Intraoperative cell salvaged blood as part of a blood conservation strategy in Caesarean section: is fetal red cell contamination important?†

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Editor’s key points

- Intraoperative cell salvage (IOCS) is increasingly used as part of a blood conservation strategy.
- Its widespread use in obstetrics has been hindered by concerns over amniotic fluid embolism and fetal red cell contamination.
- In this series of 70 patients, the incidence of red cell contamination resulting in antibody formation was very low.
- IOCS reduced the requirements for allogeneic blood.

Background. Cell salvage is used in obstetric surgery as part of a blood conservation strategy in our Trust. This carries a theoretical risk of amniotic fluid embolism and also a risk of fetal red cells being present in the re-infusion, resulting in alloimmunization. In this study, we attempted to quantify the risk of antibody formation from re-infusion of autologous blood after Caesarean section.

Methods. Women presenting for elective Caesarean section were routinely requested to consent for collection of blood by cell salvage, using one suction device. If an adequate volume of blood was collected, it was processed and, if clinically appropriate, re-infused via a leucodepletion filter. Women who received a re-infusion were followed up to test for antibody formation.

Results. Seventy women consented for re-infusion and follow-up. The median volume re-infused was 324 ml (range 118–1690 ml). The median fetal red cell contamination was 0.8 ml (range 0.2–12.9 ml). All re-infusions were given without adverse clinical signs. No antibodies were detected in 48 follow-up samples. One positive anti-S antibody was detected.

Conclusions. The implementation of a blood conservation strategy which includes the use of intraoperative cell salvage appears safe and can contribute to a reduction in the number of blood transfusions to the obstetric population. We remain uncertain of the significance of fetal red cell contamination.

Keywords: amniotic fluid embolism; blood transfusion; blood transfusion, autologous; Caesarean section

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Allogeneic blood transfusion carries potentially catastrophic risks of infection and incompatibility reactions. To conserve allogeneic blood, we revised our local transfusion guidelines, introduced i.v. iron therapy where indicated, and established intraoperative cell salvage (IOCS) into routine practice in our obstetric operating theatre.

Despite the benefits of transfusing autologous blood, there remains a perceived risk of contamination with amniotic fluid, a risk of alloimunization of the mother by fetal red blood cells (RBCs), and a belief that the introduction of IOCS will require additional resources.

We concluded from earlier work that there was little possibility for amniotic fluid contamination to enter the re-infusion system when used with a leucodepletion filter and that cell salvaged blood was safe.1 However, we were unable to quantify the significance of fetal red cell contamination or red cell antigen incompatibilities between the mother and fetus.

The aim of this study was to quantify the fetal red cell contamination of maternal salvaged blood and assess the risk of this contamination. The secondary aim was to add to the growing evidence that supports the safe use of IOCS in obstetrics.

Methods

All women undergoing elective Caesarean section at the Royal Cornwall Hospital Trust were asked to participate in the study. They were informed at the Pre Assessment Clinic of the benefits and risks of cell salvage and received a patient information sheet, and surgical consent was obtained for the use of cell salvage. Women having Category

†Presented in part at the Obstetric Anaesthetists’ Association meeting, Jersey, 2009.
2 or 3 Caesarean sections, who were able to read the patient information sheet before the re-infusion of autologous blood, were also asked to participate in the study. Category 1 emergency sections were excluded as were all women who received cell salvaged blood without a chance to read the patient information leaflet. Ethical committee approval was gained from Cornwall and Plymouth Research Ethics Committee to study the contamination of Salvaged Maternal Blood by Fetal red Cells during Caesarean section (ref: 07/H0203/257).  

During surgery, any blood lost (blood with amniotic fluid) was collected with a specific wide-bore sucker into a reservoir in a Haemonetics Cell Saver® 5 system (Haemonetics Corp., Braintree, MA, USA). The suction line was anticoagulated (30 000 IU heparin per litre of saline), pre-prepared, and attached to power of 150 mm Hg. Suction pressure was increased to a maximum of 300 mm Hg in the presence of heavy bleeding, although higher settings were avoided if possible as these can damage red cell structure. Although a Yankauer tip can be attached, it was not used routinely because it can theoretically compromise red cell integrity.  

The surgeon and assistant aimed to maximize blood collection via the wide-bore sucker as red cell retrieval was more effective from aspirated blood than blood extracted from washed swabs. However, when the swabs were heavily soiled with blood, they were washed and blood collected from the wash. Fetal blood spillage was kept to a minimum whenever possible, with the surgeons cutting the umbilical cord close to the clamp.

