Iron depletion with a novel apheresis system in patients with hemochromatosis: RBC Depletion with the Spectra Optia

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Iron depletion with a novel apheresis system in patients with hemochromatosis

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BACKGROUND: Phlebotomy represents the standard treatment option for iron overload in hemochromatosis (HC). Recently, red blood cell (RBC) apheresis has increasingly been used to remove iron. In this study we evaluated the depletion program of the newly developed Spectra Optia device.

STUDY DESIGN AND METHODS: Adult male patients (n = 11) with HC were RBC depleted with the Spectra Optia device (Terumo BCT). In total, 24 procedures were performed. A volume of 300 to 550 mL of RBCs was withdrawn per single treatment.

RESULTS: No significant adverse events were recorded. A median blood volume of 857.3 ± 23.3 mL was processed. The median procedure time was 12.0 ± 0.4 minutes. The mean reduction of Hct value in each procedure was approximately 6% (Hct pre 42.6 ± 0.5% vs. Hct post 36.6 ± 0.6%) and iron removed per procedure was 405.2 ± 23.3 mg.

CONCLUSION: The Spectra Optia device proved to be highly efficient in depleting RBCs in HC patients and allows for short procedure time. The Optia device can be safely used in this clinical setting. We recommend its use in case of severe iron overload if rapid iron depletion needs to be achieved and in case of cardiac compromise due to less blood volume removed.

Hereditary hemochromatosis (HC) is one of the most frequent causes of excess body iron in the Caucasian population. Duodenal iron absorption is inappropriately increased in HC subjects, usually due to the Cys282Tyr mutation in the HFE gene.[1,2] Another frequent cause of elevated iron stores is the dysmetabolic iron overload syndrome (DIOS), which is detected in approximately one-third of patients with nonalcoholic fatty liver disease and the metabolic syndrome. The pathogenesis is related to altered regulation of iron transport associated with steatosis, insulin resistance, and subclinical inflammation, often in the presence of predisposing genetic factors.[3,4] Iron overload is less pronounced in subjects with DIOS compared to HC and overestimated by serum ferritin (SF).[5] The current standard of treatment for these diseases is removal of body iron by whole blood phlebotomy, which must be repeated frequently during the initial phase. This treatment is inexpensive but in patients with high levels of SF it may take several months and multiple phlebotomy sessions to achieve iron depletion.[6,7] As an alternative, red blood cell (RBC) apheresis is used for selective withdrawal

ABBREVIATIONS: DIOS = dysmetabolic iron overload syndrome; HC = hemochromatosis; SF = serum ferritin.

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of RBCs. This technology facilitates to increase the amount of iron depleted two- or three-fold for each treatment.[6-8] Rapid removal of iron may be indicated in patients with symptomatic disease stage and massively elevated SF levels to stop further organ damage. Potential disadvantages of RBC apheresis are higher costs and longer treatment time for each procedure. A new apheresis system, the Spectra Optia (Terumo BCT, Lakewood, CO) has been recently introduced in the clinical setting. So far, studies about this new apheresis device report on mononuclear cell collection, on plasma-exchange procedures, and on RBC exchange, respectively.[9-13]

In this study, we performed RBC apheresis in patients with HC by using the newly developed depletion program of the Spectra Optia system to evaluate the device in this clinical setting with regard to procedure duration, efficiency of iron removal, and side effects.

MATERIALS AND METHODS

Patients

Between October 2013 and March 2014, a total of 11 male patients with hyperferritinemia were iron depleted at least once by means of RBC apheresis. Five patients were diagnosed with hereditary HC and six patients showed elevated ferritin levels in the course of a DIOS. Depending on the time point of inclusion during the study period, patients underwent up to seven apheresis procedures. Eight of these 11 patients had received phlebotomy before starting iron depletion by apheresis. If patients reached a target SF level of 50 to 100 µg/L, they were switched to phlebotomy maintenance therapy as clinically indicated.[14,15] Inclusion criteria were as follows: primary or secondary HC, hematocrit (Hct) greater than 37%, hemoglobin (Hb) greater than 125 g/L, weight 50 kg or more, and age 18 to 65 years. Exclusion criteria were as follows: malignancy, heart failure, serious cardiac arrhythmias, and epilepsy. All participants gave informed written consent and anonymous data analyses were performed with permission of the local ethics committee.

