Tranexamic Acid in Joint Replacement Surgery

Donna Berta
Blood Conservation Program Coordinator

London Health Sciences Centre
Today’s Objectives

After this presentation participants will be able to:

• to describe the basic physiology of hemostasis and fibrinolysis

• to identify Tranexamic Acid’s (TA) mechanism of action, administration, side effects, precautions, contraindications

• to examine the role of TA in knee and hip joint replacement surgery at London Health Science Centre (LHSC)
Kay’s Storey 1

• Sept 2009, for revision right hip, aseptic loosening, 4 hrs scheduled for OR
• Kay is “worried” remembers 2006 revision left hip surgery, thought she “was dying from blood transfusion reaction”

• Aug 2006 revision left hip (acetabular), 3 hrs scheduled
• 83 yrs, 171 cm, 75 kg
• Hx: Psoriatic arthritis x 30 yrs (both knees and hips replaced), GERD, severe varicose veins, smoking cessation x 10 yrs (40 pack yr hx), no: Cardiac disease, HTN, DVT/PE, CVA/TIA
• Meds: methotrexate, folic acid, pariet, ferrous gluconate

• Pre-op: Hb 125 g/L, ferritin 132 ug/L, Cr 74 umol/L
  BTL: A pos (negative antibody screen)
• Eprex pre-op day 22 and 14 (was scheduled pre-op day 15 and 7 multiple OR date changes re: spouses’ health issues)

• OR Day Hb 136 g/L retics 41
• POD # 1 Hb 93 g/L
• POD # 3 Hb 83 g/L, VS stable, c/o “dizzy” when up, mobilizing slowly
• Ortho Resident ordered 2 units RBCs with 20 mg lasix between units

• 30 minutes after 2nd unit initiated c/o SOB, nausea
  T 37.3, BP 184/78, HR 69, RR 28, O2 Sat 81 % on Rm Air
  (pre-transfusion VS T 36.1, BP 114/60, HR 70, RR 16)

• Transfusion d/c, O2 at 5 lpm, gravol IV, sample to BTL
• 30 minutes after Transfusion d/c T 37, BP 156/75, HR 80, RR 24,
  O2 Sat 100 % with O2 at 3 lpm

• 6 hrs later, c/o palpitations, BP 100/60, HR 140, RR 20
  Cardiology Consult: Dx: supra ventricular tachycardia, treated with metoprolol,
  no EKG changes, troponin negative

• Transfusion Reaction: reported “febrile reaction, post transfusion specimen no
  evidence of RBC incompatibility” (antibody screen and DAT negative)

• Discharged POD # 6 Hb 109 g/L, for follow up Holter monitor with Cardiology
Kay’s Storey 3

• Sept 2009: OR scheduled for 4 hrs, femoral and acetabular revision

• Health history essentially unchanged “just 3 yrs older”
  no further cardiology follow up since 2007
• Meds: methotrexate, folic acid, pariet, Vitamin B₁₂ PO

• Pre-op: Hb 124 g/L, ferritin 87.4 ug/L, Cr 86 umol/L
  BTL group and screen Anti–FyA antibody detected
  positive antibody screen, unidentified antibody in 4/22 cells

• Kay remembered having a medic alert bracelet “Duffy A antibody”
  after her first joint surgery in 1980’s; also she had transfusions after childbirth in 1946
  2006: Documentation reviewed, no notation of this information
  Kay “must have forgot to tell you, my husband was very sick at that time”

• BTL review of historical files noted Anti–FyA antibody
  information was not carried forward with electronic update of BTL records
  probable Kay did not receive FyA negative blood in 2006
Are there additional blood conservation strategies for Kay to limit the “need” for allogeneic transfusion ??
Today’s Objectives

After this presentation participants will be able to:

• to describe the basic physiology of hemostasis and fibrinolysis

• to identify Tranexamic Acid’s (TA) mechanism of action, administration, side effects, precautions, contraindications

• to examine the role of TA in knee and hip joint replacement surgery at London Health Science Centre (LHSC)
Hemostasis

(Stoelting & Miller, 2007)
Fibrinolysis

(Stoelting & Miller, 2007)
Today’s Objectives

After this presentation participants will be able to:

• to describe the basic physiology of hemostasis and fibrinolysis

• to identify Tranexamic Acid’s (TA) mechanism of action, administration, side effects, precautions, contraindications

• to examine the role of TA in knee and hip joint replacement surgery at London Health Science Centre (LHSC)
TA – Mechanism of Action

- Antifibrinolytic – Lysine Analogue
  - Attaches to lysine site of plasminogen and prevents its conversion to plasmin (plasmin degrades fibrin clots and fibrinogen)
  - Also inhibits the proteolytic activity of plasmin (procoagulant Factors V and VIII)
  - Prevents dissolution of the hemostatic platelet plug
TA – Administration

