

Hemosep for cell salvage

Medtech innovation briefing

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Summary

- The **technology** described in this briefing is Hemosep. It is used for cell salvage and haemoconcentration during surgery.
- The **innovative aspects** are that it can remove plasma from the blood using a membrane-controlled super-absorber instead of centrifugation. This leaves concentrated blood that contains red and white cells, platelets and clotting residuals. The filtered plasma is held as a gel matrix which is designed to make disposal safer and easier.
- The intended **place in therapy** would be as an alternative to standard cell salvage and allogenic blood transfusions in people having cardiac or trauma surgery.
- The **main points from the evidence** summarised in this briefing are from 3 studies: 2 UK-based and 1 non-UK-based randomised controlled trials including 209 adults in a tertiary care setting. The results are mixed; 1 study shows comparable outcomes between Hemosep and standard care (cell salvage), whereas in the other 2 Hemosep led to better outcomes than standard care.

- **Key uncertainties** are that there is little evidence on Hemosep, and the available studies are statistically underpowered.
- The **cost** of Hemosep is £3,875 per unit (exclusive of VAT), plus £248 in consumables per use and an additional £500 per year in maintenance costs. The **resource impact** of using Hemosep would be to add costs compared with standard care, but these could be offset if Hemosep reduced the need for allogenic blood transfusions.

The technology

Hemosep (Brightwake) is an ultrafiltration and haemoconcentration system for concentrating residual bypass blood during or after surgery. Haemoconcentration is the process of reducing the amount of plasma in the blood relative to the amount of red blood cells. It is usually done to offset haemodilution (the increase of plasma in the blood relative to red blood cells), which can be caused by administering essential fluids during surgery.

Hemosep consists of 4 main components:

- Hemosep bag and tubing (containing a filter membrane and super-absorption material in a pad, for concentrating the blood)
- Hemosep shaker unit
- 1 litre blood collection bag for concentrated blood
- intraoperative pump with suction tool and blood reservoir.

The Hemosep bag is single-use and comes in adult and paediatric sizes. Adult Hemosep bags have a maximum optimum capacity of 500 ml; paediatric Hemosep bags have an optimum capacity of 200 ml but can hold up to 250 ml if needed. More than 1 Hemosep bag may be needed per surgery, depending on the type of surgery and degree of blood loss.

Hemosep has 2 uses. It can be used to ultrafilter residual, haemodiluted blood after a bypass by connecting the Hemosep bag directly to the cardiopulmonary bypass system. It can also be used during surgery: blood is taken from the surgical site and passed into the reservoir using a heparin-infused suction tool, where it is filtered and pumped into the Hemosep bag.

However Hemosep is used, once in the bag blood is ultrafiltered using a membrane-controlled super-absorber plasma removal process. The filter membrane in the bag prevents movement of blood cells from the bag to the super-absorber pad while allowing free movement of plasma into the pad. The filtration can be helped by placing the Hemosep bag on the orbital shaker unit, which agitates the blood and encourages movement of cells across the membrane surface. The result is that concentrated blood is held within the bag while plasma is stored as a gel matrix within the super-absorber pad.

Once the concentrated blood reaches a packed cell volume of over 35%, it can be transferred to the collection bag for autotransfusion. Packed cell volume is calculated by centrifuging a small sample of the blood product and measuring the proportion of concentrated red blood cells.

The manufacturer recommends the use of a leukocyte reduction filter when reinfusing the blood.

Innovations

Concentrated blood collected using Hemosep contains not only red blood cells, as with other centrifugation cell salvage devices, but also platelets, white blood cells and clotting residuals. In this way Hemosep is designed to avoid the need for centrifugation and other blood preparation steps. It can therefore be used without the need for highly trained technical staff.

Plasma collected using Hemosep is stored in a gel, which is easier and safer to dispose of than large amounts of fluid associated with centrifugation methods.

Current NHS pathway

Cell salvage is routinely done during major surgery in the NHS when the patient is at risk of moderate blood loss. Haemodilution during surgery can cause impaired coagulation and this can increase the risk of bleeding, the need for subsequent transfusions, and morbidity.