Therapeutic RBC apheresis

For RBC apheresis we used the automated RBC depletion program of the Spectra Optia apheresis device (Terumo BCT), which requires two venous accesses. Per single treatment procedure 300 to 550 mL of RBCs were withdrawn. During the treatment the estimated removed RBC volume was replaced by normal saline. Due to the low extracorporeal volume of 170 mL and the isovolemic volume replacement of removed RBC mass by normal saline negative side effects are very rare. All RBC apheresis procedures were performed in our center.

Monitoring of treatment

Before and immediately after each procedure blood pressure and pulse of the patients were determined and blood samples were taken for analysis of Hb, Hct, and white blood cell (WBC) and platelet (PLT) count. SF, transferrin, and transferrin saturation were estimated before each RBC apheresis and at the end of the treatment period. Iron removal per procedure was calculated by the amount of RBCs collected (1 mL of RBC = 1 mg of iron).

Statistical analysis

Data are presented as arithmetic mean ± standard error of the mean (SEM). Data were tested for Gaussian distribution using the Kolmogorov-Smirnov normality test and for outliers by Grubb's test. Data were compared using paired t test. The significance level was 0.05 (95% confidence intervals). Analysis was done with computer software (GraphPad Prism 5 and GraphPad QuickCalcs, GraphPad Software, Inc., La Jolla, CA).

RESULTS

In 11 male patients a total of 24 procedures were performed with the Spectra Optia apheresis device. Patients had a mean age of 51.1 ± 2.6 years and a mean body mass index of 30.1 ± 1.7 kg/m^2. Mean total blood volume of patients was 5837.8 ± 201.3 mL. Baseline and end-of-treatment characteristics of patients are shown in Table 1. Six patients had only one apheresis procedure, two patients had two procedures, one patient had three procedures, one patient had four procedures, and one patient had seven procedures. We had a significant decrease of SF levels between baseline and end of treatment values ($p < 0.05$). There were no significant differences between baseline and end-of-treatment values of transferrin and transferrin saturation. No significant adverse events were recorded. Only two patients showed problems with blood flow rate due to venous access. ACD-A ratio was set at 1:13 in all procedures and there were no side effects due to citrate. The collection/reinfusion ratio was set at 100% (saline replacement, 371.8 ± 11.6 mL) and no circulatory side effects were observed. A mean blood volume of 857.3 ± 23.3 mL was processed during 12.0 ± 0.4 minutes. The mean reduction of Hct was approximately 6% (from 42.6 ± 0.5% to 36.6 ± 0.6%) and as an equivalent of depleted RBC volume 405.2 ± 12.6 mg of iron was removed per procedure. All apheresis variables are shown in Table 2. As expected there was a significant decrease ($p < 0.001$) of RBC counts, Hct and Hb values after the apheresis procedure. As a consequence of dilution after RBC apheresis a significant decrease of WBC and PLT counts could be observed. Pre- and postapheresis characteristics are given in Fig. 1.

