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The role of cell savers and filters in cardiac surgery

Vermeijden, Jan Wytze

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Chapter 3

Do repeated runs of a cell saver device increase the pro-inflammatory properties of washed blood?

Wytze J. Vermeijden, Ans Hagens, Willem van Oeveren, Adrianus J. de Vries

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Abstract

Background: Intra-operative cell salvage is increasingly used, especially in longer cases with continuing blood loss. However it is unknown if the quality of processed blood is affected when larger quantities of blood are processed. We hypothesized that the quality of the washed blood decreases after multiple runs.

Methods: Intra-operative cell salvage was performed in 42 consecutive patients undergoing cardiac surgery. When 1250 ml of blood was collected in the blood collection reservoir, this was processed and returned to the patient. In 21 patients more than 2500 ml of blood was collected during the whole procedure, thus allowing at least two subsequent runs with the auto-transfusion device. Blood samples were drawn from the blood collection reservoir of the cell saver device before, and from the processed blood after each run.

Results: After the first run interleukin-6 concentrations were reduced with 85% (from $21 \pm 35 \mu\text{g/l}$ to $3.1 \pm 4.4 \mu\text{g/l}$), whereas after the second run 72% was removed ($63 \pm 69 \mu\text{g/l}$ to $17.6 \pm 25.3 \mu\text{g/l}$). Leukocyte counts almost doubled after both processing runs (from $2.6 \pm 1.5 \times 10^9/\text{l}$ to $5 \pm 3.6 \times 10^9/\text{l}$) and from $3.9 \pm 2.2 \times 10^9/\text{l}$ to $7.7 \pm 5.9 \times 10^9/\text{l}$), haemoglobin concentration ($14.8 \pm 1.6 \text{ mmol/l}$ versus $15.0 \pm 1.1 \text{ mmol/l}$), free hemoglobin ($2.3 \pm 1.6 \text{ g/l}$ versus $2.1 \pm 1.4 \text{ g/l}$) and platelet counts ($18 \pm 9 \times 10^9/\text{l}$ versus $28 \pm 23 \times 10^9/\text{l}$) were not different between the two runs.

Conclusions: Our results suggest, based on interleukin-6 and free hemoglobin washout that the quality of the processed blood remains constant with multiple runs of the cell saver device.

Introduction

To minimize blood transfusion requirements during cardiac operations performed with cardiopulmonary bypass (CPB), the anti-coagulated shed wound blood can be salvaged with cardiotomy suction. However, there is pronounced inflammatory activity in cardiotomy suction blood¹, and retransfusion of cardiotomy suction blood has been shown to contribute to the post-operative inflammatory response²⁻⁴.

Mechanical cell salvage devices are therefore increasingly used as an alternative method for intra-operative blood salvage. In a cell saver the shed wound blood is collected, washed and concentrated. The red blood cell concentrate is then retransfused in the patient.

Recently, the quality of this washed and concentrated blood was addressed in several studies^{1,5,6}. It was found that processing of shed blood by a cell saver led to normalization of some, but not all, inflammatory markers in the processed blood. However, to our knowledge, these studies considered only one processing run of the cell saver. As a consequence it is unknown if the quality of processed cell saver blood is affected when larger quantities of blood are processed. We hypothesized that the quality of the washed blood decreases when, due to large blood loss, multiple runs of the cell saver are necessary. This has not been studied before and might have implications for the way cell savers are used during operations.

Therefore, in the present study we assessed the quality of the processed blood by measuring interleukin-6 (IL-6), leukocytes and free hemoglobin. After 1250 ml of wound blood was collected in the blood collection reservoir of the cell saver we measured the blood quality. After processing the collected blood we again measured the blood quality. We compared this to the quality of the collected and washed blood after a subsequent 1250 ml of wound blood was collected and processed.

Materials and methods

Patients

After written informed consent and approval by the institutional ethics committee on human research, intra-operative cell salvage was performed in 42 consecutive

patients presenting for elective coronary artery bypass surgery or first time aortic valve replacement. Excluded were patients with known coagulation disorders except for the use of aspirin or low molecular weight heparin given at least 10 h before surgery. We did not perform a power calculation, as this was a pilot study.