- Supplied as 100 mg/ml in 5 gm/50 ml vial (Sandoz)
- Administer only IV, not SC or IM; can be given PO
- Do not inject more rapidly than 100 mg or 1 ml per minute (rapid IV administration can cause hypotension)
- **Compatible**: dextrose, saline, electrolyte, amino acid, dextran solutions, heparin
- **Incompatible**: solutions containing penicillin
- Limited data in pediatrics
- Systemic half life: 2 hrs
- Diffuses rapidly to joint fluid and synovial membrane, crosses blood brain barrier, crosses placenta, passes into breast milk
- Excreted in urine (is filtered but not taken up by renal tubular cells)
- In renal impairment, IV dose adjustments suggested

<table>
<thead>
<tr>
<th>Serum Creatinine um/L</th>
<th>IV dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>120–250</td>
<td>10 mg/kg Bid</td>
</tr>
<tr>
<td>250–500</td>
<td>10 mg/kg OD</td>
</tr>
<tr>
<td>&gt; 500</td>
<td>10 mg/kg q 48 hrs</td>
</tr>
</tbody>
</table>
TA – Side Effects

- CNS: headache
- CVS: hypotension due to rapid injection
- GI: nausea, vomiting, diarrhea (more common in PO course of treatment, disappears with decreased dose)
- Ocular: visual abnormalities (if treated for several weeks)
TA – Precautions, Contraindications (e-CPS)

- Subarachnoid Hemorrhage – increased cerebral ischemia

- Acquired disturbances of color vision

- Hematuria from upper urinary tract (reports of ureteral obstruction due to clot formation)

- Patients with history or risk of thrombosis, unless it is possible to give treatment with anticoagulants

- Patients with active thromboembolic disease (DVT, PE, cerebral thrombosis)

- DIC

- Hypersensitivity to TA
Today’s Objectives

After this presentation participants will be able to:

• to describe the basic physiology of hemostasis and fibrinolysis

• to identify Tranexamic Acid’s (TA) mechanism of action, administration, side effects, precautions, contraindications

• to examine the role of TA in knee and hip joint replacement surgery at London Health Science Centre (LHSC)
• Antifibrinolytics have been inconsistently implemented for revision hip joint surgery for > 5 years

• 2006/2007 TA ordered pre-operatively for revision knee and hip joint replacement but persistent inconsistent administration intraoperatively

• 2007 – New Surgeon, requested TA for all his patients (Primary and Revision)

• March 2008 – All Surgeons requested TA for Primary and Revision joint replacement patients

• TA implemented to augment Blood Conservation Program: Pre-op patient screening early, Iron PO or IV, Eprex, Select cases of autologous blood donation, Post-op transfusion guidelines
TA at LHSC – Protocol 1

• Blood Conservation Physician: review patients with potential contraindication to TA

• Blood Conservation Nurses: write orders for TA dose pre-operatively

• Pharmacy: pre-mix TA dose in minibag, send to Surgical Prep Unit along with prophylactic antibiotics

• Anesthesiologist administers TA dose intra-operatively
Blood Conservation Physician Review if Patient history

- TVE (stroke/DVT/PE) in past 12 months
- TVE (stroke/DVT/PE) with previous joint replacement surgery
- Life long anticoagulation therapy

Blood Conservation Physician Review to
- Assess patient specific risk/benefit profile
- Advise if TA to be ordered
TA at LHSC – Protocol 3

Dose Schedule

- **Tranexamic Acid:**
  - **Dose:** 20 mg/kg
  - **Vial:** 100 mg/ml, supplied 50 ml

- **5 kg patient weight increment = 100 mg (1 ml) dose of TA** (variation minimal, up to +/- 0.9 mg/kg)

<table>
<thead>
<tr>
<th>Weight Increment (kg)</th>
<th>order</th>
<th>Tranexamic acid dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>38 to 42</td>
<td>order</td>
<td>800</td>
</tr>
<tr>
<td>43 to 47</td>
<td>order</td>
<td>900</td>
</tr>
<tr>
<td>48 to 52</td>
<td>order</td>
<td>1000</td>
</tr>
<tr>
<td>53 to 57</td>
<td>order</td>
<td>1100</td>
</tr>
<tr>
<td>58 to 62</td>
<td>order</td>
<td>1200</td>
</tr>
<tr>
<td>63 to 67</td>
<td>order</td>
<td>1300</td>
</tr>
<tr>
<td>68 to 72</td>
<td>order</td>
<td>1400</td>
</tr>
<tr>
<td>73 to 77</td>
<td>order</td>
<td>1500</td>
</tr>
<tr>
<td>78 to 82</td>
<td>order</td>
<td>1600</td>
</tr>
<tr>
<td>83 to 87</td>
<td>order</td>
<td>1700</td>
</tr>
<tr>
<td>88 to 92</td>
<td>order</td>
<td>1800</td>
</tr>
<tr>
<td>93 to 97</td>
<td>order</td>
<td>1900</td>
</tr>
<tr>
<td>98 to 102</td>
<td>order</td>
<td>2000</td>
</tr>
<tr>
<td>103 to 107</td>
<td>order</td>
<td>2100</td>
</tr>
<tr>
<td>108 to 112</td>
<td>order</td>
<td>2200</td>
</tr>
<tr>
<td>113 to 117</td>
<td>order</td>
<td>2300</td>
</tr>
<tr>
<td>118 kg or greater</td>
<td>order</td>
<td>2400</td>
</tr>
</tbody>
</table>
Blood Conservation Nurses Example Orders

