Malta Medical Journal, 33 (1): Pages (2021)
http://mmsjournals.org/index.php/mmj

MMJ

ORIGINAL ARTICLE

A comparison of intraoperative cell salvage use with cardiotomy suction in cardiothoracic surgery

Edward Muscat, Timothy Miggiani, David Sladden, Alexander Manche'

Introduction

Intraoperative cell salvage has been shown to be a safe and effective means of autologous blood recirculation in elective surgery. Most cardiac units now employ cell salvage for complex procedures but few use it routinely in all cardiac procedures requiring cardiopulmonary bypass.

Aim

To demonstrate if there was any haematological benefit of autologous transfusion using intra- operative cell salvage over single use of cardiotomy suction in patients undergoing cardiac surgery.

Methods

All patients who had operations performed by the cardiac surgical team over a twenty-month period formed part of this study including valve replacements and coronary artery bypass grafting. The patients were divided into two groups; the cell saver group and the control group. The haematological variations of these patients' blood results were analysed preoperatively, immediately post-operatively and 24 hours post-operatively.

Results

451 patients were operated on during this period. 230 patients in the control group and 221 patients in the cell saver group. Intra-operative cell salvage demonstrated better immediate post-operative haemoglobin levels (10.31 g/dL) compared to the non-cell saver group (9.99 g/dL). The p-value was 0.003 after comparison between pre-operative haemoglobin and post-operative haemoglobin in the cell saver group.

Conclusion

Intra-operative cell salvage demonstrated a minimal increment in haemoglobin levels in the immediate post-operative period when compared with cardiotomy suction alone. Even though the improvement in haemoglobin is only significant until 24 hours post-operation, overall this showed an improved haematological parameter in the immediate recovery period.

Edward Muscat, MD (Mlt), MRCS (Eng)*
Mater Dei Hospital
Msida, Malta,
North Bristol Trust,
Southmead Hospital,
Westbury-On Trym, Bristol,
edward.j.muscat@gmail.com

Timothy Miggiani, MD (Mlt)
Mater Dei Hospital
Msida, Malta,

David Sladden, MD (Mlt) MsC (Edin) FRCS-CTh (Edin)
Mater Dei Hospital
Msida, Malta,

Alexander Manche', MPhil, FRCS(CTh), FETCS
Mater Dei Hospital
Msida, Malta,

*Corresponding author

Introduction

Major surgery, especially cardiac surgery, is a challenge to the hematopoietic system. It is well known that patients with cardiac disease, namely ischaemic heart disease and hypertrophic cardiomyopathy, cannot tolerate a decrement in haemoglobin and haematocrit levels. Cardiac surgery carries a high burden in terms of blood loss and transfusion requirement, and hence transfusion related injuries. The National Blood Service in the UK advocates that 10% of its stored blood supplies are used in cardiac surgery alone.[1] The continued use of allogeneic erythrocyte transfusions is associated with adverse effects such as myocardial ischaemia, acute lung injury and an overall raised mortality index.[2] According to various authors, a haemoglobin of 10 g/dl and a haematocrit of 30% indicated desirable goals in anaemic patients undergoing cardiac surgery.[3] Blood is a limited yet costly resource and it should be utilised as sparingly as possible. The autologous options for surgical blood conservation circumvent the transfusion of allogeneic blood. Options include preoperative autologous blood donation, intra-operative haemoconcentration and blood salvage.

The cardiotomy suction apparatus was introduced first in the 1960s as an extension of the intracardiac vent to allow blood lost during the operation to be returned via the cardiopulmonary bypass (CPB) circuit. The aim was to reduce blood loss and hence the need for allogeneic blood transfusions with its known risk of increased morbidity however this is not always the case as evidence suggests that recirculated cardiotomy suctioned blood neither reduces blood loss nor transfusion requirements.[4] Intra-operative cell salvage (ICS) during cardiac surgery is widely accepted; a meta-analysis of 31 trials showed that routine use reduced the transfusion of red cells by 40%.[5]

