Alternatives to Blood Transfusion in the Perioperative Period

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State-of-the-Art Blood Saving Techniques

"With an appropriate selection of patients, all techniques can be used efficiently."

State-of-the-Art Blood Saving Techniques

"With an appropriate selection of patients, all techniques can be used efficiently."

"Any inherent risk of the transfusion alternative and any detrimental effect on perioperative risk may exceed the benefits of reduced allogeneic blood exposure"
Need for Blood Substitutes

- Complications associated with blood transfusion
  - Immune (hemolytic, non hemolytic...)
  - Non immune (infections...)
- Logistic problems associated with blood transfusion
  - Storage
  - Transport
  - Screening
- Blood availability
Epidemiology of Blood Transfusion

Blood Conservation Strategies: the "Hawthorne " Effect

Blood Conservation Techniques

Blood (units) vs. Patients (nb) graph.
Blood Conservation Techniques

Blood (units)

Patients (nb)
Blood Conservation Techniques

Blood (units)

Blood effect

Patients (nb)
Predicting Factors of Perioperative Allogeneic Blood Transfusion

- **Blood loss**
  (pre, per, and postoperative)

- **Preoperative red blood cell mass**
  (weight, height, hematocrit, gender)

- **Transfusion trigger**
  (hb - hct value, clinical criteria)
Predicting Factors of Perioperative Allogeneic Blood Transfusion

Hematocrit (%) vs. Blood loss (ml)
Predicting Factors of Perioperative Allogeneic Blood Transfusion

Hematocrit (%)

Blood loss (ml)

Perioperative blood loss
Predicting Factors of Perioperative Allogeneic Blood Transfusion

Hematocrit (%) vs. Blood loss (ml)

- Weight: 80 kg
- Weight: 40 kg

Preoperative red blood cell mass

Weight: 40 kg

Weight: 80 kg
Predicting Factors of Perioperative Allogeneic Blood Transfusion

Hematocrit (%) vs. Preoperative red blood cell mass

Weight: 80 kg

Blood loss (ml)

PVdL
Predicting Factors of Perioperative Allogeneic Blood Transfusion

Hematocrit (%)

Blood loss (ml)

Perioperative blood loss

Weight: 80 kg

Weight: 40 kg

PVdL
Predicting Factors of Perioperative Allogeneic Blood Transfusion

Hematocrit (%) vs. Blood loss (ml)

Transfusion Trigger

- Weight: 80 kg
- Weight: 40 kg

Blood loss ranges:
- 0 - 500 ml
- 500 - 1,000 ml
- 1,000 - 1,500 ml
- 1,500 - 2,000 ml
- 2,000 - 2,500 ml
- 2,500 - 3,000 ml

Blood loss triggers:
- 1,000 ml
- 1,500 ml
- 2,000 ml

PVdL
Perioperative Blood Conservation Program

Strategy

Preop RBC mass
Minimize blood loss
Reduce the Transfusion Trigger
Increase of Preoperative RBC Mass

✓ Correction of carencies
  - Iron
  - Folic acid, vitamine B12

✓ Stimulation of erythropoiesis
  - pre, per and post operative administration of erythroploietin

✓ Preoperative autologous blood donation (PABD)
Human Recombinant Erythropoietin (EPO)

**Pro**

- perioperative erythropoiesis stimulation
- facilitating PABD in anemic patients (hct < 39%)

**Con**

- hypertension
- thrombotic risk?
- **cost ($ 0.01/ unit)**

- Doses: 300-600 UI/kg SC 1-3 /week to 1/day during 14 days
  Optimal dose of perioperative EPO therapy remains to be established *(Laupacis A et al, Transfus Med 8:309-17, 1998.)*
- Iron supplementation: PO or IV
Preoperative Autologous Blood Donation

✓ Pro

- Prevents transfusion-transmitted disease
- Avoid red cell alloimmunization
- Supplements the blood supply
- Provides compatible blood for patients with alloantibodies
- Prevents some adverse transfusion reactions
Preoperative Autologous Blood Donation

✓ Con

- Does not eliminate the risk of bacterial contamination
- Does not eliminate the risk of administrative error, resulting in ABO incompatibility
- Costs more than allogeneic blood donation
- Results in discarding of blood that is not transfused
- Causes perioperative anemia and increases the likelihood of transfusion
Arthroplastie de la hanche et transfusion sanguine


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<th>1991</th>
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Blood Transfusion Costs

Costs by unit ($)

