood components were prepared with standard methods. The apheresis procedures were carried out using five Haemonetics cell separators (Haemonetics Corporation,

Baintree, MA, United States) of which five were MCS+, linked to a Haemonet Ô management server for monitoring the procedures.

The automated washing was performed with an Haemonetics ACP215.

All the RCC, both those produced by separation and those produced by apheresis, underwent quality controls, according to the numbers and frequencies established on the basis of recommendation R95(15)2005 of the Council of Europe [13]. Furthermore, the results of quality controls on all the types of blood components used during the study were analysed and a precise calculation was made of the number of units transfused and the adverse reactions occurring in the two periods.

2.5. Transfusion protocol for thalassemic patients

A hypertransfusion regime was used for the patients in the study in order to guarantee pretransfusional levels of haemoglobin (Hb) between 9 and 10 g/dL and posttransfusional Hb levels below 15 g/dL. The volume to transfuse was calculated in mL of 100% red blood cells (RBC)/kg of body weight. Buffy coat-depleted RCC filtered at the bedside were predominantly used in the first two years and RCC from whole blood, filtered prestorage in the second two years.

The transfusion protocols used were the following:

- patients without heart disease: transfusion of 15 mL/kg up to a maximum of 650 mL of 100% RBC per patient and in no case more than three units per hospital access. The overall volume of the additive solution varied between 800 and 950 mL;
- patients with thalassaemic cardiopathy:
 - transfusion of 9 mL/kg body weight to a maximum of 450 mL of 100% RBC per patient and never more than two units per access in a single administration per patient,
 - a time of infusion of at least 90 minutes per unit of RCC.

2.6. Transfusion protocol for sickle cell disease patients

We performed automatic (with cell separator Baxter CS3000 plus, Haemonetics MCS+, COBE Spectra) red blood cell exchange and we maintained the patients at the standard pretransfusion haemoglobin S (HbS) level less than 60%. Our objective after erythrocyte exchange was HbS less than 30% and the total hematocrit greater than 30% to suppress HbS production. Venous access was peripheral in all cases except for one patient whose access vein was temporary double lumen central into femoral. We processed 1.1 red blood cell volume, RBCs were removed and replaced with buffy coat-depleted RCC filtered at the bedside in the first two years and RCC from whole blood or apheresis, filtered prestorage in the second two years. All units tested negative for HbS and matched for Rh (C, c, E, e) and kell system antigens. During automatic red blood cell exchange the blood pump was: draw speed 50 ml/min, return speed 50 ml/min. Anticoagulant ratio 1:16, centrifuge

speed: Haemonetics rev min-7000, Baxter CS3000 Plus rev min-1600, COBE Spectra variable rev min. We performed clinical and biological evaluation of all patients before and after every exchange including full blood cell count, both renal and hepatic function test, the percentage of HbS, direct and indirect antiglobulin test (DAT/IAT), ferritin level, as well as HCV, HBV and HIV markers. All antibody screens were done with LISS or PEG using an anti-IgG antiglobulin test. Routine DATs were done on each specimen.

2.7. Parameters evaluated

The following parameters were evaluated for both groups of patients:

- quality control on the RCC used;
- number of units of RCC used in the first two years versus the second two years;
- mean pretransfusion Hb concentration in the patients in the first two years versus the second two years;
- number of accesses per patient in the first two years versus the second two years;
- total number of adverse reactions recorded in the recipients;
- types of adverse reactions to the transfusions;
- total number of washed RCC units used in the first two years versus the second two years;
- number of reactions in the subgroup of patients treated with filtered, washed RCC.

*Only for sickle cell disease patients:

- *number of SCD complications;
- *iron overload;
- *procedure time.

The data related to the donors and patients were drawn from the EMONET informatic system as well as from the computerised clinical records of the Day Hospital of the microcythaemia centre of the Ragusa SIMT.

3. Results

3.1. Characteristics of the RCC used

Overall, during the study period, the patients received 13,549 units of RCC. The salient characteristics of the various blood components used, derived from the results of the quality controls of the products, are summarised in Tables 3–8.

