Intraoperative Autologous Transfusion of Hemolyzed Blood

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During two cases of lumbar spine surgery with instrumentation, we used intraoperative autologous transfusion (IAT), resulting in hemolysis during collection and hemoglobinuria and coagulation abnormalities after transfusion. Hemolysis during IAT collection can lead to hemoglobinuria and binding of nitric oxide, leading to vasoconstriction. The literature suggests that stroma from damaged cells and contact of the blood with the IAT device can lead to coagulation abnormalities and other morbidities, including adult respiratory distress syndrome.
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Intraoperative autologous transfusion (IAT) of washed blood collected from the operative field has been applied in several types of surgery, including major spine procedures. The major advantages of IAT when compared with allogeneic blood include rapid availability, reduction of exposure to infectious agents transmitted by homologous blood transfusion, and a decrease in immune modulation. Furthermore, IAT has been shown to be less costly than allogeneic transfusion in surgeries in which the blood loss exceeds 1000 mL or the infused IAT blood exceeds 750 mL.[1,2]

Although a large number of studies demonstrate the value of this technique in cardiac and vascular surgery, the process is not without risk and may not be advantageous for all orthopedic procedures. We recently had two cases that highlight the potential complications of infusing IAT blood when hemolysis has occurred during IAT collection. Despite a properly functioning IAT device and experienced machine operator, IAT led to hemoglobinuria and coagulopathy with the associated medical complications which raise questions about the overall value of IAT in these spine procedures.

CASE DESCRIPTIONS

Case 1

The IRB determined permission is not required for this report. Permission to present cases was obtained from both patients. A 55-yr-old woman with a history of scoliosis and hardware placement from T_1 to S_1 presented for L4–5 hardware removal and reinstrumentation. She had no co-existing medical problems, was not taking any prescription or herbal medications known to interact with transfused products or hemostasis. General anesthesia with intraoperative neuromonitoring was conducted. After midazolam sedation, anesthesia and intubation of the trachea was accomplished with propofol, sufentanil, and vecuronium. Anesthesia was maintained with small-dose desflurane and infusions of dexmeditomidine and propofol to provide stable neuromonitoring responses. Approximately 3.5 h after induction the first IAT unit (200 mL) was transfused. Within 5–10 min, the patient had a brief episode of hypertension (systolic blood pressure exceeding 200 and diastolic blood pressure exceeding 120 mm Hg) with bradycardia, which recurred in 10–15 min. Thirty-four minutes after the IAT transfusion, hemoglobinuria was noticed and free hemoglobin (Hb) was measured in the plasma at 96 mg/dL (normal <5 mg/dL). The patient was treated with sodium bicarbonate, furosemide, and fluids to induce a diuresis. Blood drawn during the hypertension failed to form a hard clot after 1 h. A thromboelastogram (TEG®) done at that time was abnormal (α angle = 72.4 [normal 53–67], coagulation index −3.9 [normal −3 to 3], coagulation time 6.7 [normal 3–6], maximum amplitude 36.3 [normal 59–68], reaction time 14.8 [normal 10–14]) and bleeding was noted from previously hemostatic wound edges and needle puncture sites. The platelet count was recorded at 135,000/μL [normal 150,000–400,000] and serum calcium was 9.2 mg/dL [normal 8.5–10.3]. Visual inspection of a second IAT unit and residual from the first unit revealed gross hemolysis, indicating that hemolysis had occurred during the IAT process. The second IAT unit was not administered and the patient subsequently received 200 mg of calcium chloride, 2 U of packed red blood cells (PRBC), and 2 U of fresh frozen plasma (FFP) to treat coagulopathy and 1500 mL blood loss. The patient made an uneventful recovery. The cell saver device (Brat II, Cobe Cardiovascular, Quedgeley, UK) was inspected and found to be within company-specified quality assurance limits (same for Case 2).