Clinical management

Anaesthesia was induced and maintained with propofol infusion, followed by 0.1 mg/kg pancuronium to facilitate intubation. Sufentanil (1-3 µg/kg) was administered in incremental doses. Before cannulation bovine lung heparin (300 IU/kg) was administered and supplemented as necessary to obtain activated clotting times (ACT, Hemochron, New Jersey, USA) in excess of 400 s. After cardiopulmonary bypass (CPB), heparin was neutralized by protamine in a 1:1 ratio. The CPB-circuit consisted of roller pumps (Stöckert, München, Germany) and a hollow fiber oxygenator (Cobe, Lakewood, CO, USA) primed with 500 ml hydroxyethyl starch 10% (Fresenius, Bad Homburg, Germany) and 1000 ml lactated Ringer's solution. Myocardial protection consisted of cold crystalloid solution (Plegisol, Abbott laboratories, IL, USA).

Cell salvage was achieved by using the CATS system (continuous auto transfusion system, Fresenius, Bad Homburg, Germany). The cell saver device was installed identically for every patient and every run was according to the manufacturer's instructions. Washing conditions for all patients and runs were set at the automated, quality wash program, incorporated in the machine by the manufacturer. The blood collection reservoir of the cell saver was primed with 100 ml of normal saline with 30.000 IU heparin/l added. All shed wound blood during the operation including blood from the operative field during CPB was collected in the cell saver reservoir. Cardiotomy suction was not used. Thus, all cardiotomy blood was also collected in the cell saver reservoir, thereby increasing the quantity of blood to be processed. The residual blood from the heart-lung machine after CPB was also processed by the cell saver, but this blood was not analysed in this study.

When 1250 ml of shed blood was collected in the blood collection reservoir of the cell saver this was processed and returned to the patient. If another 1250 ml of blood could be collected a second processing run was performed. The amount of 1250 ml was arbitrarily chosen, as this is a volume at which a clinically relevant transfusable amount

of blood can be acquired. Furthermore this amount reflects the actual amounts lost on average in CABG operations. It is also an economical balance between cost of an allogeneic blood transfusion and the disposable centrifuge unit.

Blood samples were drawn from the blood collection reservoir of the cell saver device before each run and from the processed and washed blood after each run.

The following parameters were measured: white blood cell ($9 \times 10^9/l$) and platelet counts ($9 \times 10^9/l$), hemoglobin (mmol/l), free hemoglobin (g/l), haematocrit (%), and the concentration of the pro-inflammatory cytokine interleukin-6 (IL-6, $\mu g/l$). Samples for cytokines were collected in ethylenediamine tetraacetic acid (EDTA). The samples were centrifuged immediately and the resultant plasma was stored at $-80^\circ C$ until analysis. IL-6 was determined with a commercially available enzyme-linked immunosorbent assay (R&D Systems, Minneapolis, MN, USA) according to the manufacturer's instructions.

Statistics

Statistical analysis was performed with Wilcoxon signed ranks test as not all data had a normal distribution. A p value of less than 0.05 was considered significant. All the results are expressed as the mean \pm standard deviation.

Results

In 21 of the 42 patients at least 2500 ml of blood was collected in the blood collection reservoir of the cell saver, allowing two runs with the auto-transfusion device. Fourteen of these patients underwent coronary artery bypass grafting and seven patients had aortic valve replacement. The total amount of salvaged blood was 4718 ± 1581 ml. This also included the residual heart-lung machine blood (911 ± 330 ml), but this blood was not analysed in this study. There were no allogeneic blood transfusions during the study period. The characteristics of the patients are summarized in table 1.

Table 1: Demographics

	Euro SCORE	Age (years)	Sex (m/f)	Height (cm)	Weight (kg)	CPB (min)
Study (n=21)	3.8 ± 2.2	66 ± 8.6	17/4	1.74 ± 0.0	82 ± 14	121.7 ± 29.7

Data are presented as mean \pm SD; CPB, cardiopulmonary bypass; Euro SCORE, European System for Cardiac Operative Risk Evaluation

Processing of the blood resulted in a decrease of IL-6 in both runs. After the first run IL-6 levels were reduced with 85%, whereas after the second run 72% was removed. This difference was not significant. However the absolute reduction of IL-6 was larger in the second run. Leukocyte counts nearly doubled after each processing run (table 2).