3.2. Consumption of blood, transfusion intervals and adverse reactions in the two periods

3.2.1. Thalassaemic patients

The 76 patients evaluated received 6565 units of RCC filtered at the bed-side in the first two years and 5646 units of RCC from whole blood or from apheresis RBC filtered prestorage in the second two years. The data relating to

Table 3

Characteristics of the RCC obtained from buffy coat-depleted whole blood in the first two years

		Total (n = 186)	Males (n = 152)	Females (n = 34)	Expected values R(95) 15
Volume (ml)	Median	281	285	268	230–330 ml (including SAG-M)
	Minimum–maximum	234–327	241–327	234–308	
	S.D.	20.3	19.2	17.2	
Hb (Gr/unit) ^a	Median	54.3	56.1	50.0	Greater than 43
	Minimum–maximum	35.2–68.6	41.3–68.6	35.2–56.4	
	S.D.	5.6	5.1	4.4	
HCT (%)	Median	57.8	58.1	56.0	50–70%
	Minimum–maximum	41.4–64.3	46.3–64.3	41.4–61.4	
	S.D.	3.5	3.3	3.7	
Hb recovered (%)	Median	81	83	81	Not foreseen
	Minimum–maximum	60–89	64–89	60–89	
	S.D.	5.0	4.0	10.0	
Leukocytes 10 ⁶ /unit	Median	460	450	600	Less than 1200 × 10 ⁶ leukocytes/unit
	Minimum–maximum	70–2650	80–2650	70–1590	
	S.D.	0.43	0.40	0.40	

^a NB: poststorage filtration in the laboratory or at the bed-side in our SIMT gives a median Hb content of 49.3 g per unit, with a median volume of 281 mL (SAG-M included); S.D.: standard deviation.

Table 4

Characteristics of the RCC from whole blood filtered prestorage in the second two years

		Total (n = 200)	Males (n = 173)	Females (n = 27)	Expected values R(95) 15
Volume (ml)	Median	310	311	292	270–370 ml (including SAG-M)
	Minimum–maximum	274–350	282–350	274–318	
	S.D.	13.1	11.4	11.0	
Hb (g/unit)	Median	59.4	60.2	54.7	Greater than 40 g/unit
	Minimum–maximum	49.3–71.4	50.6–71.4	49.3–59.7	
	S.D.	4.7	4.3	3.6	
HCT (%)	Median	56.5	56.8	54.3	50–70%
	Minimum–maximum	50.0–60.7	50.0–60.7	50.7–59.5	
	S.D.	2.1	1.9	2.2	
Hb recovered (%)	Median	89	89	89	Not foreseen
	Minimum–maximum	71–93	71–93	83–93	
	S.D.	4.2	4.4	2.7	
Leukocytes 10 ⁶ /unit	Median	0.03	0.03	0.02	Less than 1,0 × 10 ⁶ leukocytes/unit
	Minimum–maximum	0.01–0.77	0.01–0.77	0.01–0.12	
	S.D.	0.49	0.53	0.03	

pretransfusion Hb levels, blood consumption, number of hospital accesses, transfusion intervals and adverse reactions to transfusions are summarised in Table 9.

From the first to the second period of two years, there was a saving of 919 units of RCC, which although substantial and very useful to us, was not a statistically significant difference ($p > 0.05$).

The pretransfusional levels of Hb were 9.81 g/dL in the first two years and 9.91 g/dL in the second two years. This increase of 0.1 g/dL, although apparently very slight, was statistically significant ($p < 0.015$).

The mean number of hospital accesses per patient in the first two years was 33.55, corresponding to a transfusion interval of 21.7 days.

Table 5

Characteristics of the RCC from erythroplasmapheresis (not filtered) in the first two years

		TOTAL (n = 76)	Expected values R(95) 15
Volume (ml)	Median	323	290–330 ml (including SAG-M)
	Minimum–maximum	288–345	
	SD	11.4	
Hb (g./unit)	Median	61.3	Greater than 40 g/unit
	Minimum–maximum	54.2–67.9	
	S.D.	2.8	
HCT (%)	Median	56.4	50–70%
	Minimum–maximum	45.7–62.7	
	S.D.	2.3	

Table 6

Characteristics of the RCC from erythroplasmapheresis filtered prestorage in the second two years

		TOTAL (n = 40)	Expected values R(95) 15
Volume (ml)	Median	289	270–310 ml (including SAG-M)
	Minimum–maximum	270–310	
	S.D.	12.3	
Hb (g./unit)	Median	56.9	Greater than 40 g/unit
	Minimum–maximum	49.6–63.1	
	S.D.	2.9	
HCT (%)	Median	56.2	50–70%
	Minimum–maximum	51.5–62.1	
	S.D.	1.7	
Leukocytes 10 ⁶ /unit	Median	0.10	Less than 1.0 × 10 ⁶ leukocytes/unit
	Minimum–maximum	0.01–0.67	
	S.D.	0.2	

Table 7

Characteristics of the RCC from single-donor red cell double apheresis (SDR) filtered prestorage