Improving the Cost-Effectiveness of PAD

✔ Optimization of Efficacy of PAD

- Factors influencing RBC production during PAD:
  - Patient's baseline hematocrit
  - Underlying disease
  - Interval between the collection of AB units and surgery
  - Number of units collected

To obtain a net gain of 200 mL of new RBCs through PAD, the patient need at least 15 days after the donation of at least 2 units of autologous blood

Minimize Perioperative Blood Loss

☑ Preoperative
  ▶ Minimize iatrogenic blood loss

☑ Intraoperative

☑ Postoperative
Allogeneic Blood Transfusion and Phlebotomies

Blood withdrawn (ml/day)

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<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
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<td>A</td>
<td>16</td>
<td>10</td>
<td>23</td>
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Phlebotomies (/day)

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<th>E</th>
<th>F</th>
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<td>1.9</td>
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<td>4</td>
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Blood withdrawn (ml)

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<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>197</td>
<td>153</td>
<td>301</td>
<td>240</td>
<td>798</td>
<td>944</td>
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</table>

A: medical unit
B: surgical unit
C-D: ICU without IBP
E-F: ICU with IBP

Allogeneic Blood Transfusion and Phlebotomies

Transfused patients

N = 100

- Definite reason for anemia: 19
- Possible reason for anemia: 13
- No reason for anemia: 4

Minimize Perioperative Blood Loss

✓ Preoperative

✓ Intraoperative
  ➤ Non pharmacological interventions
  ➤ Pharmacological interventions

✓ Postoperative
Minimize Intraoperative Blood Loss: Non Pharmacological Interventions

✓ Positioning of the patient
✓ Anesthesia technique
  ▷ general versus loco-regional anesthesia
  ▷ mode of ventilation
  ▷ optimal fluid replacement
  ▷ maintaining normothermia
  ▷ controlled hypotension
  ▷ hyperoxic ventilation
✓ Surgical technique
  ▷ HEMOSTASIS, adjuvants (tourniquets...)
✓ Preoperative plasmapheresis
✓ Acute normovolemic hemodilution (ANH)
✓ Intraoperative cell salvage (IOBS)
Controlled Hypotension

- Lowering MAP to 50-65 mmHg can decrease peroperative blood loss by about 50%

✓ Indications
  - Most effective in orthopedic and in head & neck procedures

✓ Agents
  - General anesthetics, NO donors, $\alpha$ & $\beta$ adrenergic blocking drugs...

✓ Routine monitoring
  - ECG, SpO2, ETCO2 and either NIBP or IBP

✓ Contraindications
  - Significant cerebrovascular, CAD and respiratory diseases, diabetes mellitus
Acute Normovolemic Hemodilution

✓ Pro
  ▶ Provides fresh autologous blood at room temperature
  ▶ Had few logistical problems
  ▶ Cheaper than PABD
  ▶ Improves tissue perfusion
  ▶ Combines with PABD and IOBS

✓ Con
  ▶ Efficacy ?
  ▶ Contra-indications (CAD, CHF, COPD,...)
ANH & Perioperative Allogeneic Blood Transfusion

✓ 24 RCTs - 1218 patients
  ▶ Median sample size: 30
  ▶ Mean blood volume collected: 936 ml

✓ ANH:
  ▶ Reduced the likelihood of exposure to at least 1 of allogeneic RBC
  ▶ Reduced the units of allogeneic blood transfused (-2.2 U 95% CI -3.57, -0.86)
  ▶ Had no significant effect on perioperative blood loss (-117ml 95% CI -292, -58 ml)

Acute Normovolemic Hemodilution: Technique

\[ ABV = EBV \times \frac{Ho - Ht}{(Ho + Ht)/2} \]

- **ABV**: autologous blood to be withdrawn
- **EBV**: estimated blood volume
- **Ho**: initial hematocrit
- **Ht**: target hematocrit = 20-25%

**Substitution fluids:**
- **Crystalloids**: ratio 3:1
- **Colloids**: ratio 1:1 (except with gelatins: 1.5:1)
- Blood is withdrawn from a venous or an arterial line, collected in **labelled** CPD bags (450 mL /bag) and stored at room temperature for up to 6 hours.
Minimize Perioperative Blood Loss

✓ Pharmacological interventions
  ▶ Surgical glues
  ▶ Antifibrinolytics
    ▶ Tranexamic acid, EACA
  ▶ Serine protease inhibitor
    ▶ Aprotinin
  ▶ Vasopressin analog
    ▶ Desmopressin
      (only very specific indications)
Minimize Perioperative Blood Loss: Pharmacological Interventions