TABLE 1. Baseline and end of treatment characteristics of 11 HC patients*

Patient	Number of procedures	SF (µg/L)		Transferrin (mg/dL)		Transferrin saturation (%)	
		Start	End	Start	End	Start	End
1	7	1427	35	243	343	46	11
2	4	5570	3999	197	206	84	81
3	3	853	93	320	350	10	9
4	2	420	154	196	198	68	65
5	2	474	151	193	250	79	21
6	1	569	436	251	274	30	31
7	1	837	539	251	244	28	22
8	1	142	NT	298	NT	31	n.t.
9	1	332	282	218	219	40	49
10	1	699	513	239	260	37	30
11	1	333	156	288	319	20	17
Mean		1059.6	635.8	244.9	266.3	43.0	33.6
SEM		463.1	360.3	13.0	16.5	7.3	7.2
p value		$p < 0.05$		NS		NS	

* In one patient end of treatment values for SF, transferrin, and transferrin saturation were not determined.
NS = not significant; NT = not tested.

TABLE 2. Variables of 24 apheresis procedures*

Number of procedures	24
ACD-A	
Total (mL)	65.9 ± 1.8
In the bag (mL)	16.9 ± 0.6
To the patient (mL)	43.9 ± 1.4
Blood volume processed (mL)	857.3 ± 23.3
Procedure time (min)	12.0 ± 0.4
Entered Hct (%)	37.0 ± 0.5
Iron removal/procedure (mg)	405.2 ± 12.6
Saline replacement (mL)	371.8 ± 11.6

* Data are shown as mean ± SEM. Iron removal per procedure was calculated by the amount of RBCs collected (1 mL of RBC = 1 mg of iron).

DISCUSSION

RBC apheresis of HC patients has become increasingly popular in recent years, since it allows for an effective treatment in removing excess in body iron.[6,7] To our knowledge, this is the first published evaluation of efficiency and safety of RBC apheresis in HC patients with the recently developed Spectra Optia apheresis system. The mean procedure time of the Spectra Optia is reduced by more than 50% in comparison to other RBC apheresis systems.[16] Therefore, a monthly treatment regimen with short treatment duration by apheresis may be easier to tolerate for patients than a biweekly phlebotomy. Although the costs for a single RBC apheresis procedure are higher than for phlebotomy, treatment may be cost-effective taking into account total treatment costs of the fewer procedures required and fewer lost hours absent from work.[6]

The use of apheresis technology with lower extracorporeal volume and saline replacement is known to reduce adverse events during the procedure.[10,16,17] In comparison to other apheresis systems, such as the Alyx system (Fenwal, Lake Zurich, IL) and the MCS+ system (Haemonetics Corp., Braintree, MA), the extracorporeal volume of the Spectra Optia device is reduced by approximately 50%.[16] In this study, no significant adverse events were recorded. However, all patients included in the study were male and had a mean body mass index of 30.1 kg/m^2.

A disadvantage of the Spectra Optia device is that the depletion program uses a two-needle system. Therefore, this therapy is restricted to patients with optimal vein conditions. In two patients treatment was declined due to suboptimal veins after the first procedure.

In our study, RBC apheresis resulted in a mean removal of more than 400 mg of iron per single procedure. Therefore, RBC apheresis resulted in two to three times higher iron depletion per single procedure than whole blood phlebotomy.[18] The removal of iron per procedure is comparable to data from HC patients, in which the apheresis device MCS+ was employed.[6] Notably, this increased depletion volume did not induce anemia even in patients after multiple apheresis procedures. After achieving the target SF level of 50 to 100 µg/L patients receive standard phlebotomy maintenance therapy as clinically indicated. Generally, this strategy is sufficient to stabilize SF levels at low-normal values.[14,15] Of note, this target SF level was not the primary endpoint of our study. Patients were depleted by means of apheresis at different time points of their therapy. Two patients reached the target SF level due to early inclusion during the study period. These patients were then switched to phlebotomy maintenance therapy. The other patients are still receiving further treatment.

Another advantage of RBC depletion by apheresis is the preservation of plasma proteins, PLTs, WBCs, and clotting factors by returning these blood components to the patient. Therefore, RBC apheresis can be beneficial in patients with low PLT counts or hypoproteinemia due to liver disease.

