Novel Ultrafiltration Technique for Blood Conservation in Cardiac Operations

Serdar Gunaydin, MD, and Terence Gourlay, PhD

Department of Cardiovascular Surgery, University of Kirikkale, Golbasi-Ankara, Turkey, and Bioengineering Unit, University of Strathclyde, Glasgow, United Kingdom

Purpose. The performance characteristics and clinical outcome of a novel hemoconcentrator, the HemoSep (Brightwake, Nottingham, United Kingdom), for reusing salvaged blood postoperatively were evaluated.

Description. HemoSep concentrates blood by removing the fluid component from a pooled volume of blood salvaged at the end of the operation from the heart-lung machine. During a 6-month period, 102 patients were prospectively randomized into two groups. In group 1 (n = 52), salvaged blood in the venous reservoir after the cessation of cardiopulmonary bypass was reused by the HemoSep device and the processed blood was retransfused to the patients. In group 2 (n = 50), the control group, the operation proceeded using conventional method without using the hemoconcentrator.

Evaluation. The mean amount of processed blood was 775 ± 125 mL. The efficacy of the HemoSep device was confirmed by the percentage concentration of the hematocrit at 15 and 40 minutes. Serum albumin and factor VII levels were concentrated more than threefold at 40 minutes vs baseline measurements. Patients who received processed blood had significantly less need for an allogeneic transfusion.

Conclusions. The HemoSep device functions as designed and without technical failures, offering a complementary technique in blood management during cardiac operations.

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The 2011 update to the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists Blood Conservation Clinical Practice Guidelines reached the consensus that some form of pump salvage and reinfusion of residual pump blood at the end of cardiopulmonary bypass (CPB) is reasonable as part of a blood management program to minimize blood transfusion (Class IIa, Level of Evidence C). Centrifugation instead of direct infusion of residual pump blood is cited as reasonable for minimizing post-CPB allogeneic red blood cell transfusion (Class IIa, Level of Evidence A) [1–5].

A number of technologies have evolved to fulfill the hemoconcentration task in recent decades. These include the use of modified dialysis technology and, more commonly, the use of centrifuge devices to concentrate cell populations and remove excess water and plasma [6–8]. These devices are fairly complex and require specialist technical knowledge to operate. In addition to the concentrated blood product, these devices also produce a liquid waste effluent that may represent a contamination risk.

In a prospective randomized design, we studied the performance, characteristics, and clinical outcome after retransfusion of the end product of a novel hemoconcentrator, the HemoSep (Brightwake, Nottingham, UK), which uses membrane-controlled superadsorber technology in high-risk patients (European System for Cardiac Operative Risk Evaluation [EuroSCORE] >6) undergoing coronary revascularization.

Technology

The novel HemoSep technology was created at Strathclyde University (Glasgow, United Kingdom), and the clinical evaluation was conducted in patients who were treated at University of Kirikkale-Turkey (Golbasi-Ankara, Turkey). The study was approved by the University of Kirikkale-Turkey Institutional Ethics Board for Clinical Research (Ref No. 2011/0588) on Jan 12, 2011.

Patient Selection and Design

During a 6-month period, 102 patients at EuroSCORE exceeding 6, undergoing coronary artery bypass grafting (CABG) were prospectively randomized by closed envelope allocation into two groups:

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Address correspondence to Dr Gunaydin, University of Kirikkale, Department of Cardiovascular Surgery, Ankaville Sitesi, D-13, Kizilcasar mah, 1233. sok No:3/28, 06836 Golbasi-Ankara, Turkey; e-mail: sgunaydin@isnet.net.tr.

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Group 1 (n = 52)—After the cessation of CPB, salvaged blood in the venous reservoir was reused by the HemoSep hemoconcentrator and the processed blood was retransfused back to the patients.

Group 2 (n = 50)—The operation proceeded using conventional methods without using a hemoconcentrator. This group acted as the control patients for the assessment of blood loss and transfusion requirements for comparative purposes.

The primary objective was to evaluate the efficacy of the HemoSep hemoconcentrator device by demonstrating the level of the increase in the percentage concentration of red blood cells, leukocytes, and platelets in the end product compared with the baseline levels. The secondary objectives were to determine the benefit of the retransfusion of the end product in the reduction in blood loss and the need of donor blood during the patient's the clinical course, to evaluate the acceptability of the device, and to measure the effect of the device on circulating levels of proinflammatory cytokines from the processed blood product.

The study included patients aged 18 years or older with coronary primary artery disease suitable for elective operation using CPB, a preoperative EuroSCORE exceeding 6, and who were capable of providing written informed consent. Patients aged younger than 18 years, who had undergone previous open-heart operations, who were participating in another therapeutic trial, or who were pregnant were excluded.