		Total (n = 81)	Expected values R(95) 15
Volume (ml)	Median	554	540–620 ml (including SAG-M)
	Minimum–maximum	520–597	
	S.D.	17,0	
Hb (g/unit)	Median	111,5	Greater than 80 g/unit
	Minimum–maximum	102,8–126,7	
	S.D.	4,9	
HCT (%)	Median	58,9	50–70%
	Minimum–maximum	54,2–63,4	
	S.D.	1,7	
Leukocytes 10 ⁶ /unit	Median	0,19	Less than 2.0 × 10 ⁶ leukocytes/unit
	Minimum–maximum	0,05–0,88	
	S.D.	0,23	

The mean number of hospital accesses per patient in the second two years was 31.34, corresponding to a transfusion interval of 23.3 days. Both the reduction in the number of accesses and the increase in the number of days between each transfusion were statistically significant ($p < 0.05$)

3.2.2. Sickle cell disease patients

All 10 patients followed the scheduled treatment with automatic red blood cell exchange with cell separator. We performed 206 automatic red blood cell exchanges with cell separator. Mean duration of the automatic procedure was 240 min with Baxter CS3000+, 180 min with MCS+

Table 8

Quality control of the washing of RCC filtered prestorage

		Manual washing (n = 61)	Automated washing with Haemonetics ACP215 (n = 50)	Expected values R(95) 15
Volume (ml)	Median	217	272	200–240 ml (manual) 240–280 (ACP215)
	Minimum–maximum	133–259	225–315	
	S.D.	18.7	22.0	
Hb (g./unit)	Median	53.0	54.5	Greater than 40 g/unit
	Minimum–maximum	33.2–62.0	41.8–66.8	
	S.D.	5.5	5.6	
HCT (%)	Median	72.4	59.7	65–75% (manual) 55–65% (ACP215)
	Minimum–maximum	60.7–80.2	51.7–62.7	
	S.D.	4.8	2.8	
Free Hb %	Median	0.18	0.16	Less than 0.8%
	Minimum–maximum	0.06–0.52	0.04–0.33	
	S.D.	0.12	0.07	
Protein content in the supernatant (g/unit)	Median	0.20	0.15	Less than 0.5 g/unit
	Minimum–maximum	0.07–0.48	0.02–0.36	
	S.D.	0.09	0.09	

Table 9

Statistical comparison of the number of units transfused, pre-transfusion Hb value, number of hospital accesses, transfusion interval and transfusion reactions between the two periods for thalassemic patients

Total patients <i>n</i> = 76	Number of units transfused	Quantity (L of 100% RBC)	Pre-transf. Hb (g/dL)	Total n. of accesses	Mean n. of accesses/patient	Transfusion interval (days)	Transf. reactions/n. of patients
1 st two years	6,565	1,142,070	9.81	2550	33.55	21.7	13/12
2nd two years	5,646	1,121,544	9.91	2382	31.34	23.3	25/18
Difference	– 919 (NS)	– 20,526	+ 0.10 (<i>p</i> < 0.015)	– 168	– 2.21 (<i>p</i> < 0.05)	+ 1.6 (<i>p</i> < 0.05)	+ 12/+ 6 (<i>p</i> < 0.05)

NS: not significant.

Table 10

Sickle cell disease patients results

Number of red cell exchange

Paz	Manual	Automatically			Clinical	Ferritin level	Dat/Iat	Hbv/Hcv/Hiv	Dfo	HbS < 30% after EXC
		Baxter CS300+	Haemonetics MCS+	COBE Spectra						
1 G.G.		9	7	8	Improvement	230 ↓	Neg/Neg	Neg/Pos/Neg Hcv Rna Neg	N	Y
2 D.G.		16	6	8	Improvement	1200 ↑	Neg/Neg	Neg/Neg/Neg	Y	Y
3 P.G.		15	5	6	Improvement	425 ↔	Neg/Neg	Neg/Neg/neg	N	Y
4 A.G.		5	7	5	Improvement	2800 ↔	Neg/Neg	Neg/Pos/Neg Hcv Rna Neg	N (Compl)	Y
5 B.V.		5	5	1	Improvement	1500 ↓	Neg/Neg	Neg/Pos/Neg Hcv Rna Pos	N (Compl)	Y
6 Pe.G		8	8	6	Improvement	600 ↔	Neg/Neg	Neg/Pos/Neg Hcv Rna Pos	N (Compl)	Y
7 S.A.			8	7	Improvement	280 ↔	Neg/Neg	Neg/Neg/Neg	N	Y
8 L.F.		7	6	4	Improvement	60 ↓	Neg/Neg	Neg/Pos/Neg Hcv Rna Pos	N	Y
9 T.A.		3	8	5	Improvement	170 ↓	Neg/Neg	Neg/Neg/Neg	N	Y
10 B.F.			2	2	Improvement	100 ↓↓	Neg/Neg	Neg/Neg/Neg	N (Compl)	Y

B.W.: body weight; Prev treated: previously treated; Y: yes; N: no; Dat: direct antiglobulin test; Iat: indirect antiglobulin test; SDRC: single donor red blood cell; SRC: standard red cell, ↑: increased; ↑↑: more increased; ↓: reduced; Dfo: deferoxamine; N (compl): no compliance; Neg: negative; Pos: positive.