Case 2

A 46-yr-old man had posterior T_{10} to S_1 spinal osteotomy with instrumentation and fusion after removal of old hardware from T_8 to S_1. He had no co-existing medical problems,

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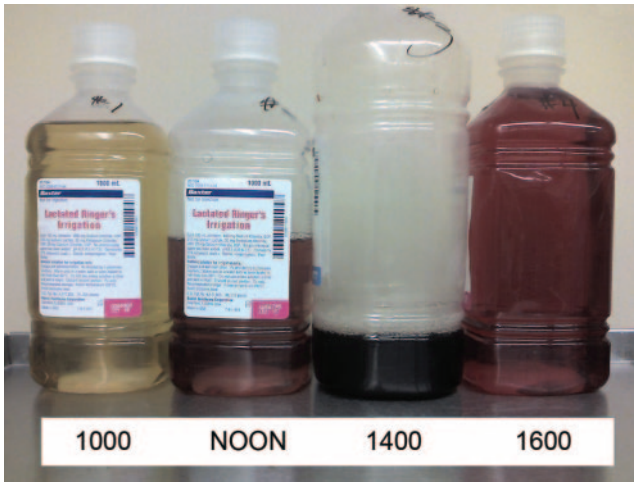

Figure 1. Urine collected during Case 2. Shown is the urine collected from the start of the case (7:30) until 10:00 (left), the urine collected between 10:00 and noon, the urine collected between noon and 14:00, and the urine collected between 14:00 and 16:00. Shown is the progressive darkening of the urine associated with hemoglobinuria and the initial resolution after 14:00 with diuresis.

was not taking any prescription or herbal medications known to interact with transfused products or the coagulation system or known to cause discoloration of the urine. General anesthesia with intraoperative neuromonitoring was conducted. After midazolam sedation, induction and intubation of the trachea were performed at 0730 using propofol, fentanyl, and vecuronium. Anesthesia was maintained with infusions of propofol, ketamine, and sufentanil to provide stable neuromonitoring responses. The initial TEG® obtained before IAT was normal (α angle = 53.1, coagulation index −4, coagulation time 5.3, maximum amplitude 55.7, reaction time 18.3). During the first 2.5 h, his urine output was clear (Fig. 1, 10:00), serum calcium was 8.6 mg/dL and platelet count of 139,000/μL. The blood loss was approximately 400 mL/h; however, after the transfusion of a 300 mL IAT blood, there was a marked increase in the blood loss to approximately 600 mL/h reaching a maximum of 1600 mL/h at the end of the procedure. IAT blood continued to be transfused during surgery. By 4.5 h hemaglobinuria was documented and apparent on visual inspection (Fig. 1, noon). There was a progressive darkening of the urine (Fig. 1, 1400) and increasing coagulopathy. A TEG® done at 1335 was abnormal (α angle = 38.5, coagulation index −4.7, coagulation time 9.7, maximum amplitude 48.6, reaction time 12.2) and a coagulation profile shortly, thereafter, was also abnormal (prothrombin time (PT) = 16.9 s [normal = 12–14.6], partial thromboplastin time (PTT) = 33.7 s [normal = 23.8–33.5], international normalized ratio (INR) = 1.4 [normal = 0.9–1.1]). One gram of calcium chloride in divided doses, crystalloids, furosemide, mannitol, and additional blood products were administered. At the conclusion of surgery the coagulation profile demonstrated a severe coagulopathy (TEG®-α angle = 43.2, coagulation time = 9.3, maximum amplitude = 40.7, reaction time = 80; PT = 20 s, PTT = 48.8 s; INR of 1.2; fibrinogen = 37 mg/dL [normal 150–400]). He received 4500 mL IAT blood, 683 mL FFP, 2 U of PRBC, 251 mL platelets (8 U) for an estimated 6900 mL blood loss. His Hb ended at 10.1 gm/dL from an initial 15.2. Postoperatively in the intensive care unit, his laboratory values were consistent with disseminated intravascular coagulation (DIC) (PT = 27.3, PTT = 56.4, INR = 2.3, fibrinogen = 57 and DDimer = 9640 mg/dL [normal <500]). He made a full recovery.