One method is to re-transfuse salvaged, heparinised blood (such as from a bypass machine) directly back into the patient. Another is centrifugation cell salvage, which involves taking blood from the surgical site and mixing it with anticoagulants in a collection

reservoir. The reservoir filters the blood before it is centrifuged to separate the red blood cells from other blood products. These are then washed with saline solution while still in the centrifuge, displacing any remaining blood products. The concentrated blood is then pumped into a bag ready for reinfusion.

Allogenic blood transfusions may also be used during and after high blood loss surgeries, but these are reliant on the availability of donor blood.

Hemosep would be used as an alternative to current cell salvage methods for autologous blood transfusion, and could be used instead of allogenic blood transfusions.

NICE's guideline on [blood transfusions](#) advises the use of intraoperative cell salvage with tranexamic acid for patients who are expected to lose a high volume of blood. NICE interventional procedures guidance on [radical prostatectomy or radical cystectomy](#) states that cell salvage during surgery may cause the reinfusion of malignant cells, and guidance on [intraoperative blood cell salvage in obstetrics](#) states that it may cause amniotic fluid embolism and haemolytic disease in the mother in future pregnancies. Safety guidelines produced in 2009 by the [Association of Anaesthetists of Great Britain and Ireland \(AAGBI\)](#) recommend cell salvage because it is cost effective compared with red blood cell transfusions, but state that it should not be used in the presence of bowel content unless there is a catastrophic haemorrhage.

NICE is aware of the following CE-marked devices that appear to fulfil a similar function to Hemosep:

- Hemobag (Global Blood Resources).

Population, setting and intended user

Hemosep would be used in a tertiary care setting during and after routine cardiac and trauma surgery in which the patient had moderate to high blood loss. It can be used in both adults and children. It would most likely be used by a clinical perfusion scientist, perfusionist, blood conservation co-ordinator or anaesthetist. Around 1 hour's training is needed to use Hemosep; the manufacturer provides this at no extra cost. The device comes with a training manual and quick reference guide.

Costs

Technology costs

The manufacturer estimates the average cost per treatment to be £240 ([Advancis Surgical, 'The true cost of cell salvage compared to Hemosep'](#)). Table 1 shows the cost of Hemosep and the associated consumables.

Table 1: Device and consumables costs

Description	Cost	Additional information
Hemosep orbital shaker unit	£3,500	Reusable
Shaker unit maintenance (annual)	£500	Reusable
Reservoir attachment, IV pole and fittings	£375	Reusable
Adult or child kit (1 Hemosep bag and 1 collection bag)	£80	Single-use, purchased individually
Suction kit	£143	Single-use
1-to-3 adapter	£25	Optional; connects the blood collection reservoir to up to 3 Hemosep bags

Costs of standard care

Using the Dideco Electa Cell Salvage device as an example, the average total cost of cell salvage (including consumables) is £296.72 per transfusion, based on a costing statement from the NICE guideline on [blood transfusion](#). This does not include the cost of the device itself. The same costing statement estimates that allogenic blood transfusion costs £170.14 for the first unit of red blood cells and £162.01 per subsequent unit. However, this does not include transfusion of any other blood, or blood components, so is likely to be an underestimate for surgery in practice.

Resource consequences

Because cell salvage devices are commonly provided to the NHS at no charge, Hemosep would cost more than current cell salvage methods. This could be offset if Hemosep reduced the need for allogenic blood transfusions because of the cost of additional blood components needed per transfusion.

A [national comparative audit of blood transfusions](#) (PDF) from 2011 states that, on average, 2 units of red blood cells are used per transfusion episode. Based on cost estimates from this and the NICE costing statement, Hemosep could save around £332.15 per transfusion compared with use of donor red blood cells. These savings may be greater if additional blood components are transfused.

