

Tranexamic Acid

Where We Use It And Why

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Overview

- Blood Conservation Strategies
- Hemostasis
- Fibrinolysis
- Antifibrinolytics
 - Tranexamic Acid
 - Aprotinin
- Tranexamic Acid and Cardiac Surgery
- Use of Tranexamic Acid in Other Surgeries
- Literature
- Cost

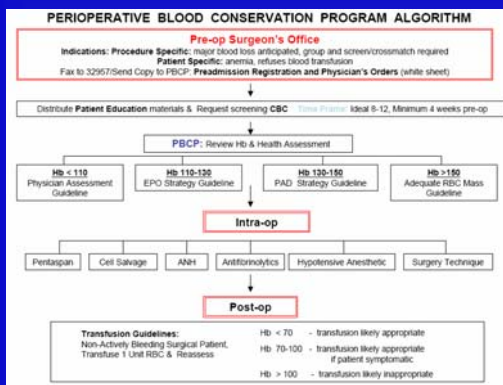
Blood Conservation Strategies

- Preoperative:
 - Iron
 - Erythropoietin
 - Autologous blood donation
 - Decreasing / stopping anticoagulant and antiplatelet medications
- Intraoperative:
 - Surgical technique
 - Acute normovolemic hemodilution (ANH)
 - Intraoperative blood salvage
 - Antifibrinolytics
 - Regional anesthesia
- Post-operative
 - Anemia management algorithms

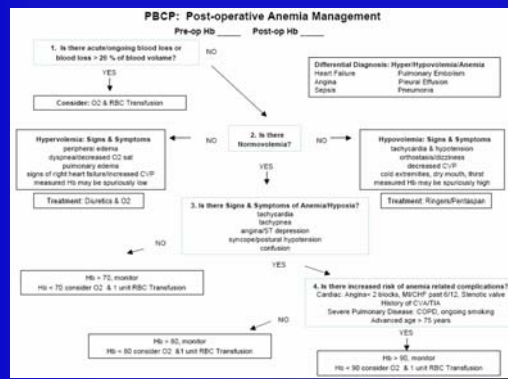
Blood Conservation Strategies

TIME UNTIL SURGERY	BLOOD CONSERVATION STRATEGIES AVAILABLE
> 35 days	<ul style="list-style-type: none"> • Investigate and treat anemia • Delay surgery until anemia corrected • Iron
14-35 days	<ul style="list-style-type: none"> • Delay surgery until anemia corrected • Autologous blood donation • Erythropoietin weekly dosing regimen • Iron
10-13 days	<ul style="list-style-type: none"> • Delay surgery until anemia corrected • Erythropoietin daily dosing regimen • Iron
< 10 days before surgery	<ul style="list-style-type: none"> • Delay surgery until anemia corrected
Intraoperative	<ul style="list-style-type: none"> • Attention to surgical hemostasis • Antifibrinolytics and DDAVP • Intraoperative cell salvage • Regional anesthesia • Other measures, mainly investigational • Adherence to strict transfusion guidelines