DISCUSSION

Both of these patients developed hemoglobinuria and abnormal clotting shortly after the first unit of IAT blood. Evaluation of the IAT processed blood revealed gross hemolysis before transfusion. Both patients had unanticipated intensive care unit stays. In Case 1, coagulation abnormalities and hemoglobinuria were noted after the first 200 mL of IAT blood, suggesting the hemolyzed blood contributed to both of these problems. In Case 2, the patient developed hemoglobinuria and DIC after transfusion of IAT blood. In this case the hemolyzed blood likely contributed to the early onset of hemoglobinuria, but due to marked blood loss it is unclear to what extent the transfusion of the hemolyzed blood contributed to the ultimate development of DIC.

Unfavorable effects of IAT have been reported.[3–5] In one study of 56 patients, the use of IAT was associated with a higher incidence of respiratory complications (40% vs 12.5%), greater transfusion of blood (5.8 vs 3.6 U) and FFP (4.4 vs 1.5 U), and a longer hospital stay (9.3 vs 5.6 days) than in patients who did not receive IAT.[4] Of note, the amount of banked blood transfused was disproportionately increased in patients receiving more than 3000 mL of IAT. The authors recommended limiting IAT transfusions to 3000 mL. In another study of IAT in lumbar spine fusion surgery, the number of postoperative transfusions was not reduced such that the authors concluded IAT was neither necessary nor cost-effective.[5] However, it is worthy to note that larger volumes of infused blood may also be associated with other factors leading to increased postoperative morbidity (e.g., longer surgery, more complex operations, more comorbidities).

The IAT process may lead to these complications. Shed blood is suctioned from the operative field into heparinized or citrated isotonic crystalloid where cell trauma can occur. After filtration to remove large debris, including aggregates of white blood cells, platelets, and tissue fragments, the solution undergoes a centrifugal washing which causes red blood cells (RBCs) and materials of similar density to collect on the outer wall of the bowl, whereas less dense materials are washed away by a saline solution. Therefore, the blood may receive trauma during collection, is exposed to plastic surfaces, and unwanted products may be inadequately washed in the centrifugal washing device.

Cell trauma and hemolysis are inevitable with collection. In a study of five IAT devices when used in cardiac surgery, free Hb in the collection reservoir ranged between 49.9 and 4689.9 mg/L (mean of 651 mg/L), demonstrating hemolysis with the collection process.[6] The free Hb in the washed processed cells was between198.2 and 2645 mg/L (mean of 705 mg/L), demonstrating that the centrifugal processing and washing does not remove all stroma-free hemoglobin.

Hemolysis during collection may be caused by several mechanisms, and these may be more of a problem during spine surgery accounting for a difference in outcome between these applications. Since larger diameter suction devices and suctioning of large pools of blood are used in cardiac surgery and major joint replacement surgery, the effects of collection may be less traumatic on the cellular components than with spine surgery in which a smaller diameter device is used to "skim" blood from a large surface in the operative field in spine surgery. This technique causes more mechanical trauma and aspirates air, increasing the amount of blood-air interface which promotes cell rupture.[7] Some studies have shown that dilution of the blood before suctioning results in less cell damage; however, the advantages of this technique have not been fully explored.[7] Hemolysis can also occur secondary to the use of hypotonic irrigation fluids, excessive suction pressure (>100 mm Hg), and aspiration of clotted blood. Cell rupture can also be caused by the collection of the blood with povidine-iodine, hydrogen peroxide, alcohol or bone cement.[8] None of these factors was present in these two cases.

The levels of free Hb in IAT may exceed 2000 mg/L, which are higher than in allogeneic PRBC (typically 2–20 mg/L).[9] In addition, there are many more non-cellular components in IAT than PRBC, making the total dose of free Hb and RBC stroma higher. Unlike potassium, the density of free Hb and ruptured RBC stroma causes some of these materials to be retained in the centrifugal washing device with the RBCs and included in the product to be transfused.[9] The observation of gross hemolysis in the IAT units of Case 1 and the elevated serum-free Hb confirmed that hemolysis occurred.