It works by collection, washing, and re-infusion. Collection involves the use of a double-lumen suction device. One lumen drains blood from the operative field and the other lumen adds a dose of heparinized saline to the drained blood. The anticoagulated blood is then passed through a filter, which is then collected in a reservoir. Centrifugation splits the blood into separate components. The red blood cells (RBCs) are then isolated and washed which are then filtered across a semi-permeable membrane. The free haemoglobin, plasma, platelets, white blood cells, and heparin become removed at this stage. The same RBCs are infused in normal saline transforming the haematocrit to 50–80%. Blood can then be transfused immediately or within a six-hour time frame.[6]

ICS is purported to feature benefits such as a decreased need for allogeneic blood transfusions and increased cost-effectiveness. It has been argued that ICS has financial benefits over erythrocyte transfusion in the setting of homologous blood is becoming more expensive. Furthermore, leucodepletion of blood in the post Creutzfeldt-Jakob disease era has quadrupled the cost of allogeneic blood transfusion.[7] It also avoids the potential side effects such as the transmission of viral illnesses, transfusion reactions and immunosuppressive infections associated with blood transfusions.[8] In addition, it can be associated with a lower risk of cerebral lipid embolism.[9]

The principal drawback of ICS in the literature is dilutional coagulopathy as blood that is salvaged lacks clotting factors. It has also been argued that since the introduction of drugs,

lower priming volumes and intravascular shunts blood loss has been minimised to the extent that ICS is no longer warranted.[1] At the time of writing this study there have been many publications highlighting the benefits of cell saver over cardiotomy suction but few recommend its routine use in cardiac surgery. Its use needs to be justified by analysing post-operative improvement in haemoglobin and haematocrit levels.

Therefore, the aim of our clinical study was to evaluate the effects of autologous cell saver blood transfusion on blood loss and changes in haemoglobin and haematocrit concentrations in the cardiac operations done in between over a one year period in Mater Dei Hospital in Malta. The literature has shown that the values of blood markers (number, size, function) produce changes during the early phase of cardiac surgery, steady recovery during the postoperative period achieving preoperative values 2-6 months after surgery.[10]

Materials and Methods

This study included all patients who had operations performed by the cardiac surgical team over a twenty-month period. Inclusion criteria consisted of all major cardiac surgical operations within this period including valve replacements (aortic and/or mitral). coronary artery bypass grafting (emergency or elective), aortic graft, cardiac tamponade and aortic root replacement. All patients underwent a general anaesthetic and standard practice of cardiopulmonary bypass.

The selected patients were organised into two groups namely the control (non-cell saver) and the cell saver groups. Data collection included patient demographics and hospital numbers, which were processed by the local hospital clinical manager software, iSoft, in order to retrieve their individual haematology results. The main focus of this study was primarily interpretation of trends of Haemoglobin (Hb) and Haematocrit (Hct). In order to accurately measure the trend of haematological variation throughout the patients' hospital stay blood results preoperatively, immediately post-operatively and 24 hours post-operatively (delayed) were obtained for analysis. All statistical analysis was performed using the SAS statistical software programme. We considered results to be significant at p value < 0.05.

The cell saver system was implemented in the year of 2015 in Mater Dei Hospital, Malta. Therefore, acquisition of control group patients was historical and occurred prior to the cell saver group being between January 2014 to September 2014. An equivalent number of control cases were recorded before the introduction of the cell saver machine and this included matching criteria. These weren't case matched on an individual basis however the average group demographics were consistent with similar risk factors and co-morbidities. Data for the cell saver group was collected prospectively as the operations were performed over time. The two cohorts were matched overall by a separate researcher prior to data collection of blood levels. All operations were performed by the same three cardiothoracic surgeons using relatively similar surgical methods and bypass times.

