Tranexamic Acid in Trauma: What is it and why don't we use it?

Laura MacCall, PharmD
PGY2 Pharmacy Resident, Emergency Medicine; Salt Lake City, Utah

Objectives:
- Describe the use of tranexamic acid (TXA) in trauma
- Discuss the benefits and risks of TXA
- Identify barriers for the use of TXA
Oncologic Emergencies

Metabolic
- Hypercalcemia
- SIADH
- Tumor Lysis Syndrome

Hematologic
- Febrile Neutropenia
- Hyperviscosity Syndrome
- DIC

Structural
- Spinal cord compression
- Malignant pericardial effusion
- Superior vena cava syndrome
- Increased ICP

Treatment related
- Extravasation
- Infusion reaction
Objectives

Identify common oncologic emergencies and care to initiate in the ER, urgent care, or clinic prior to admission

Discuss care for metabolic, structural, and infectious emergencies specific to oncology patients

Contrast how the care of neutropenic patient differs from that of an immunocompetent patient with SIRS/Sepsis

Identify neutropenic patients appropriate for outpatient antimicrobial care

Identify key points specific to cancer treatment that may impact ED care
Cancer Care Key Points: Trends in Therapy

Targeted therapy
- Specific gene mutations in cancer genetics
- Gene sequencing

Immunotherapy
- Ipilimumab (Yervoy)
  - Started in Melanoma treatment, now being widely used for many oncologic/hematologic malignancies
- Nivolumab
- Pembrolizumab (Pembro)

Traditional chemotherapy (key points)
# Cancer Care Key Points: Immune-mediated Adverse Reactions

<table>
<thead>
<tr>
<th>System</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI</td>
<td>Enterocolitis, Pancreatitis</td>
</tr>
<tr>
<td>ENDOCRINE</td>
<td>Hypopituitarism, Adrenal insufficiency, hyper- or hypothyroidism, thyroiditis</td>
</tr>
<tr>
<td>SKIN</td>
<td>Dermatitis, psoriasis, leukocytoclastic vasculitis</td>
</tr>
<tr>
<td>NEURO</td>
<td>Sensory/Motor Neuropathy, Guillain-Barre Syndrome, Myasthenia Gravis, Polymyositis</td>
</tr>
<tr>
<td>LIVER</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>HEME</td>
<td>Hemolytic anemia</td>
</tr>
<tr>
<td>CV</td>
<td>Angiopathy, myocarditis, pericarditis, temporal arteritis, vasculitis</td>
</tr>
<tr>
<td>OCULAR</td>
<td>Blepharitis, conjunctivitis, episcleritis, iritis, scleritis, uveitis</td>
</tr>
<tr>
<td>ID</td>
<td>Meningitis</td>
</tr>
<tr>
<td>MSK</td>
<td>Arthritis, polymyalgia rheumatic</td>
</tr>
<tr>
<td>RENAL</td>
<td>Nephritis</td>
</tr>
<tr>
<td>PULM</td>
<td>Pneumonitis</td>
</tr>
</tbody>
</table>

**TREATMENT:** CORTICOSTEROIDS 1-2mg/kg/day

For severe or life-threatening symptoms until symptoms improve, then slow taper.
# Cancer Care Key Points: Toxicity Grading Criteria