Table 2: Results

Variable	Run 1: reservoir	Run 1: processed	Run 2: reservoir	Run 2: processed
IL-6 (µg/L) (n=18)	21 ± 35	3.1 ± 4.4 ^a	63 ± 69 ^d	17.6 ± 25.3 ^{b,c}
Leukocytes (x10 ⁹ /L) (n=21)	2.6 ± 1.5	5 ± 3.6 ^a	3.9 ± 2.2 ^d	7.7 ± 5.9 ^{b,c}
Free haemoglobin (g/L) (n=20)	2.2 ± 1.0	2.3 ± 1.64	2.3 ± 1.3	2.1 ± 1.4
Haemoglobin (mmol/L) (n=21)	2.7 ± 0.9	14.8 ± 1.6 ^a	3.5 ± 0.9 ^d	15.0 ± 1.1 ^b
Haematocrit (n=21)	12 ± 0	71 ± 0 ^a	16 ± 0 ^d	72 ± 0 ^b
Platelets (x10 ⁹ /L)(n=21)	72 ± 29	18 ± 9 ^a	87 ± 32	28 ± 23 ^b

Data are shown as mean ± SD

^a p< 0.01 for reservoir versus processed 1; ^b p< 0.01 for reservoir 2 versus processed 2; ^c p<0.01 for processed 1 versus processed 2; ^d p<0.01 for reservoir 1 versus reservoir 2.

The concentrations of IL-6, leukocytes, hemoglobin and haematocrit significantly increased in the unprocessed blood during the course of the operation (table 2, reservoir 1 vs. reservoir). The concentration of free hemoglobin in the blood collection reservoir of the cell saver did not increase in the unprocessed blood (table 2, reservoir 1 vs reservoir 2). Processing of blood from the cell saver blood collection reservoir resulted, in both runs, in a significant increase in hemoglobin, haematocrit and a significant decrease of platelets. The hemoglobin concentration, free hemoglobin concentration and platelet counts were not different between the two processed runs (table 2).

Discussion

The results of the present study demonstrate that repeated processing runs of shed wound blood with a cell saver leads to a similar reduction of the concentration of the pro-inflammatory cytokine IL-6. Leukocytes are retained. Hemoglobin, free hemoglobin, haematocrit and platelet concentrations were also not different between

the two processed runs. Thus, we showed that subsequent runs with a cell saver do not diminish the washout ability of pro-inflammatory markers.

Our IL-6 concentrations in the salvaged wound blood were relatively low compared to other studies that investigated the IL-6 concentrations in salvaged wound blood. An explanation may be that in this study only salvaged wound blood was used whereas in other studies the residual heart-lung machine blood was also processed ^{5,6}. As in earlier studies we found a high standard deviation of IL-6 values between and in patients ¹. We did not measure the IL-6 concentration in the patients, as in this pilot study we were only interested in the blood quality aspect of the cell saver. The significant increase in IL-6 in the unprocessed blood between the two runs is most likely due to the ongoing inflammatory response during the course of the operation and CPB ^{3,7}. Hemodilution by priming of the cell saver reservoir is a less likely explanation for the lower IL-6 concentrations in the first blood collection reservoir. The priming volume was 100 ml and would thus have a dilution effect of 8%.

Free hemoglobin levels were not reduced. Approximately 0.5% of erythrocytes are being damaged during and after the washing procedure, resulting in new hemoglobin release ⁸.

Our study also demonstrates a concentrating effect of leukocytes after each run. This has been demonstrated previously ^{1,9} and might be explained by the centrifugation process itself. White blood cells, which are larger but not heavier than red blood cells, are spun to the rim of the washing chamber, the so-called buffy coat. With on-going centrifugation and washing the buffy coat becomes so concentrated with debris that leukocytes pass with the red blood cells into the process bag. The formation of such a layer of debris has been demonstrated before ^{9,10}.

The consistent performance of red blood cell saving can be explained by the operating process of the cell saver itself. A light sensor reacts on the red blood cell concentration and starts the pump to transport the processed blood to the collection bag. Thus one would, given time, always expect similar hemoglobin and haematocrit in subsequent runs.

The device used in this study is the CATS cell saver. This is a continuous auto-transfusion system, which means that the system runs continuously until the blood collection reservoir is empty. This is in contrast to a bowl system, which operates by

using batches of blood from the blood collection reservoir. In the current study we used this continuous system as a bowl collection system for a clear separation of the amount of blood processed.

In retrospect in a few patients it would have been possible to perform a third processing run. It would have been interesting to see the effect of a further processing run on the blood quality. Furthermore, measurement of leukocyte activation in the processed blood could have shown if leukocytes are activated by the blood processing process, giving further information on processed blood quality. In conclusion, our results suggest that with repeated runs blood quality is maintained. With repeated runs of the cell saver device leukocytes are retained. This is probably due to a concentration effect.

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