Results

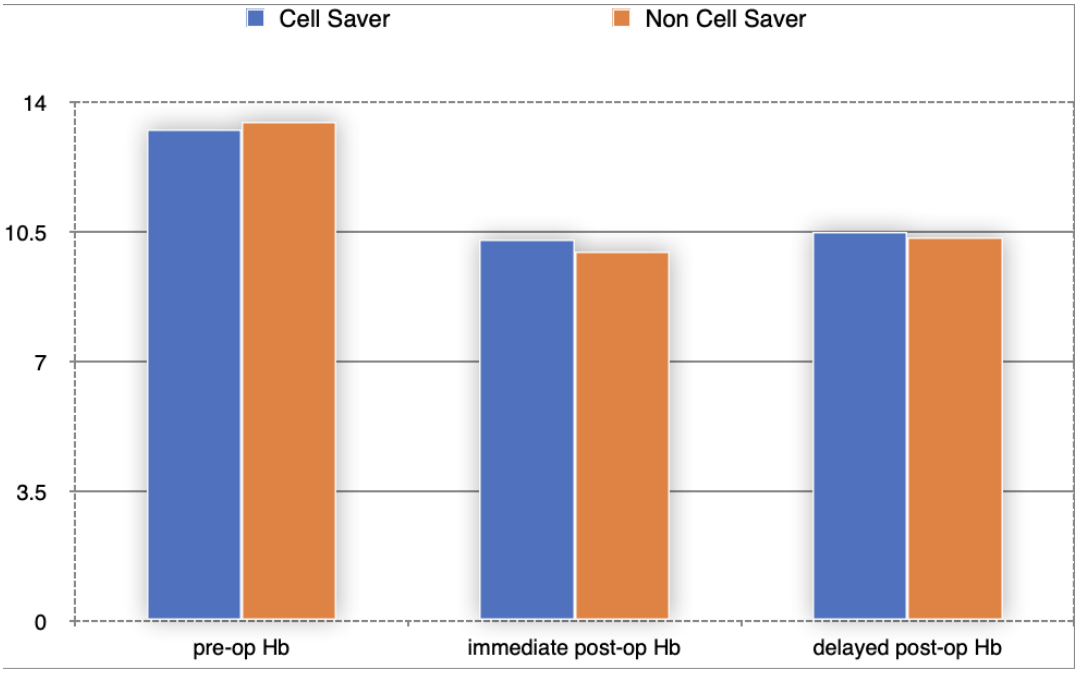
The total number of patients were 451 with a mean age of 64.75 years. 230 patients were in the control group and 221 patients in the cell saver group. The total number of operations is shown in table format in Table 1. The overall pre-operative haemoglobin mean was 13.28g/dL in the cell saver group and 13.47g/dL in the control group. The overall

mean preoperative haematocrit was 38.79% in the cell saver group and 39.15% in the control group. In both groups the average number of units of whole blood transfused to the patients were the same.

Table 1 Table including the categories of cases in this study

	Control	Cell saver
Total patients	230	221
Number of total AVR cases	54	60
Number of total MVR cases	17	27
CABG cases	169	139
Combined AVR + MVR cases	1	2
Combined CABG +VR	13	10

Figure 1 Bar graph showing the comparison of haemoglobin values between cell saver and non-cell saver cardiac operations pre and post-operation.



An important result from both group findings was mainly the *p*-value of 0.003 after comparison between pre-operative haemoglobin and post-operative haemoglobin in the cell saver group which is statistically significant for this study being that confidence intervals were all 95% *(Figure 1)*. The same cannot be said for delayed post-operative haemoglobin which did not show any statistical significance when comparing pre-operative haemoglobin *(p*=0.143*)*. Therefore, an increment was found amongst the cell saver

patients compared to control group patients in terms of immediate post-operative haemoglobin levels considering the pre-operative Hb even was lower for the cell saver grouped patients. Minor haematocrit difference was observed between both groups both immediately post-operation *(p*=0.643*)* and delayed post- operation *(p*=0.766*).*

Discussion

Intraoperative autologous red cell salvage during cardiac surgery is an attractive alternative to the continued single use of cardiotomy suction. From our study we have observed that ICS was associated with better post-operative haemoglobin results compared to the control group in the immediate post-operative period. Similar results were also mentioned by Marcoux et al in his study where post-operative haemoglobin concentrations, in cardiac surgical patients, were significantly higher in the ICS group consequently spending significantly less time in the Intensive Care Unit (ICU).[11] In terms of delayed post-operative haemoglobin results both groups had similar results with the cell saver group having haemoglobin levels that were, again, slightly higher.