http://www.eortc.be/services/doc/ctc/

<table>
<thead>
<tr>
<th>Gastrointestinal disorders</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adverse Event</strong></td>
<td><strong>1</strong></td>
</tr>
<tr>
<td><strong>Diarrhea</strong></td>
<td>Increase of &lt;4 stools per day over baseline, mild increase in ostomy output compared to baseline</td>
</tr>
<tr>
<td><strong>Definition:</strong> A disorder characterized by frequent and watery bowel movements.</td>
<td></td>
</tr>
<tr>
<td><strong>Dry mouth</strong></td>
<td>Symptomatic (e.g., dry or thick saliva) without significant dietary alteration; unstimulated saliva flow &gt; 0.2 ml/min</td>
</tr>
<tr>
<td><strong>Definition:</strong> A disorder characterized by reduced salivary flow in the oral cavity.</td>
<td></td>
</tr>
<tr>
<td><strong>Duodenal fistula</strong></td>
<td>Asymptomatic; clinical or diagnostic observations only; intervention not indicated</td>
</tr>
<tr>
<td><strong>Definition:</strong> A disorder characterized by an abnormal communication between the duodenum and another organ or anatomic site.</td>
<td></td>
</tr>
</tbody>
</table>
Cancer Care Key Points: Diagnosing Cancer in the ER

Referral to Oncologist
- Urgency depends on clinical presentation
- Send records/imaging

Arrange a biopsy

Life expectancy
- Difficult to discuss unless you know type and stage of cancer
- Home health vs palliative care vs hospice

NCCN guidelines
Cancer Care Key Points: NCCN Guidelines

NCCN.org
FREE
Patient or Provider
Cancer site specific guidelines
- Disease information
- Work-up
- Staging
- Treatment

Invasive Breast Cancer

CLINICAL STAGE

WORKUP
- History and physical exam
- Diagnostic bilateral mammogram; ultrasound as necessary
- Pathology review
- Determination of tumor estrogen/progesterone receptor (ER/PR) status and HER2 status
- Genetic counseling if patient is at high risk for hereditary breast cancer
- Breast MRI (optional), with special consideration for mammographically occult tumors
- Fertility counseling if premenopausal
- Assess for distress

For clinical stage I-IIA, consider additional studies only if directed by signs or symptoms:
- CBC
- Liver function tests and alkaline phosphatase
- Bone scan indicated if localized bone pain or elevated alkaline phosphatase
- Abdominal and pelvic diagnostic CT or MRI indicated if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, or abnormal physical examination of the abdomen or pelvis
- Chest diagnostic CT (if pulmonary symptoms present)

If clinical stage IIIB (T3, N1, M0) consider:
- CBC
- Liver function tests and alkaline phosphatase
- Chest diagnostic CT
- Abdominal and pelvic diagnostic CT or MRI
- Bone scan or sodium fluoride PET/CT (category 2B)
- FDG PET/CT (optional, category 2B)
Cancer Care Key Points: Discussing New Diagnosis

**Setting**
Ensure patient privacy. Review your communication plan before entering the room.

**Perception**
Find out what the patient’s Perception and understanding of his or her condition is. Pay attention to the patient’s words. Make a mental note of the discrepancies between medical facts and patient’s perspective.

**Invitation**
Obtain a clear Invitation by the patient to give the information: “How would you like me to handle the information that we will obtain from these tests?”; “Are you the sort of person who wants all the details on their condition?”

**Knowledge**
Use the patient’s current understanding of his or her condition as a starting point to provide Knowledge and medical facts. Use the same level of language as the patient uses. Give the information in small chunks. Check for patient understanding at each step.

**Empathy**
Be Empathic: “This must be very hard for you.” Recognize that crying and anger are normal responses when receiving bad news. Provide realistic hope: “You will survive the best available treatment.”
Cancer Care Key Points: Increased ICP

Pt with primary or metastatic CNS disease

Sudden increased lethargy, confusion, AMS
  ◦ Evaluate for recent steroid taper

Treat underlying cause: chemo, resume steroids, XRT, surgery

Seizure prophylaxis
Case Study: Febrile Neutropenia (FN) (inpatient)

44yo man with Ewing sarcoma, currently receiving chemotherapy and abdominal radiation

Chemotherapy: Ifosfamide/Etoposide with Neulasta on day 5

Presents on day 8 with nausea, vomiting, dizziness, got 2L IVF in radiation department for dehydration, but BP still low

Reports shaking chills and night sweats x2 days, no clear fever

Dehydrated, sleeping a lot, near-syncopal episodes

VS- T 36.6, HR 117, RR 14, BP 88/49

Chem panel unremarkable (Na 135)