Blood Conservation Strategies



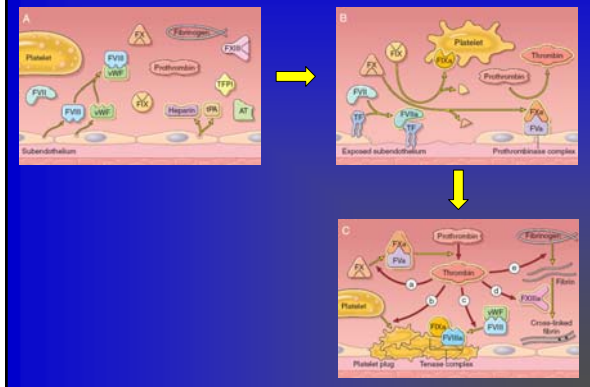
Blood Conservation Strategies



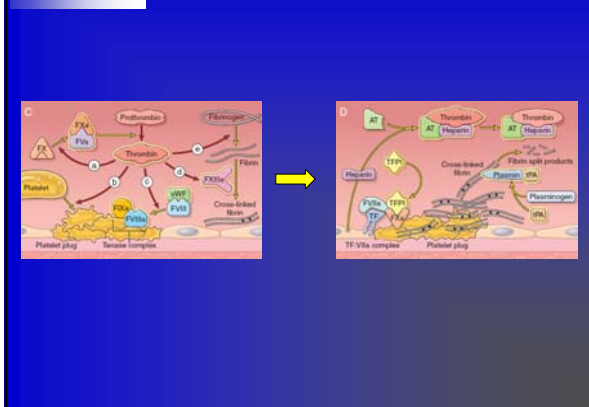
Blood Conservation Strategies

- Intraoperative:
 - Surgical technique
 - Acute normovolemic hemodilution (ANH)
 - Intraoperative blood salvage
 - Antifibrinolytics
 - Regional anesthesia

Hemostasis



Fibrinolysis



Fibrinolysis

- Fibrinolysis During Cardiac Surgery:
 - Initiated by incision and sternotomy
 - Augmented by CPB
 - Peaks toward the end of extracorporeal circulation
 - Evidence for bypass-associated fibrinolysis:
 - Presence of FDPs during and after CPB
 - tPA levels increase during CPB (tPA is released from endothelium and activates plasmin)
 - Increased plasmin levels

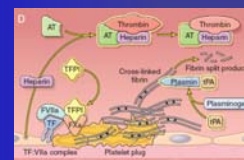
Antifibrinolytics

- Tranexamic Acid
- Aprotinin
 - 1993: approved for used during CABG
 - 2006: increased risk of renal failure, myocardial infarction, stroke, and death
 - 2008: BART
 - Aprotinin vs. Lysine Analogues in cardiac surgery
 - Reduced risk of massive postoperative bleeding
 - Reduced need for postop administration of blood products
 - Increased risk of death at 30 days

BART = Blood Conservation Using Antifibrinolytics in a Randomized Trial

Tranexamic Acid

- Antifibrinolytic
- Lysine Analogue
 - Attach to the lysine site of plasminogen and prevent its conversion to plasmin
 - Inhibits the proteolytic activity of plasmin
- Half life: 80 min
- Excretion: Renal



Tranexamic Acid

- TA and Cardiac Surgery:
 - Decrease in blood loss
 - Decrease in transfusion requirements
- Side Effects:
 - Hypotension (only if given too fast IV)



Risks

Risk of Event	Factor
1 in 10	Fabry's non-hemolytic transfusion reaction per pool of 5 donor units of platelets (5 donor exposures) per unit of component
1 in 100	Minor allergic reactions (urticaria)
1 in 300	Fabry's non-hemolytic transfusion reaction per unit of RBC (5 donor exposures)
1 in 700	Transfusion-associated circulatory overload per transfusion episode
1 in 5,000	Transfusion-related acute lung injury (TRALI)
1 in 7,000	Delayed hemolytic transfusion reaction
1 in 10,000	Symptomatic bacterial sepsis per pool of 5 donor units of platelets
1 in 40,000	Death from bacterial sepsis per pool of 5 donor units of platelets
1 in 40,000	ABO-incompatible transfusion per RBC transfusion episode
1 in 40,000	Serious allergic reaction per unit of component
1 in 82,000**	Transmission of hepatitis B virus per unit of component
1 in 100,000	Symptomatic bacterial sepsis per unit of RBC
1 in 100,000	Death from bacterial sepsis per unit of RBC
~ 1 in 1,000,000	Transmission of West Nile Virus
1 in 3,000,000	Transmission of HTLV per unit of component
1 in 3,100,000	Transmission of hepatitis C virus per unit of component
1 in 4,700,000	Transmission of human immunodeficiency virus (HIV) per unit of component

Tranexamic Acid

- No definite evidence that TA (or any other antifibrinolytics) can produce thrombosis
 - Case reports in literature of DVT, PE, renal thrombosis, carotid artery thrombosis, cerebral artery thrombosis but no clear association could be made
- Common misconception that antifibrinolytics are procoagulants and that they will increase blood clotting