When first introduced in the 1980s, some authors had opposing views against the use of ICS, because it would neither decrease the costs nor the requirement of autologous blood. Since then, several studies have emerged highlighting the advantages in the use of ICS being that it increases haemoglobin concentration and utilizes less use of allogenic blood transfusion in the post-operative period.[12] Several other studies have shown advantages in the use of the cell salver. Almeida et Leitao also mentioned that use of a cell saver mechanism results in shorter hospitalization time in ICU (one day less) and a reduction of the use of red blood cell units during inpatient stay for cardiac surgical patients.

Currently, misconceptions regarding the use of cell saver systems portray them as expensive, ineffective, and inappropriate for use in certain clinical situations. Several authors have demonstrated that the lack of use of red blood cells in the postoperative period decreases not only the morbidity but also intra and postoperative mortality. In a recent study, Coté et. al. retrospectively analysed outcomes of ICS in cardiac surgery revealing ICS group were less likely than the control group to be exposed to packed red blood cells, coagulation products or any blood products in the peri-operative period.[13] Since whole blood transfusion is used after cardiac surgery as a means to enhance cardiac output it was not analysed as a variable for cell saver performance in our study. Both groups had cardiotomy suction available providing an added benefit. In our study we had not noticed any significant difference in the number of units of blood products between both groups but as this is a pilot study of cardiac operations the patients received similar transfusion units post operatively and perhaps the team will become more confident in the ability of the cell saver system over the years. However, despite this postoperative hemoglobin levels increased in the cell saver group in the immediate setting. Few ICS studies stated as to whether or not remaining cardiopulmonary bypass contents were processed through the cell saver via cardiotomy suction. Those of which that did found a significant decrease in red blood cell transfusion and a decrease in postoperative chest tube drainage.[14] Interestingly, a randomised controlled trial (RCT) by Westerberg et al. comparing re-transfusion of ICS and cardiotomy suctioned

blood effects in cardiac surgery showed cardiotomy suctioned blood being quite vasoactive decreasing the mean arterial pressure (MAP). The vasodilation was proportional to the release of inflammatory cytokines from cardiotomy suctioned blood and this is significantly reduced by using it alongside ICS.[15]

Cardiopulmonary suction alone involves a highly turbulent flow of the suction which causes shear stresses at the air-fluid interface resulting in the stimulation of humoral cascades as part of the systemic inflammatory response. The shearing stress caused by a cardiotomy suction results in an increased amount of free haemoglobin due to mechanical haemolysis.[7] Perhaps this is as to why there is a slight difference between the cell saver and control group blood results. It is well documented that not only does the single use of the cardiotomy suction in cardiopulmonary bypass (CPB) surgery is associated with a systemic inflammatory response but also a resulting coagulopathy as it exacerbates the microembolic load. High quantities of free haemoglobin can cause platelet disfunction and damage to renal tubular cells. Processing cardiotomy suctioned blood with a cell saver device is important factor to effectively reduce these inflammatory responses, yet this in itself might also have potential harmful effects for the patient[16]. In terms of safety with cell saver we know that heparin coated CPB circuit with the uncoated cardiotomy reservoir may be less biocompatible than the identical CPB set used together with cell saver mechanism. Borowiec et. al mentioned that cardiotomy suction produces a marked reduced ability to produce oxygen free radicals by the whole blood at 45 minutes of CPB.[17] Fat microembolic load is decreased by the cell saver by as much as 85%.[18] In a prospective randomised trial analysing fat percentage in recirculated blood in cardiac surgery the percentage reduction in fat weight achieved by cell saver and cardiotomy suction alone was 87% and 45% respectively.[19]

In a RCT by Lau et al. recirculation of blood in the operative field significantly decreased the number of packed cells, platelets, and total blood products received in the test group when compared with the control group.[20] 200 patients were randomised prospectively undergoing first time CABG to control or cell salvage (washed). The cell salvage group was significantly less likely to receive a homologous blood transfusion and they received significantly fewer units of blood or platelets than controls. Larger systematic reviews have been completed to address this clinical question.[21] The Cochrane systematic review of Carless et al. did not differentiate between studies with washed and unwashed blood, but overall a similar result suggesting benefit of this technology.[22]