If the surgeon or anaesthetist judged the blood loss to potentially require replacement and there was sufficient blood aspirated into the reservoir, then the collection was processed. The final decision to re-infuse was made jointly by the obstetrician and anaesthetist in discussion with the woman whenever possible, and this discussion was documented. The salvaged blood bag was labelled with a Patient Identification Label which corresponded to the patient’s wristband and was prescribed in the usual way on the i.v. fluids prescription chart. Before a decision to use the blood, the bag remained at the patient’s bedside and was not stored in a fridge. If the blood was to be re-infused, a patient blood sample was obtained for test of fetal red cell contamination, before re-infusion.

Re-infusion of the salvaged blood usually took place within 2 h of collection but had to occur within 6 h of the start of the collection. Written informed consent was obtained from all women who received a re-infusion. This consent was usually obtained after delivery, but when significant blood loss was predicted, the consent was taken before surgery. All women received the processed washed blood through a leucodepletion filter (Pall LeukoGuard® RS Filter, Pall Europe, Europa House, Portsmouth, UK). Blood warmers and pressurized bags were not used. Routine observations were continued throughout the re-infusion.

A monitoring sheet was completed for all cases, even if collection only (no processing or re-infusion) occurred (see Supplementary Appendix 1).

A blood sample was obtained from the post-filtration re-infusion bag. Initially, the protocol required no further sampling direct from the patient; however, an amendment to the original protocol (January 2010) included a patient sample to be obtained before re-infusion. Samples were sent directly for processing to test for full blood count and using the Kleihauer–Betke technique to detect fetal red cells.

Consenting patients agreed to return for a follow-up appointment 3–6 months after surgery, at which time, a sample of venous blood was obtained to screen for any maternal antibodies. Any positive antibody screens were investigated further, discussed with the Consultant Haematologist and Consultant Obstetrician, the significance assessed, and, where appropriate, communication with the patient was undertaken by a consultant and the Ethics Committee informed.

**Results**

Seventy women were enrolled to the study, with mean age 33 yr (range 22–43 yr). All were ASA class I or II. Forty-eight of the 70 women recruited were undergoing elective surgery (Category 4 Caesarean section). Nineteen were having Category 3 or 2 sections, eight of whom had some bleeding before operation. The remaining three cases were women who were taken to the operating theatre because of bleeding.

The mean preoperative haemoglobin (Hb) concentration was 11.3 g dl⁻¹ [SD 1.0 (range 8.7–13.3 g dl⁻¹)]. These higher concentrations reflect that the majority of cases were undergoing elective operations and not bleeding before surgery. The median estimated blood loss during the procedure was 900 ml (range 400–7000 ml). Collected blood was only processed if there was an estimated blood loss of more than 1 litre and only re-infused if a full bowl was processed.

When possible, before re-infusion, postoperative Hb concentrations were measured either with a HemoCue (HemoCue AB, Angelholm, Sweden) device at the bedside or a formal laboratory sample. The mean Hb concentration after operation was 9.0 g dl⁻¹ [SD 1.3 (range 6.6–11.5 g dl⁻¹)].

Re-infusions were offered to all women, regardless of the postoperative Hb concentration. With informed consent, some women chose to have the re-infusion of autologous blood, despite normal Hb concentrations.

The median total collected and processed volume was 2339 ml (range 1458–6723 ml). This resulted in a median RBC re-infusion volume of 324 ml (range 118–1690 ml).

Thirteen of the 70 women who received autologous blood also had alloimmune blood ordered and issued, and went on to receive one or more units of blood in addition to the re-infusion, ranging from one to 16 units. Four women received other blood products (fresh frozen plasma, cryoprecipitate, and platelets) in addition. Two of the four women who received additional blood products were bleeding before operation and had a ruptured uterus. The other two women were not bleeding before operation; one had an elective section for a fibroid and the other a Category 3 section for placenta praevia/accreta.
Twelve of the 13 women received their allogeneic blood transfusion in the delivery suite and one in the post-natal ward.

Samples obtained from the processed re-infusion packs were collected into EDTA and processed on a Bayer Advia 120 Full Blood Count analyser (Bayer, Newbury, UK), providing Hb and haematocrit (Hct). Samples were also tested to quantify any fetal RBCs present, using the Kleihauer–Betke technique.

The mean Hb concentration of the processed blood was 14.2 g dl$^{-1}$ [so 2.0 (range 10.8–18.9 g dl$^{-1}$)] with a mean Hct of 0.418 [0.06 (range 0.322–0.541)].