When infused, free Hb is rapidly bound to haptoglobin forming a complex which is removed by monocytes and macrophages.[10] However, larger doses exhaust the haptoglobin levels in patients and free Hb rapidly increases in the plasma and then in the urine.[11] The circulating free Hb binds nitric oxide (NO) producing nitrate and methemoglobin. The Hb-NO complex is thought to be the most important pathway for eliminating NO bioactivity.[10,12] Since NO regulates vascular tone, smooth muscle tone and platelet activation, the reduction in NO can lead to hypertension, smooth muscle dystonias, gastrointestinal contractions, erectile dysfunction, and increased clot formation.[10,12] The binding of NO by free Hb is 600–1000 fold more than Hb confined within RBCs, and free Hb can diffuse into the subendothelial space, placing it closer to the source of NO thereby having a more profound effect on NO-dependent functions.[10,13,14]

The loss of NO results in vasoconstriction and a dose-dependent increase in systolic and diastolic blood pressure in the systemic and pulmonary circulation.[10] These hypertensive effects (such as those seen in Case 1) have been described as the primary cause of morbidity and mortality with stroma-free Hb as a blood substitute such that the newest generation of Hb substitutes contain mutations designed to minimize the interaction with NO.[12] These effects are also thought to play a role in the clinical problems and organ dysfunction seen in patients with paroxysmal nocturnal hemoglobinuria, sickle cell disease, thalassemias, malaria, and cardiopulmonary bypass.[10,12–14]

The reduction of NO increases the potential for thrombus formation.[10] In addition, free Hb and its breakdown product (heme) promote procoagulant effects, including platelet activation and release of inflammatory substances, that can contribute to vascular obstruction.[10]

Intravascular hemolysis also occurs after transfusion of blood. This is most frequently due to attack by antibodies and complement from transfusion of ABO-incompatible blood, although antibody-mediated destruction can occur extravascularly in the reticuloendothelial system. Similar to transfusion of already hemolyzed blood, renal injury and coagulation abnormalities are the major consequences. The activation of the intrinsic clotting system is thought to occur through erythrosin released with RBC stroma.[15] Hypotension is common and thought to be due to the vasodilatation effect of bradykinin produced by activation of the kallikrein system.[15] Because hemoglobinuria occurred in our patients before transfusion of non-IAT blood, the initial hemoglobinuria is consistent with the hemolysis seen in the IAT blood prepared for transfusion. However, since our patients had received transfusions in a prior surgery, it is possible that intravascular hemolysis from this effect might have played a role during the transfusion of banked blood in the later portions of these cases, especially Case 2.

Of greater concern in these two cases was the development of a coagulopathy when no other cause was apparent. No preexisting bleeding tendency was known to be present and the degree of bony trauma was thought to be insufficient to release tissue plasminogen activator or urokinase, which activate the fibrinolytic system.[16] Since the IAT devices were working properly, heparin would normally be adequately washed and unlikely a cause of coagulopathy.[6] Reinfusion of substantial IAT volume (>3.5 L of IAT blood[6] or where the transfused IAT blood exceeded 70 mL/kg[17]) produces a dilutional coagulopathy due to the removal of platelets and coagulation factors. This is unlikely in these patients because the onset of coagulopathy occurred well below these volumes.

Coagulopathy and DIC have been documented with IAT. For example, since IAT blood is deficient in coagulation factors and platelets, a coagulopathy may develop if these other components are not transfused.[18] One study in vascular and trauma cases noted this effect with large volumes of IAT.[19] Specific coagulopathy attributed to IAT blood has been observed when combined with aprotinin in abdominal aortic

aneurysm surgery[20] and in patients receiving transfusions of postoperative drainage blood or unwashed mediastinal blood collected after cardiopulmonary bypass surgery.[21–24] Contaminated IAT blood has also been associated with coagulation abnormalities as seen in trauma patients receiving more than 15 U of IAT[25] and in neuromuscular scoliosis patients in whom it was thought that osteopenic bone fragments were suctioned with the shed blood.[17] Two of these reports noted hemoglobinuria, but the coagulation abnormalities were not attributed to transfusion of hemolyzed IAT blood.[17,20] In addition, if chelating agents (e.g., EDTA) are used in the collection process or in transfused banked blood, a coagulopathy may develop due to deficient calcium levels. In our two cases, these factors do not seem to have been a factor in the early stages of the cases but may have played a role in the later aspects of the cases, particularly the second case. There, large volumes of IAT blood were used and the correction of hypocalcemia and the amounts of FFP and platelets would be important in correcting the contribution to the coagulopathy resulting from transfusing only RBCs (regardless of whether these were from IAT or banked blood).