Fat particles have been linked with neurologic disfunction associated with CPB which have been due to the presence of small capillary and arteriolar dilatations (SCADs) shown in the brain in post- mortem studies. Unprocessed cardiotomy blood has also resulted in the production of thrombin during cardiac surgery including markers of inflammation such as tumor necrosis factor, interleukin-6 (IL-6), complement and neuron-specific enolase.[23] Even though the use of cardiotomy suctioned blood poses a microvascular risk, Rubens et.al stated that there is no clinical evidence of any neurologic benefit with this approach in terms of postoperative cognitive function.[24] This decrease in blood product utilization translated into a significant cost savings per patient in the available literature. We have not

analysed cost in this study as the cell saver device was initially a donation to the local department but it would be an interesting feature to do so in the future. In the same RCT Rubens et.al also stated there was less postoperative bleeding and less use of blood transfusions amongst the cell saver group in cardiac surgery.[24] Our results are fairly consistent with other studies demonstrating that ICS results in increased post-operative haemoglobin rates, especially in cardiac surgical patients. Cardiac surgery patients are most at risk of myocardial ischaemia when haemoglobin levels fall and as a consequence are also at most risk of transfusion related complications especially acute lung injury.

It has been suggested that cardiotomy suction alone produces an unbalanced ratio of pro and anti-inflammatory cytokines. A RCT by Gabel et. al discovered that cell savage in combination with cardiotomy suction decreased the concentrations for such cytokines improving the postoperative balance.[25] Damgaard et al. suggested that ICS decreases circulatory levels of pro-inflammatory markers IL-6 and IL-8 and increased immediate Hb levels at 6 hours post CPB[26]. Engels et al supports this with his RCT of inflammatory cytokines in cardiac surgery which indicated lower levels of Clara cell 16 kD proteins (CC16) resulting in less lung injury in the ICS group compared to controls. The ICS group had shorter ventilation times.[27]

Cell salvage is not however entirely without its problems. The air-fluid interface remains, however, the presence of heparin at the tip of the suction reduces the activation of the clotting and inflammatory cascades. It is almost predicable that if very large volumes of blood are processed through a cell saver it will deplete that volume of blood of platelets and clotting factors, careful monitoring and replacement of these may be necessary[6]. Shen et. al performed a RCT on high-risk cardiac surgical patients and discovered that ICS could impair blood coagulation and found excessive bleeding post operatively in this group[28]. Even though complications associated with the use of ICS are rare, studies have shown no overt increase in the rate of complications in patients who receive ICS.[29]

Conclusion

This study recommends the use of the cell saver system in cardiac surgery to reduce the probability of severe postoperative anaemia. As also stated by the ASA guidelines, we support the recommendation to keep its availability for immediate use 24 hours a day in any center undertaking surgery where blood loss is a recognised potential complication.[30] Although the use of ICS did not decrease the rate of red blood cell transfusion there were higher postoperative hemoglobin levels in immediate post-operative settings compared with cardiotomy suction alone. The literature seems to support use of combined ICS with cardiotomy suction as they effectively decrease inflammatory cytokines which can cause complications. However, excess cell saver use alone may decrease circulating clotting factors in high risk bleeding cardiac surgery.[31] Therefore, we do not recommend cell saver use without cardiotomy suction in cardiac surgery. It would be worth comparing both groups in terms of post-operative bleeding in future cohorts.

Summary Box

What is already known about this subject:

- Benefits of ICS include less time in ICU, shorter ventilation times and a shorter hospital stay in surgical patients.

- ICS causes a depletion of clotting factor and platelets due to hemofiltation of recirculated blood.
- Cardiotomy suction alone causes mechanical hemolysis increasing transfusion requirements whilst maintaining clotting factors.

What are the new findings:

- Immediate post-operative haemoglobin levels are increased with the use of ICS in cardiac surgery compared with cardiotomy suction alone.
- No significant changes in hemoglobin found in the late post-operative period using the cell

  saver. No significant changes in hematocrit using a cell saver mechanism.
- An addition to the literature to support a combination of cell saver mechanism with cardiotomy suction in cardiac surgery.

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