Haemonetics, and 70 min with COBE Spectra cell separator (Tables 10 and 11).

The exchange procedures were extremely well-tolerated by the patients and adverse effects were limited to symptoms of hypocalcaemia during automatic red blood cell exchange with cell separator.

The 10 patients evaluated received 710 units of RCC filtered at the bed-side, with a mean of 6.9 units of RBCs exchanged per automatic procedure, in the first two years and 628 units of RCC from whole blood or from apheresis RBC filtered prestorage, with a mean of 6.1 units of RBCs exchanged per automatic procedure, in the second two years. After every red blood cell exchange, we obtained HbS level less than 30%. No patients developed a clinically significant alloantibody and/or transfusion reaction.

Table 11

Procedure time

	Baxter CS3000 Plus	MCS+ Haemonetics	COBE Spectra	Total
Number of procedures	68	78	60	206
Mean procedure time (minute)	240	180	70	

All patients treated with chronic red blood cell exchange had a reduced number of complications per year (less than two per year) with clinical improvement with good compliance and clinical benefit.

Moreover, patients had limited iron overload making chelating therapy easier.

Adverse reactions: during the four years of the study, there were 38 adverse reactions to 13,549 units of RCC administered. Of the 38 transfusion reactions, 37 were grade I and one was grade II; this latter occurred in a topic child with constantly high levels of plasma IgE. All the reactions resolved rapidly and completely.

The number of washed units decreased from 523 in the first two years to 378 in the next two years, which, in percentage terms was a decrease from 7.9 to 6.6% of units used.

4. Discussion

The first conclusion that can be drawn from these data is that, using RCC from whole blood or from apheresis RBC filtered prestorage, the expected rise in Hb or Ht after transfusion was more predictable.

We have defined these RCC as having a high Hb concentration, since the three products used in our centre in

the next two years had an average Hb content per prestorage leucodepleted unit greater than 56 g compared to the approximately 50 g in the concentrates used in the first two years. Compared to the R95-15 recommendation (40 g for RCC filtered prestorage and 43 g for the buffy coat-deprived RCC), the products are 45 and 25% better [13].

Consequently, all of our patients had an improvement of the quality of their life, in fact, our thalassemic patients, who obviously want to have as few hospital accesses as possible, had a reduction in the average number of hospital accesses, which decreased by 2.21 per patient in the second period of two years compared to in the first two years.

Regarding our sickle cell disease patients, they had a reduced number of complications per year (less than two per year) with clinical improvement with good compliance and clinical benefit, moreover they had a reduction in the average number of units exchanged which decreased to 6.1 per automatic procedure in the second period of two years compared to 6.9 per automatic procedure in the first two years.

The RCC high Hb concentration is the result of precise working choices, including tailored donation, prestorage filtration of whole blood and the use of RBC obtained from MCC apheresis, filtered prestorage.

The tailored donation used in our centre consists of using a donor for one type of donation rather than another according to a classification of haematological and clinical characteristics listed in Table 12. The aim is to identify the ideal and most appropriate donation for a given donor's clinical and haematological profile [11,12,14,15].

As a result of using this system, of the 13,980 donations made in 2005 at our ISO 9000 certified collection centre, 4776 (34.2%) were made by women, but only 1613 units of whole blood (17.3% of the donations of whole blood, accounting for 11.5% of all donations) were from women. The mean haemoglobin content/bag from female donors was 54.7 ± 3.6 g, compared to 60 ± 4.3 g in the bags from male

donors. All the RBC obtained by apheresis were from male donors.

The choice of systematically adopting *prestorage filtration of whole blood*, a choice made on the basis of data reported in the literature [16–20] and in consideration that the primary therapeutic aim of our centre is the treatment of anaemia, enabled us to have RCC with a mean Hb content of 59.4 g. This was achieved by eliminating the loss of haemoglobin (about 10%) that poststorage filtration, either in the laboratory or at the bed-side, causes. Furthermore, there is a considerable organisational advantage from filtering whole blood rather than poststorage filtration of RCC in the laboratory or at the bed-side. Fewer centrifugations mean less stress to the RBC, less work for the staff and lower costs.