In all samples obtained from the processed re-infusion packs, fetal RBCs were detected, with a median contamination volume of 0.8 ml (range 0.2–12.9 ml). Two cases were excluded from calculations due to being significant outliers with contamination of more than 25 ml. There were potentially user errors in the sampling method, resulting in poor quality of the Kleihauer–Betke slides.

All women consented for re-infusion consented for follow-up and were contacted between 3 and 6 months for a follow-up appointment. Eighteen women were uncontactable. Forty-eight women attended follow-up and had samples tested for antibody formation. One positive antibody was detected. Investigations confirmed this as anti-S. The clinical significance of this antibody in obstetrics is unknown. The remaining four cases are due for a follow-up appointment in the next few months.

As part of the blood conservation programme, figures for the consumption of blood throughout the Trust were also compared with those used in obstetrics. Data from the previous 3 yr demonstrated a reduction in blood transfusion in the obstetric population.

Fifty-eight patients (in 2007/08) needed an allogeneic blood transfusion during or immediately after delivery. Sixty-two were transfused in 2008/09 and 40 in 2009/10. The total number of units transfused decreased from 244 (2007/08) to 241 (2008/09) to 197 (2009/10), with the percentage of overall transfusions used in obstetric practice decreasing from 2.3% to 1.7%. The birth rates in each year were similar. The use of IOCS increased during the study period and was greatest during 2009/10, which may in part account for the greater reduction in the figures for this period.

Discussion

Cell salvage and autologous blood transfusion is an established method of blood conservation for surgical procedures that are anticipated to involve significant blood loss. However, despite the endorsement of the AAGBI, OAA, and NICE, its use is not established in obstetric practice.\textsuperscript{3, 4} We found that the introduction of IOCS has been associated with a reduction in allogeneic blood transfusion in obstetric practice over the past 3 yr. This has been demonstrated in other units and specialty areas, and we were keen to establish cell salvage as part of our blood conservation strategy in obstetrics, where surgical cases can cause unpredictable and significant blood loss.\textsuperscript{5, 6} The risks of allogeneic blood are significant, leading to a review of the triggers for transfusion and implementation of other strategies to conserve blood.\textsuperscript{7, 8} For the 70 women having IOCS in this study, the availability of autologous blood resulted in an over-estimation of the need for allogeneic blood, with blood ordered being either all or partly returned unused (14 and 13 women, respectively).

One reason for the slow adoption of IOCS in obstetrics has been the perceived risk of amniotic fluid embolism. In earlier work, we demonstrated $\alpha$-fetoprotein is significantly reduced post-wash after cell-salvage, to concentrations well within the normal range for the general population, before passing through the filter. Heparin is also eliminated, and while the washing process does not eliminate the presence of squame cells, their significance in the circulation remains unknown.\textsuperscript{1} Squame cells present post-wash are significantly reduced post-filtration. It is therefore recommended to re-infuse through a leucodepletion filter which removes any remaining fetal contaminant. As there is little or no possibility of amniotic fluid contamination re-entering the re-infusion system and, of the 1.1% of reports to SHOT associated with autologous transfusion reactions, there have been no reports of death or major morbidity indicative of a sudden obstetric collapse, this risk remains entirely theoretical.\textsuperscript{7}

Other perceived barriers to implementing IOCS are costs, manpower planning, and training. We have overcome these issues by establishing the cell saver into routine practice. In our unit, the set-up and use of IOCS is included into the routine preparation of the obstetric operating theatre and is entirely run by the normal quota of obstetric theatre staff. This has been aided by the introduction of a competency training programme for operating department practitioners (ODP) and we use one ODP to both assist the anaesthetist and operate the cell saver machine. No additional manpower has been required to facilitate the use of cell salvage and it is currently used for more than 40% of all our Caesarean sections. We only use one suction device, as the washing process is effective in removing $\alpha$-fetoprotein, and contamination is similar using one or two suction devices; using one suction device reduces waste and improves blood collection volumes.\textsuperscript{1} The suction line is pre-prepared, enabling theatre personnel to commence IOCS, even in urgent or emergency cases. Over the last 2 yr, blood has been collected but not processed in 450 patients. Thus, costs have been minimized by processing only those collections where significant blood loss occurs and allogeneic transfusion is likely. All re-infusions have been administered through a leucodepletion filter by gravity alone. No haemodynamic changes were observed during the re-infusions, although recent case reports have reported hypotension after rapid re-infusions through a leucodepletion filter.\textsuperscript{9} Transfusion-induced hypotension is a recognized phenomenon and has been reported both with and without the use of bedside leucocyte removal.
In cases requiring rapid resuscitation, we use volume resuscitation with little or no perioperative transfusion of allogeneic blood, allowing the subsequent administration of the slower re-infusion of cell salvaged blood. In patients who decline allogeneic blood, such as Jehovah’s Witnesses, we would consider removing the filter from the re-infusion.\(^1^0\)\(^1^1\)