CBC- WBC 0.12, Hgb 10.7, HCT 30.2, PLT 48, ANC 0
Febrile Neutropenia Key Points

Sepsis protocols and EMR triggers may not identify patients
- FN= SIRS
- Time to Nadir

Typical Patient
- Fever 7-10 days after myelosuppressive chemotherapy
- Post radiation therapy (pelvis/spine)
- Low-grade fever w/ or w/o other localizing symptoms

Neutropenia= ANC <1000
Severe Neutropenia= ANC< 500
mEWS (modified Early Warning System)

<table>
<thead>
<tr>
<th>Measure</th>
<th>3</th>
<th>2</th>
<th>1</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature</td>
<td>35.1-36.0</td>
<td>36.1-38.0</td>
<td>38.1-39.0</td>
<td>39.1-42.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>6-8</td>
<td>9-11</td>
<td>12-20</td>
<td>21-25</td>
<td>26-30</td>
<td>31-40</td>
<td></td>
</tr>
<tr>
<td>Pulse</td>
<td>30-40</td>
<td>41-50</td>
<td>51-100</td>
<td>101-110</td>
<td>111-130</td>
<td>131-160</td>
<td></td>
</tr>
<tr>
<td>Systolic BP</td>
<td>70-79</td>
<td>81-90</td>
<td>91-100</td>
<td>101-150</td>
<td>151-190</td>
<td>191-220</td>
<td>221-250</td>
</tr>
</tbody>
</table>
Risks for NP patients

Age >65

Comorbidities: DM, organ dysfunction (CHF, COPD, liver disease, etc)

Combination therapy

Break in mucosal barriers

Immune deficits
  ◦ secondary to chemo
  ◦ Decreased phagocytic activity
  ◦ Cancers produce abnormal antibodies
The incidence of toxic effects from chemotherapy increases with age. In a study in 299 postmenopausal women with breast cancer treated with CMF grade 3 neutropenia (ANC 500 $10^6$/L to 1000 $10^6$/L) was twice as common in women aged 65 or older as in younger women. Significant age-related differences were also seen in the rates of grade 3 mucositis and overall grade 3 toxic effects. Adapted from Crivellari et al.[19]
Pathogens Causing NP Fever

Source identified in 30% of cases
- Of those identified 80% arise from normal (endogenous) flora
  - Translocation of GI flora

Gram negative bacteria (40-60%)
- E. coli, Klebsiella, pseudomonas

Gram positive bacteria (5-10%)
- Staph/Strep

Fungi (less common)
- Candida, aspergillus

Viral

Prior to broad spectrum antibiotics, NP fever accounted for 75% of the mortality related to chemotherapy
Treatment

Surviving sepsis guidelines:

- Early goal directed therapy
  - Fluid resuscitation
  - Empiric broad-spectrum antibiotics
    - Gram negative coverage
    - Cefepime or a carbapenem
  - Expand to include gram positive coverage if hypotension, mucositis, central line infection, MRSA colonization
  - Continue abx until NP resolves
  - IDSA guidelines (idsociety.org)
Role of G-CSF

2015 guidelines from ASCO, EORTC, IDSA, and NCCN

Prophylactic use if incidence of FN is 20% or higher with a given regimen

Primary vs secondary prophylaxis

Neulasta vs Neupogen

Bone pain- Antihistamines
Case Study: Febrile Neutropenia (outpatient)

27 year-old woman with Hodgkin’s lymphoma, s/p cycle #6 ABVD, now day #14
Left ear pain x3 days, sinus pressure, fever 101F, left tooth pain/pressure
No OTC meds, only warm salt water gargles
VS- T 37.8C, HR 96, BP 103/74, RR 12, O2 100%
PE: left TM cloudy, left maxillary sinus pain
Labs: WBC 2.8, ANC 600
**MASCC Risk Index**