The clotting system can be activated in IAT by several means. Leukocytes and platelets damaged during collection or activated when they come in contact with the plastic IAT centrifuge bowl surface can release clotting activators.[26–29] This contact is postulated to increase when the surface of the bowl is not sufficiently covered by RBCs due to dilute collection fluid.[26–30] The released procoagulant, leukotactic, and inflammatory mediators are thought to contribute to the development of DIC and acute respiratory distress syndrome. Fortunately, activated polymorphonuclear leukocytes seem to be washed from the blood before transfusion.[6,26,31,32]

The coagulation process can also be initiated by cytokine and complement released from damaged RBCs and leukocytes.[9,33,34] Consistent with this, complement, lipid mediators, pro and antiinflammatory cytokines, and leukocyte adhesion molecules have been detected in IAT blood.[35] DIC can also be induced by the reinfusion of thrombin or Gelfoam collected from the wound by IAT.[8,36]

Coagulopathy with IAT blood in spine cases has been observed by Bull and Bull[27] who coined the term "salvaged blood syndrome." McKie and Herzenberg[8] reported a coagulopathy which developed in a patient having scoliosis correction with IAT. DIC had its onset 30 min after infusion of the first IAT unit similar to our cases. This patient also developed cardiovascular collapse and respiratory distress syndrome similar to transfusion-related acute lung injury. Similarly, Gause et al.[37] observed a significant increase in blood loss and the number of blood transfusions after IAT use. In our cases, the coagulopathy was noted by changes in TEG®, PT, PTT, INR and clinical observation; however, in our second case, DIC may have also developed secondary to bony trauma or as a result of the multiple transfusions of IAT or banked blood products. Studies by Horlocker et al.[38] suggest that the PT, PTT and INR are the best tests to detect a developing coagulopathy in instrumented spinal fusion.

The substantial amount of free Hb in our cases is illustrated by the appearance of Hb in the urine of both patients who had no other cause of hemolysis when it started and hemolysis observed in the IAT blood (Fig. 1). There is a correlation between the total free Hb load and the subsequent renal dysfunction due to the precipitation of free Hb in the renal tubules.[39] One prospective study in thoracic-aorta surgery concluded that more than 5 U of IAT blood contributed to renal failure.[40] This hemoglobinuria suggests RBC damage with release of Hb and cell stroma into the IAT system.

Cell damage during the initial collection and release of substances seemed to promote coagulopathy in our patients. The large volume of IAT transfused in Case 2 suggests an ongoing process that may explain the disproportionate morbidity seen in patients receiving large IAT volumes.[4] Hemolysis potentially serves as a marker for the cellular trauma and release of RBC and leukocyte cell stroma that contributed to the coagulopathy. The American Association of Blood Banks has indicated that assessing the quality of IAT blood for residual albumin, free Hb, leukocytes, bacteria, and complement fractions may be of value; however, the time and resources involved in this would reduce the readily availability of IAT during surgery when active bleeding is occurring.[41] Potassium could be used as a marker of hemolysis in the collection fluid, but not in the final product as it is effectively removed during IAT washing.[9]

These cases suggest IAT should be evaluated for its risk-benefit in individual cases. Concern should be raised if hemolysis is noted in the IAT blood before transfusion. Studies are necessary to determine ways to reduce hemolysis and cellular damage during the collection process or IAT processing to reduce these potential complications in instrumented spine surgery.