- **Hip** joint replacement surgery:
  Send to Surgical Prep Unit
  Tranexamic acid 2000 mg (wt 101 kg), in 50 cc NaCl IV, administer 10 minutes prior to skin incision
  v/o Dr. F. Ralley/_____ PBCP RN

- **Knee** joint replacement surgery:
  Send to Surgical Prep Unit
  Tranexamic acid 2000 mg (wt 101 kg), in 50 cc NaCl IV, administer at patellar clamping
  v/o Dr. F. Ralley/_____ PBCP RN
TA at LHSC – Costs

• TA Vial: 50 ml (100 mg/ml) $62.45
  1 ml costs $1.25
  (Sandoz generic brand– contract costing)

• 75 kg patient; dose 1500 mg (15 ml)
  TA Costs: $ 18.75
  Minibag/Pharmacy work $  4.00
  Total $ 22.75

• Alternative: Cyklokapron (Pfizer)
  10 x 10 ml (100 mg/ml) vials $ 81.91
  1 ml costs $ 0.82
LHSC – Orthopedic Surgery DVT Prophylaxis

- LHSC Standard Care:
  Fragmin 5000 u sc OD for 14 days post-op; then ASA 325 mg OD for 1 month

- If patient has history of DVT/PE or Cancer:
  Fragmin 5000 u sc OD for 30 days post-op

- If patient was taking coumadin pre-op:
  Fragmin 5000 u sc OD until INR > 2, coumadin restarted POD # 1
# TA at LHSC – Outcomes

2008 SABM Poster, 2009 AAOS Conference
2010 Clinical Orthopedics and Related Research

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>April 1 to June 30, 2007</td>
<td>89</td>
<td>110</td>
<td>145</td>
<td>150</td>
</tr>
<tr>
<td>April 1 to June 30, 2008</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N transfused</td>
<td>12</td>
<td>4</td>
<td>19</td>
<td>3</td>
</tr>
<tr>
<td>% transfused</td>
<td>13.5 %</td>
<td>3.6 %</td>
<td>13.10 %</td>
<td>2.0 %</td>
</tr>
<tr>
<td>Ave Hb change*</td>
<td>46 g/L</td>
<td>39 g/L</td>
<td>45 g/L</td>
<td>36 g/L</td>
</tr>
<tr>
<td>Std dev Hb change*</td>
<td>12 g/L</td>
<td>12 g/L</td>
<td>12 g/L</td>
<td>11 g/L</td>
</tr>
<tr>
<td>Ave Hb Pre-op</td>
<td>139 g/L</td>
<td>139 g/L</td>
<td>139 g/L</td>
<td>139 g/L</td>
</tr>
<tr>
<td>Std dev Hb Pre-op</td>
<td>12 g/L</td>
<td>11 g/L</td>
<td>11 g/L</td>
<td>11 g/L</td>
</tr>
<tr>
<td>Ave Hb Discharge</td>
<td>99 g/L</td>
<td>102 g/L</td>
<td>97 g/L</td>
<td>104 g/L</td>
</tr>
<tr>
<td>Std dev Hb Discharge</td>
<td>14 g/L</td>
<td>13 g/L</td>
<td>10 g/L</td>
<td>12 g/L</td>
</tr>
</tbody>
</table>

* Ave Hb change = pre-op Hb – lowest recorded Hb
The Important Part, The Patient

Are there additional blood conservation strategies for Kay to limit the “need” for allogeneic transfusion ???
Kay’s Storey 6

- Sept 2009: Feramax 150 mg OD, Eprex pre-op day 15 and 7
- OR Day Hb 135 g/L, retics 124
- Tranexamic acid 1500 mg in 50 ml NaCl given 10 minutes prior to skin incision
- Cell salvage intra-op: 150 ml RBCs transfused
- POD # 1 Hb 94 g/L
- POD # 3 Hb 100 g/L
- POD # 5 Transfusion not required, Discharged
- Post-op 2 months: Physio, doing “great”
Thank you !!!

Dr. Fiona Ralley and Dr. Ian Chin−Yee

UH Orthopedic Surgery – Surgeons especially Dr. Doug Naudie, Dr. Jamie Howard
Secretaries, Nurse Practitioners,
LHSC Library Services – Erin Boyce
UH Pharmacy – Ian McKechnie, Manager
Colleague – Valerie Binns

My Husband and Kids