There remains a risk of alloimmunization of the mother by re-infusion of fetal RBCs in the final washed product. These may be significant in cases of red cell antigen incompatibility between the mother and fetus. However, the potential for sensitization can occur throughout pregnancy and at delivery, as concentrations of fetal RBCs in the maternal circulation increase during pregnancy. Peak transplacental haemorrhage (TPH) occurs at delivery, with nearly 1% of women in the third trimester having TPHs of \(>2.5\) ml and 0.3% having \(>15\) ml.\(^1^4\) We previously reported similar amounts of contamination in parturients with a median fetal RBC volume of 0.48 ml (range 0–4.6 ml) before delivery and a maximum of 9 ml after delivery, although many of these women had an obvious TPH during delivery.\(^1^5\) Therefore, re-infusing a median fetal red cell volume of 0.8 ml (range 0.2–12.9 ml) in cell salvaged blood is comparable with that found normally in the maternal circulation after delivery. The maximum we have re-infused has been 12.9 ml, and in two cases (excluded from the analysis), contamination volumes were \(>25\) ml. Both these re-infusions (320 and 280 ml) were to women who delivered twins. Other reported volumes of fetal RBCs collected by cell salvage range from 0.2 to 19 ml.\(^1^6\)\(^1^8\) The critical volume of contamination required to provoke an antibody response or an immune response to red cell antigens (Kell, Duffy, and Rh, for example) is unknown.

Data from a 3 yr period show that 0.4% of obstetric patients at our Trust have a clinically significant antibody. Some of these antibodies resulted from pregnancy or, fewer, after an allogeneic blood transfusion (Table 1). The formation of anti-D in mothers of an Rh(D)-positive fetus, although clinically significant, has been reduced by the use of routine prophylactic anti-D treatment throughout the pregnancy. Less commonly, other clinically significant antibodies, such as anti-K, anti-c, anti-Fy(a), and anti-Jk(a), have been implicated in haemolytic disease of the newborn.\(^1^9\)

Follow-up of 48 cases has detected one case of anti-S antibodies. This was not detected antenatally and the clinical significance of this is unknown. We were unable to establish whether the anti-S was produced due to the cell salvage re-infusion or due to contamination from multiple antenatal bleeds suffered by this patient from 33 weeks gestation or from the significant placental abruption requiring delivery by Caesarean section. Estimated blood loss at the time of operation was 2.5 litre; 400 ml autologous blood was re-infused. We feel it was more likely that the antibody anti-S was produced due to the multiple TPH during pregnancy and delivery, although we cannot exclude cell salvage with certainty.

Table 1 Origin of antibodies detected

<table>
<thead>
<tr>
<th>Formation of antibody (%)</th>
<th>Unknown cause</th>
<th>Due to pregnancy</th>
<th>Due to allogeneic blood transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007/08 (n=26)</td>
<td>65</td>
<td>31</td>
<td>4</td>
</tr>
<tr>
<td>2008/09 (n=25)</td>
<td>40</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>2009/10 (n=23)</td>
<td>43</td>
<td>48</td>
<td>9</td>
</tr>
</tbody>
</table>

Owing to the low incidence of antibody formation and relatively small numbers of patients followed up, it is impossible to speculate if the incidence of antibody formation or alloimmunization after autologous blood transfusion is greater, less, or the same as that which occurs in pregnancy. Despite this, there already has been a suggestion that the risk of alloimmunization is unlikely to be greater than that incurred in a normal vaginal delivery.\(^2^0\)

Large numbers of women need to be followed up to assess the incidence of antibody formation and also to evaluate the introduction of cell salvage into routine practice.\(^2^1\) We suggest that a central database is formed to collate this information and assess the risk of alloimmunization.

In conclusion, the introduction of cell salvage in obstetric surgery can reduce allogeneic blood transfusions. The procedure is efficient, and IOCS has been introduced with minimal manpower or resource implications. The significance of the risk of alloimmunization by fetal RBCs is uncertain after a re-infusion of cell salvaged blood. Further work and collaboration is required to assess this risk and we recommend that all women are followed up to test for antibody formation 3–6 months after re-infusion.

**Supplementary material**

Supplementary material is available at *British Journal of Anaesthesia* online.

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**Conflict of interest**

None declared.

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