When compared on a cost per transfusion basis with cell salvage methods, Hemosep could save around an estimated £56.72 per transfusion. This is mainly because of a reduced need for additional blood components and specialist staff. Hemosep could also provide a viable option for patients who cannot have donor blood transfusions.

There are likely to be few practical issues because Hemosep needs minimal staff training and no additional technical staff.

Hemosep is currently used routinely in 1 NHS trust.

Regulatory information

Both adult and paediatric Hemosep bags were CE marked as class IIb devices, the intraoperative suction kit (including the pump) was CE marked as a class IIa device and the Hemosep shaker unit was CE marked as a class I device, all in August 2012.

A search of the Medicines and Healthcare Products Regulatory Agency website revealed that no manufacturer field safety notices or medical device alerts have been issued for this technology.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In

producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

During cardiac surgery, women are more likely to have allogenic red blood cells, platelets and a greater quantity of blood compared with men ([Rogers et al. 2007](#)). Sex is a protected characteristic under the Equality Act 2010.

Hemosep may be of particular benefit to people with certain beliefs who are unwilling to accept blood transfusions.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the [interim process and methods statement](#). This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

This briefing summarises 3 randomised controlled trials including 209 patients. Two are fully published journal articles (n=155) and the other is a conference abstract reporting results from a 2016 trial (n=54). Table 2 summarises the clinical evidence as well as its strengths and limitations.

Overall assessment of the evidence

There are very few published studies using Hemosep, and those that exist have small sample sizes and are most likely underpowered to detect a true difference between groups. Two of the studies were part-funded by the manufacturer.

Two of the 3 studies in this briefing were done in the UK, making their results relevant to NHS practice.

Larger trials are needed to improve the evidence base for the effectiveness of Hemosep compared with standard care. Hogan et al. (2015) commented that larger trials could compare Hemosep with other haemofiltration methods, centrifugation cell salvage methods, bagged pumped blood and allogenic blood transfusion. They estimated that around 176 patients would be needed per group for adequate statistical power for their study design.

Table 2: Summary of included studies

<u>Boyle et al. (2016)</u>	
Study size, design and location	RCT including 54 low-risk cardiac patients from St Thomas' NHS Trust, London.
Intervention and comparator(s)	The intervention group received autologous blood returned from the Hemosep device. The comparator group had autologous red blood cells returned from cell salvage.
Key outcomes	Cell saver volume was significantly higher in the intervention group. PT was shorter in the intervention group postoperatively. aPTT was increased in the intervention group following transfusion. DDimer and ETP were higher in the comparator group following transfusion.
Strengths and limitations	NHS-based, has good relevance to NHS practice. Conference abstract and so limited details of the study are available.
<u>Gunaydin et al. (2013)</u>	
Study size, design and location	RCT including 102 cardiac patients with a EuroSCORE exceeding 6 from University of Kirikkale (Turkey).
Intervention and comparator(s)	The intervention group received autologous blood returned from the Hemosep device. The comparator group had blood salvaged by conventional methods without the use of a haemoconcentrator.

Key outcomes	<p>Within the Hemosep group, haematocrit, white blood cells, serum albumin and blood coagulation factor VII levels were all statistically significantly concentrated after 15 and 40 minutes compared to baseline.</p> <p>Levels of post-operative bleeding were not significantly different between groups.</p> <p>Patients in the control group received statistically significantly more perioperative allogenic RBCs compared to the intervention group.</p> <p>Statistically significantly more patients within the control group needed a transfusion perioperatively compared to patients within the intervention group.</p>
Strengths and limitations	<p>Not UK-based and so generalisability to the NHS is unclear.</p> <p>Doesn't fully explain what is meant by standard care.</p> <p>Funded by Brightwake.</p> <p>General lack of discussion.</p>
<u>Hogan et al. (2015)</u>	
Study size, design and location	RCT including 53 patients with a EuroSCORE above a mean of 4.8 from Papworth Hospital NHS Foundation Trust.
Intervention and comparator(s)	<p>The intervention group received residual blood concentrated using Hemosep.</p> <p>The comparator group received heparinised (but not concentrated) residual cardiopulmonary bypass blood.</p>
Key outcomes	<p>There was no difference between groups in haemoglobin concentration, platelets, PT or aPTT after autotransfusion.</p> <p>There was no difference between groups in the rate of red blood cell, platelets or FFP transfusions with 12 hours after surgery.</p> <p>There was no difference in blood loss within 12 hours after surgery between groups.</p> <p>The intervention group did show a reduction in weight of blood compared to the comparator group.</p>
Strengths and limitations	NHS-based, has good relevance to NHS practice. Brightwake provided an unrestricted educational grant.