Tranexamic Acid

- Other Surgical Specialties:
 - Orthopedic Surgery
 - Liver (incl. Transplant)
 - Urology
 - Trauma
 - Obstetrics
 - Gynecology
 - ENT

Orthopedic Surgery

- Total Knee Arthroplasty
 - Hiippila et al. Tranexamic acid radically decreases blood loss and transfusions associated with total knee arthroplasty. *Anesthesia and Analgesia* 84: 839-844 (1997).
 - 75 patients
 - 15 mg/kg bolus, then 2 10 mg/kg boluses postop
 - Significant decrease in surgical blood loss (689 ml vs 1509 ml)
 - Significant decrease in PRBCs transfused (1.0 vs 3.1)
- LHSC – University Hospital
 - 20 mg/kg TA for TKA and THA (prepared by pharmacy)
 - Better postop Hb
 - Decreased transfusion rates
 - TKA: 2% (vs 13.1%)
 - THA: 3.6% (vs 13.5%)
- Many other studies show similar benefits in TKA

Orthopedic Surgery

- Spine Surgery
 - Reduced blood loss
 - Most studies (not all) show decreased # blood products transfused
- Pediatric Scoliosis Surgery
 - Antifibrinolytic agents for reducing blood loss in scoliosis surgery in children. *Cochrane Database Syst Rev.* 2008 Jul 16;(3)
 - Review of six studies
 - Antifibrinolytics decreased blood loss and the number of blood products transfused

Other Surgeries

- Liver Transplantation
 - Efficacy and safety of antifibrinolytic drugs in liver transplantation: a systematic review and meta-analysis. *Am J Transplant*. 2007 Jan;7(1):185-94
 - Decreased transfusion requirements
 - No increased incidence of thrombosis
- Obstetrics
 - Cesarean section
- Gynecology
 - Dysfunctional uterine bleeding
 - Menorrhagia
- Oral and Maxillofacial Surgery
- Urology
 - TURP (prostate releases IPA)

Trauma

- Insufficient evidence at this time to support or refute a treatment effect for TA in trauma
 - Antifibrinolytic drugs for acute traumatic injury. *Cochrane Database Syst Rev*. 2004 Oct 18;(4)

Subarachnoid Hemorrhage

- Antifibrinolytic therapy for aneurysmal subarachnoid haemorrhage.
 - *Cochrane Database Syst Rev*. 2003;(2)
 - 9 trials included
 - No evidence of benefit for poor outcome (death, vegetative state, severe disability)
 - Antifibrinolytic treatment reduced the risk of re-bleeding
 - Treatment increased the risk of cerebral ischemia in 5 trials

Patients

- Jehovah's Witness
- Hemophilia A
- Hemophilia B
- Hereditary Coagulation Factor Deficiency
- Von Willebrand's Disease
- Liver Disease
- Cancer



Costs

- Tranexamic Acid: 5g vial = \$62
- 20 mg/kg dose for 70 kg male = 1.4 g = \$17.50

Item	Price
Red blood cells	\$400
Autologous (whole) blood	\$400
Erythropoietin 40,000 IU/week for 2 to 4 weeks	\$1,140 - \$2,280†
Erythropoietin 1,000 IU	\$14,251†
5 units platelets	\$500
4 units buffy coat derived platelets	\$500
1 unit single donor (apheresis) platelets	\$500
1 unit HLA-matched single donor (apheresis) platelets	\$1,250
Apheresis fresh frozen plasma	\$220
4 units frozen plasma	\$700
8 units cryoprecipitate	\$225
Blood group (ABO, Rh D)	\$10
Antibody screen	\$25
Crossmatch (no antibody)	\$15
Crossmatch (antibody positive patient)	\$45

Limitations

- Human Nature
- Education
- Research

Summary

- Number of methods exist to reduce patient exposure to blood products
- Tranexamic acid has been shown to reduce blood loss and exposure to blood products in a variety of patients and surgical procedures
- More education needed
- More research needed

- Protocols

- Money