Device

The HemoSep system consists of three major components: the HemoSep bag, a fixed-rate orbital shaker, and a transfer pack for the collection of processed blood. The bag element is the active processing section of the device. It consists of a polyvinyl chloride blood bag with a polycarbonate membrane bag suspended within it, which is a sheet of superadsorber material. The superadsorber element is the driving force behind the transport of fluid (plasma) from the blood pool, through the control membrane, and into the superadsorber section.

The key to the HemoSep device is its simplicity. Rather than removing water, it actually removes plasma and does not spare proteins. In this regard it is very similar to the centrifuge technology, with the key difference that it spares all cell species. The priming process ensures an initial intimate contact between the fluid component of the blood product and the wetted, activated, superadsorber. This creates channels for the fluid to be drawn into the superadsorber material through the controlling pores.

The mobility of the superadsorber component of the HemoSep device is restricted by two factors: firstly, the gelling property of the material itself, and secondly, the presence of the containing control membrane. One gram of superadsorber will adsorb up to 240 mL/g of fluid before reaching saturation, and the 12 g of superadsorber used in the device is therefore capable of removing up to 3 L of fluid before becoming saturated.

Levels of acrylate associated with the presence of the superadsorber in the resultant fluid were measured using an acrylate assay for this purpose. No measurable acrylate was found in the samples from devices that had been handled. There is therefore no apparent risk of superadsorber mobilization from devices handled in accordance with the information given. Laboratory and clinical studies confirm that there is no increase in plasma levels of free hemoglobin in blood processed using this device.

Although the HemoSep device is capable of concentrating blood cells passively, the time taken to achieve the desired concentration is considerably shortened by using some agitation of the device. A fixed rate of 120 cycles/min has been determined as the most efficient frequency for the system, leading to maximal improvement in the exchange performance with no effect on cellular damage.

The device consists of a polyvinyl chloride blood bag, sized 12 × 7 inches, which is flat packed when presented for use. This processing bag, which is the main functional component device, weighs less than 100 g.

Technique

Before blood was introduced into the HemoSep bag, the system was first primed using 150 mL normal saline solution. The bag was then gently rotated by hand to ensure that the polycarbonate control membrane was adequately wetted, until the priming liquid was entirely adsorbed into the superadsorber pad. Once the volume of blood was introduced, the inlet and outlet tubes were clamped and the bag was placed into the orbital shaker chamber. The shaker was switched on and orbital, periodic bidirectional agitation initiated at a rate of 120 cycles/s for 40 minutes. At the conclusion of the predetermined time, the HemoSep bag was removed from the orbital shaker and held upright with the blood outlet port at the bottom. With the blood collection bag connected to the outlet port, the outlet clamp was released and the processed blood was drained into the collection bag.

Blood Samples and Assays

Samples were obtained through the port of the bag in potassium-ethylenediaminetetraacetic acid tubes from processed blood at baseline, 15, and 40 minutes to document hematologic and inflammatory parameters. Complete blood count, activated partial thromboplastin time, and levels of fibrinogen and factor VII were evaluated. Standard blood biochemistry; especially the albumin fraction, was documented. Serum interleukin 6 (IL-6) levels were measured by enzyme-linked immunosorbent assay (Bender Medsystems, Vienna, Austria; coefficient of variation < 10%, sensitivity < 1.4 pg/mL). Hemolysis was evaluated by plasma determination of free plasma hemoglobin (Behring Diagnostics, Westwood, MA).

Statistical Analysis

Data are expressed as the mean ± the standard error of the mean. The Mann-Whitney *U* test was used to compare demographic and nonparametric data. Two-way analysis of variance with factor of group and repeated factor of time was used to analyze differences over time in

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Table 1. Preoperative Evaluation of Patient Groups[a]

Variable[b]	HemoSep (n = 52)	Control (n = 50)
Age, y	69.1 ± 10	72.4 ± 10
Female sex	38	32
Body surface area, m^2	1.79 ± 0.05	1.74 ± 0.05
Diabetes	35	29
CABG[c]	6	8
Pre-op ejection fraction[d]	0.38 ± 0.08	0.35 ± 0.08
EuroSCORE	7.7 ± 1.5	8.4 ± 2.3

[a] $p < 0.05$ for comparisons between groups for all variables. [b] Continuous data are shown as the mean ± standard error of the mean and categoric data as number of patients. [c] Includes associated valve and carotid operations. [d] As detected by echocardiography.

CABG = coronary artery bypass grafting; EuroSCORE = European System for Cardiac Operative Risk Evaluation.

each group and for differences between groups. A post hoc test with Bonferroni correction was applied whenever a significant difference was detected. A p value of less than 0.05 was considered significant. Data were analyzed using SPSS software (SPSS Inc, Chicago, IL).

Clinical Experience

The preoperative evaluation of patients is reported in Table 1. The mean amount of processed blood was 775 ± 125 mL at the end of 40 minutes. The clinicians reported no technical failures with the HemoSep device and were pleased with its ease of use and overall performance.