REFERENCES

1. Kelley-Patteson C, Ammar AD, Kelley H. Should the Cell Saver Autotransfusion Device be used routinely in all infrarenal abdominal aortic bypass operations? J Vasc Surg 1993;18:261–5
2. Tawes RL Jr. Blood replacement and autotransfusion in major vascular surgery. In: Rutherford RB, ed. Vascular surgery. Philadelphia: WB Saunders, 1995
3. Freischlag JA. Intraoperative blood slavage in vascular surgery-worth the effort? Critical Care 2004;8:S53–6
4. Posacioglu H, Apaydin AZ, Islamoglu F, Calkavur T, Yagdi T, Atay Y, Buket S. Adverse effects of cell saver in patients undergoing ruptured abdominal aortic aneurysm repair. Ann Vasc Surg 2002;16:450–5
5. Reitman CA, Watters WC III, Sassard WR. The Cell Saver in adult lumbar fusion surgery: a cost-benefit outcomes study.[see comment]. Spine 2004;29:1580–3

6. Burman JF, Westlake AS, Davidson SJ, Rutherford LC, Rayner AS, Wright AM, Morgan CJ, Pepper JR. Study of five cell salvage machines in coronary artery surgery. Transfus Med 2002;12:173–9
7. Waters JH, Williams B, Yazer MH, Kameneva MV. Modification of suction-induced hemolysis during cell salvage. Anesth Analg 2007;104:684–7
8. McKie JS, Herzenberg JE. Coagulopathy complicating intraoperative blood salvage in a patient who had idiopathic scoliosis. A case report. J Bone Joint Surg Am 1997;79:1391–4
9. Szpisjak DF, Edgell DS, Bissonnette B. Potassium as a surrogate marker of debris in cell-salvaged blood. Anesth Analg 2000;91:40–3
10. Rother RP, Bell L, Hillmen P, Gladwin MT. The clinical sequelae of intravascular hemolysis and extracellular plasma hemoglobin: a novel mechanism of human disease. JAMA 2005;293:1653–62
11. Henn A, Hoffmann R, Muller HA. [Haptoglobin determination in the serum of patients following intraoperative autotransfusion using the Haemonetics Cell Saver III. Studies on the loading of patients with free hemoglobin in retransfused erythrocyte concentrate]. Anaesthesist 1988;37:741–5
12. Rochon G, Caron A, Toussaint-Hacquard M, Alayash AI, Gentils M, Labrude P, Stoltz JF, Menu P. Hemodilution with stroma-free [correction of stoma-free] hemoglobin at physiologically maintained viscosity delays the onset of vasoconstriction. Hypertension 2004;43:1110–5
13. Kim-Shapiro DB, Schechter AN, Gladwin MT. Unraveling the reactions of nitric oxide, nitrite, and hemoglobin in physiology and therapeutics. Arterioscler Thromb Vasc Biol 2006;26:697–705
14. Schechter AN, Gladwin MT. Hemoglobin and the paracrine and endocrine functions of nitric oxide.[see comment]. N Engl J Med 2003;348:1483–5
15. Lopas H, Birndorf NI, Bell CE Jr, Robboy SJ, Colman RW. Immune hemolytic transfusion reactions in monkeys: activation of the kallikrein system. Am J Physiol 1973;225:372–9
16. Kahmann RD, Donohue JM, Bradford DS, White JG, Rao GH. Platelet function in adolescent idiopathic scoliosis. Spine 1992;17:145–8
17. Murray DJ, Gress K, Weinstein SL. Coagulopathy after reinfusion of autologous scavenged red blood cells. Anesth Analg 1992;75:125–9
18. Page P. Perioperative autotransfusion and its correlation to hemostasis and coagulopathies. J Extra Corporeal Technol 1991;23:14–21
19. Homann B, Klaue P, Hauptvogel S. [Intraoperative autotransfusion and its influence on the blood-clotting-system]. Anaesthesist 1977;26:606
20. Milne AA, Drummond GB, Paterson DA, Murphy WG, Ruckley CV. Disseminated intravascular coagulation after aortic aneurysm repair, intraoperative salvage autotransfusion, and aprotinin. Lancet 1994;344:470–1