✓ Aprotinin
  ▶ Pro
  ▶ Decreases allogeneic blood exposure in cardiac surgery, liver transplantation and orthopedic surgery
  ▶ Improves survival in cardiac surgery?
  ▶ Con
  ▶ Allergic reactions
  ▶ Cost

✓ Antifibrinolytics
  ▶ Pro
  ▶ Decreases allogeneic blood exposure in cardiac surgery, liver transplantation, orthopedic and urologic (?) surgeries
  ▶ Con
  ▶ Prothrombotic effect?
### Pharmacological Interventions & Cardiopulmonary bypass

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<th></th>
<th>EACA</th>
<th>Tranexamic acid</th>
<th>Aprotinin</th>
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<td>150 mg/kg</td>
<td>15-20 mg/kg</td>
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<tr>
<td><strong>CPB prime dose</strong></td>
<td></td>
<td></td>
<td>2.000000 KIU</td>
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<tr>
<td><strong>Infusion rate</strong></td>
<td>10-15 mg/kg.h</td>
<td>1-2 mg/kg.h</td>
<td>500000 KIU</td>
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<tr>
<td><strong>Cost/case</strong> *</td>
<td>$ 39</td>
<td>$ 26</td>
<td>$ 900</td>
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* for an 80 kg patient undergoing 3 hours of treatment

From Gravlee GP. Annual Refresher Course Lectures, 1994 p512
Peroperative Blood Salvage

✓ Red cell salvaging with processing: centrifuged-based system requiring anticoagulant

✓ Pro

  ▶ Supplies 200-250 mL of washed RBcs (hct 55-60%), with normal half-life, P50 and 2-3 DPG

  ▶ Indicated in elective and urgent surgeries

✓ Con: complications

  ▶ Dilutional coagulopathy, reinfusion of anticoagulants

  ▶ Air embolism
Peroperative Blood Salvage

✓ Indications
  ▶ Estimated blood loss > 20% of the patient blood volume
  ▶ Blood ordering usual for the procedure
  ▶ > 10% of the patients undergoing the procedure require transfusion
  ▶ Blood volume transfused usually for the procedure > 1 unit

✓ Limitations
  ▶ Rapid hemorrhage (> 300 mL/min)
  ▶ Massive hemorrhage
Perioperative Blood Salvage

✓ Autotransfusion of unprocessed salvaged blood

✓ Pro

  ➤ Ease of usage, low cost and quick turnover from hemorrhage to reinfusion
    ➤ Blood recovered from serous cavities or the mediastinum does not require anticoagulation
    ➤ Blood collected from a wound require anticoagulation

✓ Con: complications
  ➤ Hemolysis
  ➤ Disseminated intravascular coagulation

Upper limit: 1000-1400 ml within 6 hours
Perioperative Blood Salvage

✓ Contraindications
  ▶ Malignancy
  ▶ Septicemia & infection at the site of surgery
  ▶ Contamination of the surgical field with fluids or hemostatic substances

✓ Precautionary measures
  ▶ Use of adequate filters (<40µ)
  ▶ Avoidance of strong surgical suction
  ▶ Reduction of air/blood contacts
  ▶ Use of adapted anticoagulation programs
  ▶ Appropriate replacement of hemostatic factors
Autologous Transfusion: the Costs

- Allogeneic blood
  - ± 70 $/unit
- PABD
  - ± 100 $/unit
- ANH
  - ± 20$/unit
- PBS with processing
  - Machine: ± 30,000 $
  - Disposable: ± 150 $
- PBS without processing
  - ± 150 $/unit
Minimize Perioperative Blood Loss

✓ Preoperative

✓ Peroperative

✓ Postoperative
  - Active rewarming
  - Postoperative blood salvage
  - Monitoring of coagulation and algorithm therapy
Perioperative Transfusion Algorithm

PLT Count

- <50 Platelets
  - PT; aPTT > 1.8 MVB +
    - YES FFP
    - NO PLT RX
  - YES PT; aPTT > 1.8
    - YES FFP
    - NO PLT RX
- 50 to 100 Platelets
  - PT; aPTT > 1.8
    - YES FFP
    - NO PLT RX
- >100 Platelets
  - PT; aPTT > 1.5
    - YES FFP
    - NO PLT RX

The Transfusion Trigger

✓ Optimal hemoglobin versus critical hemoglobin level

✓ Maintenance of tissue O2 delivery during normovolemic anemia:

► Compensatory mechanisms
  ◦ increased cardiac output
  ◦ increased tissue oxygen extraction

► Metabolic demand (rest > exercise)
Risks of Anemia

Blood Transfusion

EFFICACY

RISKS
Transfusion Requirements in Critical Care

**Average units/patient**

- **RestRICTive**: 8.5 ± 0.7 g/dl
- **Liberal**: 10.7 ± 0.7 g/dl

**30-day mortality (%)**

- APACHE II < or = 20:
  - **Restrictive**: 8.7, 16.1, p=0.03
  - **Liberal**: 18.7, 23.3, p=0.11

- **Patients < 55 years**:
  - **Restrictive**: 5.7, 13, p=0.02
Transfusion Requirements in Critical Ill Patients with CVD

Patients with CVD (N=357)
30 day mortality (%)

Patients with ischemic heart disease (N=257)
30-day mortality (%)

Symptoms Requiring RBC Transfusion During Normovolemic Anemia

- Syncope
- Dyspnea
- Postural hypotension
- Tachycardia
- Angina
- Transient ischemic attack
Perioperative Transfusion Trigger

✓ Preoperative period
  ▶ Definition of anemia
  ▶ Surgical risk
  ▶ Patient's clinical status

✓ Peroperative period
  ▶ Volemia
  ▶ Blood losses
  ▶ Hemodynamic response

✓ Postoperative period
  ▶ Metabolic needs
  ▶ Complications

RBC Transfusion: Role of Audit & Practice Guidelines

Total number of transfusion decreased by 43 %

Blood Transfusion Requirements

- Red Cell Transfusion Strategies
  - Administer transfusion(s) on a unit-by-unit basis
  - Evaluate the patient after each unit

- Standardized multidisciplinary approach!!!
Effect of a standardized multidisciplinary approach of blood transfusion strategy on allogeneic transfusion exposure?
Standardized Blood Transfusion Strategy

✓ Aggressive prebypass hemodilution (CPB Hct ± 20%)
✓ Aprotinin, Cell Saver, Ultrafiltration:
  ▸ standardized indications
✓ Allogeneic transfusion trigger:
  ▸ hemoglobin level
  ▸ clinical status
  ▸ potential risk of complications

Standardized Blood Transfusion Strategy

Acute normovolemic hemodilution (%)

- Group 1: 72.8
- Group 2: 89.2

p=0.000

Acute normovolemic hemodilution (mL)

- Group 1: 500 mL
- Group 2: 1000 mL

p=0.000
Standardized Blood Transfusion Strategy

Patients (%)

- Group 1: 48.6% Aprotinin, 25.9% Others
- Group 2: 51.4% Aprotinin, 28.1% Others
Standardized Blood Transfusion Strategy

Group 1: 340 units in 108 patients; Group 2: 161 units in 57 patients

Allogeneic blood transfusion (%)

Group 1: 33%, Group 2: 18%

p=0.000

Allogeneic blood (U)

p=0.000
Standardized Blood Transfusion Strategy

Patients transfused (%)

- Perop: Group C: 5.6, Group T: 3.2
- JPO 1: Group C: 17.5, Group T: 8.9
- JPO 2-7: Group C: 23.4, Group T: 13

P-values: p=0.001
Perioperative Hemoglobin Level

Hemoglobin (g/dL)

- Group 1: N=321
- Group 2: N=315

Pre-op | POD1 | POD2 | POD5 | Discharge
### Perioperative Hemoglobin Level

<table>
<thead>
<tr>
<th>Hemoglobin (g/dL)</th>
<th>Pre-op</th>
<th>POD1</th>
<th>POD2</th>
<th>POD5</th>
<th>Discharge</th>
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<td>Group 1: N=321</td>
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</tr>
<tr>
<td>Group 2: N=315</td>
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* p<0.05, ** p<0.01 vs previous measurement
Perioperative Blood Transfusion Strategy

- Preop RBC mass
- Periop blood loss
- Reduce the Transfusion Trigger

depending on:

- Surgical procedure and technique
- Patients limitations
- Health Care environment
- Immediate and long term costs
Developing a Blood Conservation Strategy

 ✓ Reliable data base

 ✓ Choice of alternative techniques
   ▶ Surgical procedure and technique
   ▶ Patients limitations
   ▶ Health Care environment
   ▶ Immediate and long term costs

 ✓ Continuous monitoring

 ✓ Multidisciplinary approach: anesthesiologists, surgeons, blood bankers...