No significant difference in plasma free hemoglobin, international normalized ratio, activated clotting time, and partial thromboplastin time levels were demonstrated. Table 2 presents the data before and after HemoSep application. Serum fibrinogen levels were also increased significantly at 15 minutes (345 ± 85 mg/dL; $p = 0.043$) and 40 minutes (425 mg/dL; $p = 0.0034$) vs baseline (195 mg/dL). Hemoconcentration and ultrafiltration reduced IL-6 levels at the end of 40 minutes of processing (75 ± 20 pg/dL) vs baseline (210 ± 100 pg/dL; $p = 0.0022$).

Perioperative follow-up of the patients who received processed blood is documented in Table 3.

Table 2. Data Before and After HemoSep[a] *Application*

Variable[b]	Baseline	15 min	40 min
Hematocrit, %	22.5 ± 4.8	29.5 ± 5.2[c]	36.9 ± 6.1[c]
p Value		0.043	0.014
White blood cells, $\times mm^3$	8.80 ± 3.1	11.40 ± 3.6[c]	14.20 ± 4.2[c]
p Value		0.031	0.0022
Platelet count, $\times 1{,}000\ mm^3$	110 ± 34	146 ± 40	193 ± 40[b]
p Value			0.025
Serum albumin, g/dL	1.6 ± 0.05	3.2 ± 0.08[c]	4.95 ± 0.07[c]
p Value		0.008	0.0002
Factor VII, %	56 ± 11	147 ± 18[c]	210 ± 21[c]
p Value		0.0038	0.0011

[a] Brightwake, Nottingham, United Kingdom. [b] Data are shown as mean ± standard error of the mean. [c] Statistically significant vs baseline.

Comment

The objective of the HemoSep development was to design a hemoconcentration technology that does not require centrifugation and associated blood transfer steps and can be used without the need for highly trained technical personnel. An additional benefit of the HemoSep technology is that it produces a gelatinous waste product, essentially plasma in a gel matrix, which is safer and easier to dispose of than the large volumes of fluid associated with the more common centrifugation processes.

Our study is the first clinical evaluation of HemoSep technology. Similar technologies are available that depend on ultrafiltration for blood salvage. The Hemobag (Global Blood Resources, Somers, CT) device concentrates residual blood from the CPB circuit during and after the bypass period. Substantial reductions were achieved in allogeneic blood product avoidance and cost to the hospital with use of this device [9].

Some cell-saving devices use a comparatively older technique to process salvaged blood after open heart operations. Studies demonstrated that these devices also reduced systemic levels of the proinflammatory markers IL-6 and IL-8 at 6 hours after CPB [10]. The HemoSep application reduced IL-6 levels from 210 ± 100 pg/dL at baseline to 75 ± 20 pg/dL at the end of 40 minutes of processing ($p < 0.05$).

The blood product produced by processing with the HemoSep device was very similar to the preoperative sample, with the exception of the white cell count, which was elevated in the processed blood. This is largely due to the normal patient cellular expression response to CPB and the effective sieving of white blood cells by the HemoSep membrane control mechanism. In terms of cell concentration, the HemoSep device functioned as expected, delivering a blood product that was in most respects very similar to the preoperative native blood in its essential composition.

Table 3. Perioperative Follow-Up of the Patients

Variable[a]	HemoSep[b] (n = 52)	Control (n = 50)	*p* Value
Post-op bleeding (24 h), mL	545 ± 180	725 ± 200	>0.05
Transfusion, units			
Red blood cells	1 ± 0.8	2.4 ± 1	0.032
Fresh frozen plasma	0.95 ± 1.2	2.4 ± 3	>0.05
Patients with no transfusion	38 (73)	19 (38)	0.012

[a] Continuous data are shown as mean ± standard error of the mean and categoric data as number (%). [b] Brightwake, Nottingham, United Kingdom.

The comparison between patients receiving HemoSep-derived autotransfusion blood and those receiving no autotransfusion, which is normal practice in this clinical center, demonstrated that the use of the HemoSep device was associated lower postoperative blood transfusion requirements.

Overall, the study demonstrated that the HemoSep device functions as designed and without technical failures. The resultant blood product was superior to that of the salvaged blood in terms of all active cell species studies, suggesting some possible clinical advantage in its deployment. Transfusion of the processed blood functioned well to contribute blood management strategies postoperatively. Large-scale comparative studies are warranted for the evaluation of other currently available ultrafiltration and autotransfusion systems.

Disclosures and Freedom of Investigation

The study was funded by University of Kirikkale Research Fund, Turkey (2011/223) and Brightwake Ltd., Nottingham, United Kingdom. The authors were free from outside interests in controlling the design of the study, acquisition of data, collection, analysis and interpretation of data and have freedom to fully disclose all results. The devices were provided at no charge.

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