The collection of *red cell concentrates by MCC apheresis* produces greater standardisation of the product. In fact, all the quality controls on the RBC produced by apheresis showed better standardisation than that of the concentrates produced from whole blood. The standard deviation of the Hb content in the products produced by erythroplasmapheresis and SDR was 2.9 compared to a standard deviation of 4.7 for the RCC from whole blood filtered prestorage.

Tailored donation, which, in our opinion, is always recommendable, becomes essential if the aim is to produce standard RCC with a high Hb content; on the other hand, this strategy has less importance if apheresis is used, since the collection technique using a cell separator enables the RBC to be concentrated according to the procedure set by the software, thus guaranteeing a standardised final haemoglobin content.

About the observed frequency of transfusion reactions in our patients, it was very low respect data reported in the literature [21–23] of 8% of units transfused. In the haemovigilance section of the French EFS report, in 2004, the overall incidence of reactions to approximately 2,500,000 transfusions was 3%. This haemovigilance system, which also collects data on grade I and II reactions, showed that in 2004 allergic reactions alone

Table 12
Haematological and clinical characteristics used for tailored donation

	Haematological and clinical characteristics of the donor	Recommended donation
1	Plt > 200,000 < 299,000, Hb > 11.5 < 14.4 Total proteins > 6.0 < 8.5 g/dL	P-Plt
2	Plt > 200,000 < 299,000, Hb > 14.5 < 15.4 Ferritin > 20 ng/mL, Weight > 60 kg	R-Plt or WB
3	Plt > 300,000, Hct < 40%, Plt-Plt	Plt-plt
4	Plt < 200,000, Hb > 14.5 < 15.5 Ferritin > 20 ng/mL, Total proteins > 6.0 < 8.5, Weight > 60 kg	R-P or WB
5	Hb > 1.5*, Ferritin > 50 ng/mL*, (in the last three donations*) Must get author to correct Weight > 70 kg	R-R
6	Female donors: Hb > 12.5 < 13.5 Total proteins > 6.0 < 8.5 Plt < 200,000	P
7	Male donors: Hb > 13.5 < 14.5 Total proteins > 6.0 < 8.5	WB alternated with P
8	Thalassaemic trait, Total proteins > 6.0 < 8.5	P or P-Plt or Plt-Plt if as n. 1-3
9	Group AB, Hct < 45%, Total proteins > 6.0 < 8.5	P

P: plasma; Plt: platelets; R: red blood cells; WB: whole blood; R-R: double unit of red blood cells; Plt-Plt: double unit of platelets.

accounted for 57% of all the reactions [24]. Our population is very different from the general French population, since our patients are multiply transfused and sensitised and, therefore, at a higher risk of adverse reactions.

The use of RCC filtered prestorage allowed us to reserve washed RBC to only those patients with a clinical history of repeated or severe allergic episodes. We did not find particular advantages from manual washing of the products with respect to close circuit automated washing, apart from the fact that this latter gives us the possibility of preparing the product in advance or deferring its transfusion. Only subjects with a history of clinically relevant allergic reactions that cannot be prevented in other ways, still need washed RBC even if filtered. Washing leads to a modest loss of haemoglobin per unit and potential mechanical stress to the red blood cells, which could reduce their mean life-span.

Closed circuit automated washing offers the great advantage of being able to store the washed RCC for seven days, enabling these products to be prepared in advance or for their transfusion to be postponed.

5. Conclusion

This study was focused on the most suitable characteristics of blood components for use in thalassaemics and sickle cell disease patients, showing the clinical advantages for patients derived from good selection of the donor and good practices in the production of the blood components.

We believe that the optimal characteristics of the RCC are aged less than 10 days from time of collection; Hb content greater than 56 g per unit; Hct: 55–60%; volume (including additive) 300 mL $\pm$ 20%; leucodepleted to less than 200,000 leukocytes per unit; low cytokine content (achievable by prestorage filtration carried out between two and 24 hours after the collection); lack of microaggregates (achievable by prestorage filtration or filtration in the laboratory); protein content less than 0.5 g per unit for patients allergic to plasma proteins (achievable with manual or automated washing). It is still recommended to transfuse respecting Rh and Kell system phenotypes and the use of RCC with a high content of Hb(greater than 56 g per unit) is strongly recommended, because our study clearly shows that this reduces the number of exposures to donors and the number of accesses to hospital, thus improving the patients' quality of life.

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