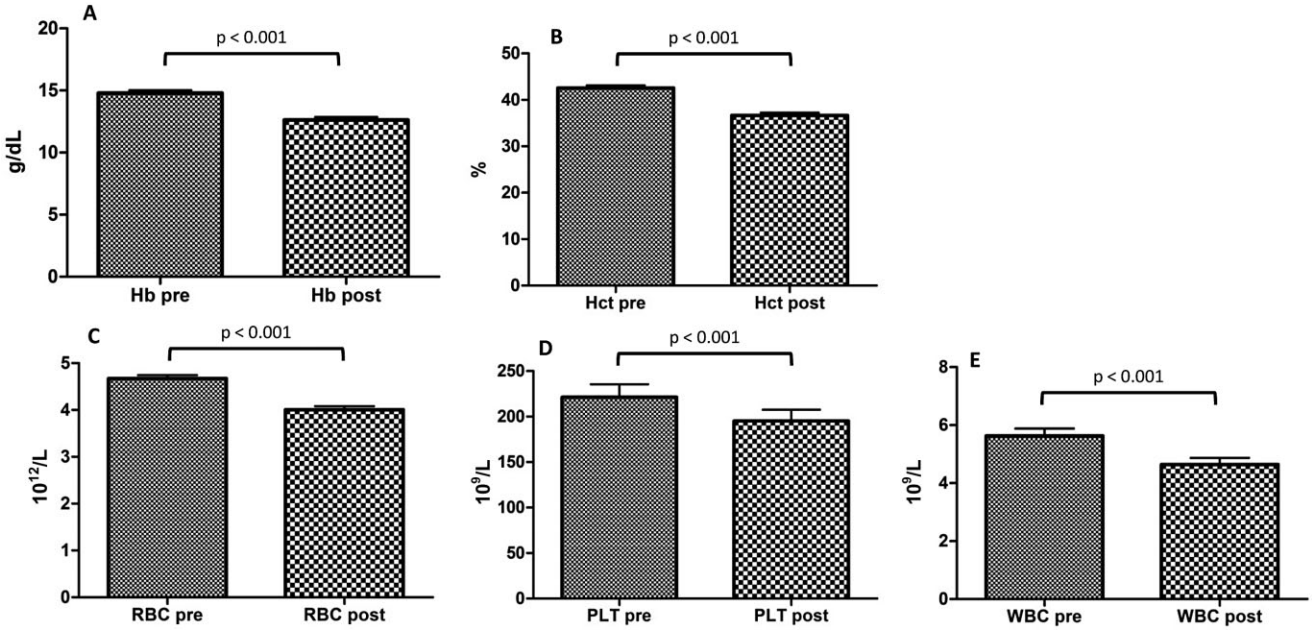

Fig. 1. Results were obtained with the Spectra Optia apheresis system and shown as before (pre) and after (post) RBC depletion. Data are means ± SEM. Significance was determined by two-tailed and paired t test of preapheresis versus the respective postapheresis conditions. Significance was determined by two-tailed and paired t test. (A) Hb; (B) Hct; (C) RBCs; (D) PLTs; (E) WBCs.

Additionally, the clinical condition of some HC patients prohibits required frequency of phlebotomy and adequate blood removal. Therefore, RBC apheresis may provide efficient iron depletion in these patients.

A limitation of RBC apheresis is that this therapy needs specialized apheresis equipment and trained staff. Therefore, patients with primary or secondary HC should be monitored by a specialist outpatient clinic with proximity to an apheresis center.

Although this technology is not available at every facility and is more expensive for the hospital and more time-consuming for the clinical staff, the Spectra Optia apheresis device was demonstrated to be a good option for RBC apheresis in HC patients due to short procedure time and safe use. Overall, our data do not provide evidence for a general recommendation of RBC apheresis in HC patients. However, our findings support its use in cases of severe iron overload if rapid iron depletion needs to be achieved as well as in cases of cardiac compromise due to volume-sparing removal of RBCs.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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