Abbreviations: ETP, endogenous thrombin potential; FFP, fresh frozen plasma; RBC, red blood cell; RCT, randomised controlled trial; PT, prothrombin time; aPPT, activated partial thromboplastin time.

Recent and ongoing studies

No ongoing trials were identified.

Specialist commentator comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

One out of 3 specialist commentators was familiar with this technology.

Level of innovation

The specialist commentators all agreed that Hemosep is a variation on existing cell salvage technology; 1 felt that this was a minor variation and another thought that it was somewhat novel.

Potential patient impact

One commentator felt that by reducing the need for allogenic blood transfusions, Hemosep could reduce risks such as potential blood mismatch and transmission of viral infections. They suggested that Hemosep could be useful for patients who are expected to lose over 20% of their blood volume, such as those having cardiac surgery, or after major trauma or major obstetric haemorrhage. However, another commentator stated there could be problems when using Hemosep for high blood loss surgery or uncontrolled haemorrhage because of the possibility of reinfusing activated white blood cells and platelets. They suggested that more research is needed in this area. The same commentator felt that Hemosep could be particularly useful in low to moderate blood loss surgeries such as routine open heart surgery, hip replacements and elective aortic surgery.

Potential system impact

All commentators agreed that Hemosep might reduce the need for allogenic blood transfusions, which could lead to shorter hospital stays and reduce the need for donor blood. Implementing Hemosep would need few infrastructural changes but all commentators felt that it could result in savings to the NHS. Two of the commentators felt that it may be difficult to encourage use of Hemosep because it is competing with bagging of the pump blood, which is very cheap and effective, and with cell salvage devices that are already used in most centres. One commentator noted that NICE's estimate of the costs of cell salvage was inflated and may not have taken into account high-use centres.

All commentators agreed that minimal training would be needed. One stated that the availability of staff trained in cell salvage can sometimes be a problem, so having a device like Hemosep that is easy to use and does not need any specialist training would be beneficial.

General comments

One commentator felt that there was a need for additional research using this device in high blood loss surgery, uncontrolled haemorrhage or in patients in intensive care. This research should focus on inflammatory markers after reinfusion of the concentrated blood to look at frequency of complications. Studies should investigate the possible risk of reinfusing activated white blood cells and platelets into these groups, which can lead to pulmonary dysfunction and disseminated intravascular coagulopathy.

One commentator stated that there could be time constraints associated with Hemosep. The manufacturer recommends allowing 40 minutes to ultrafilter the blood, but this could cause problems if the patient needs blood volume very quickly, which happens often. The commentator noted that volume can be achieved very quickly through bagging of the pump blood or using a cell saver, which they felt made Hemosep a less attractive option in this scenario.

Specialist commentators

The following clinicians contributed to this briefing:

- Charles McCollum, professor of surgery and head of department of surgery, University of Manchester. Has shareholdings in and acts as a medical advisor to Independent Vascular Services, Rinicare, Advanced Therapeutic Materials and Piur Imaging. None of these businesses develops medical products that compete against or are involved in the same field of medicine as Hemosep.
- Ajit Walunj, consultant anaesthetist, Good Hope Hospital, Sutton Coldfield. No conflicts of interest declared.
- Tony Meakin, chief clinical perfusion scientist, Morriston Hospital, Swansea. No conflicts of interest declared.

Development of this briefing

This briefing was developed for NICE by Cedar. The [interim process and methods statement](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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