21. Dietrich W, Barankay A, Heinemann G, Blumel G, Wendt P, Richter JA. [Changes in blood clotting due to the autotransfusion of postoperative drainage blood]. Beitr Infusionther Klin Ernahr 1987;18:90–3
22. Sieunarine K, Lawrence-Brown MM. Haematological effects of reinfused mediastinal blood after cardiac surgery. Med J Aust 1991;155:347
23. Griffith LD, Billman GF, Daily PO, Lane TA. Apparent coagulopathy caused by infusion of shed mediastinal blood and its prevention by washing of the infusate.[see comment]. Ann Thorac Surg 1989;47:400–6
24. Schaff HV, Hauer JM, Bell WR, Gardner TJ, Donahoo JS, Gott VL, Brawley RK. Autotransfusion of shed mediastinal blood after cardiac surgery: a prospective study. J Thorac Cardiovasc Surg 1978;75:632–41
25. Horst HM, Dlugos S, Fath JJ, Sorensen VJ, Obeid FN, Bivins BA. Coagulopathy and intraoperative blood salvage (IBS). J Trauma 1992;32:646–52
26. Bull BS, Bull MH. Enhancing the safety of intraoperative RBC salvage. J Trauma 1989;29:320–5
27. Bull BS, Bull MH. The salvaged blood syndrome: a sequel to mechanochemical activation of platelets and leukocytes? Blood Cells 1990;16:5–20
28. Bull BS, Bull MH. Hypothesis: disseminated intravascular inflammation as the inflammatory counterpart to disseminated intravascular coagulation. Proc Natl Acad Sci U S A 1994;91:8190–4
29. Bull MH, Bull BS, Van Arsdell GS, Smith LL. Clinical implications of procoagulant and leukoattractant formation during intraoperative blood salvage. Arch Surg 1988;123:1073–8
30. Ridler BMF, Thompson JF. The qualities of blood reinfused during cell salvage. Transfus Altern Trasfus Med 2003;5:466–71
31. Innerhofer P, Wiedermann FJ, Tiefenthaler W, Schobersberger W, Klingler A, Velik-Salchner C, Oswald E, Salner E, Irschick E, Kuhbacher G. Are leukocytes in salvaged washed autologous blood harmful for the recipient? The results of a pilot study. Anesth Analg 2001;93:566–72
32. Sandoval S, Alrawi S, Samee M, Satheesan R, Raju R, Cunningham JN, Acinapura AJ. A cytokine analysis of the effect of cell saver on blood in coronary bypass surgery. Heart Surg Forum 2001;4:113–7
33. Sieunarine K, Lawrence-Brown MM, Goodman MA, Prendergast FJ, Rocchetta S. Plasma levels of the lipid mediators, leukotriene B4 and lyso platelet-activating factor, in intraoperative salvaged blood. Vox Sang 1992;63:168–71
34. Quinley ED. Immunohematology: principles and practice. New York: Lippincott Williams and Wilkins, 1998
35. Tawes RL Jr, Sydorak GR, Duvall TB, Scribner RG, Rosenman JE, Beare JP, Harris EJ. Avoiding coagulopathy in vascular surgery. Am J Surg 1990;160:212–6
36. Ansell JE, Widrich WC, Johnson WC, Maizels M, Robbins AH, Nabseth DC, Deykin D. Gelfoam and autologous clot embolization: effect on coagulation. Invest Radiol 1978;13:115–20
37. Gause PR, Siska PA, Westrick ER, Zavatsky J, Irrgang JJ, Kang JD. Efficacy of intraoperative cell saver in decreasing postoperative blood transfusions in instrumented posterior lumbar fusion patients. Spine 2008;33:571–5
38. Horlocker TT, Nuttall GA, Dekutoski MB, Bryant SC. The accuracy of coagulation tests during spinal fusion and instrumentation. Anesth Analg 2001;93:33–8
39. Klodell CT, Richardson JD, Bergamini TM, Spain DA. Does cell-saver blood administration and free hemoglobin load cause renal dysfunction? Am Surg 2001;67:44–7
40. Godet G, Fleron MH, Vicaut E, Zubicki A, Bertrand M, Riou B, Kieffer E, Coriat P. Risk factors for acute postoperative renal failure in thoracic or thoracoabdominal aortic surgery: a prospective study. Anesth Analg 1997;85:1227–32
41. Guidelines for blood salvage and reinfusion in surgery and trauma. Bethesda, MD: American Association of Blood Banks, 1993