Identify low risk patients with febrile neutropenia for outpatient treatment

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>WEIGHT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burden of febrile neutropenia with no or mild Symptoms(^1)</td>
<td>5</td>
</tr>
<tr>
<td>No hypotension (systolic BP &gt; 90 mm Hg)</td>
<td>5</td>
</tr>
<tr>
<td>No chronic obstructive pulmonary disease(^2)</td>
<td>4</td>
</tr>
<tr>
<td>Solid tumor or hematological malignancy with no previous fungal infection(^3)</td>
<td>4</td>
</tr>
<tr>
<td>No dehydration requiring parenteral fluids</td>
<td>3</td>
</tr>
<tr>
<td>Burden of febrile neutropenia with moderate Symptoms(^4)</td>
<td>3</td>
</tr>
<tr>
<td>Outpatient status</td>
<td>3</td>
</tr>
<tr>
<td>Age &lt;60 years</td>
<td>2</td>
</tr>
</tbody>
</table>
Outpatient Treatment of FN: MASCC Score

Low-risk patients that are eligible by guidelines to treat OP:

1) MASCC score ≥ 21
2) Expected neutropenia ≤ 7 days
3) ANC > 100
4) Few co-morbidities
5) Able to take PO
6) Socially reliable / live within 1 hour of medical facility
7) Close f/u with PCP/oncologist planned
8) Appropriate support at home
Outpatient Treatment for FN

Typical antibiotics for OP are:

Best evidence: Augmentin 875 PO BID + Cipro 500 PO BID

or Levo 750 PO qDay or Cipro monotherapy 750 PO q12

Or Clinda 300 PO QID if PCN allergy + Cipro 500 PO q12

IV is ok if home infusion feasible (generally for use with other allergies or if previously on FQ prophylaxis)
TIME HEALS ALL WOUNDS?

FALSE.

SEPSIS CAN BE FATAL.
Case Study: Tumor Lysis Syndrome

66 year-old woman with extensive stage small cell lung cancer
Cycle #1 Etoposide and carboplatin
Presents with hypotension
On day 1 chemo developed hyperglycemia (>500) thought to be due to dex, insulin increased
Day 2 developed watery diarrhea (>6BM), none since taking Imodium
Day 3 took her regular Lisinopril 10mg and oxycodone for pain, arrived for appointment BP 70/40

VS- BP 88/37, Pulse 102, Temp 36.7C, Resp 24, SpO2 98%
PE: + **thrush**, **tachycardic**, lungs clear, + **left sided abdominal pain**, 3+ edema LE
## Case Study: PH

<table>
<thead>
<tr>
<th>CBC</th>
<th>WBC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7.3</td>
</tr>
<tr>
<td>Hgb</td>
<td>9.5</td>
</tr>
<tr>
<td>Hct</td>
<td>31%</td>
</tr>
<tr>
<td>PLT</td>
<td>134</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CMP</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>138</td>
</tr>
<tr>
<td>K</td>
<td>4.7</td>
</tr>
<tr>
<td>Cl</td>
<td>102</td>
</tr>
<tr>
<td>CO2</td>
<td>19</td>
</tr>
<tr>
<td>BUN</td>
<td>45</td>
</tr>
<tr>
<td>Crt</td>
<td>1.1</td>
</tr>
<tr>
<td>Glucose</td>
<td>507</td>
</tr>
<tr>
<td>Ca</td>
<td>7.7</td>
</tr>
<tr>
<td>Total Protein</td>
<td>5.3</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.1</td>
</tr>
<tr>
<td>Alk Phos</td>
<td>258</td>
</tr>
<tr>
<td>AST</td>
<td>321</td>
</tr>
<tr>
<td>ALT</td>
<td>111</td>
</tr>
<tr>
<td>Anion Gap</td>
<td>17</td>
</tr>
<tr>
<td>Lactate</td>
<td>4.5</td>
</tr>
<tr>
<td>Uric Acid</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Phos</td>
<td>5.6</td>
</tr>
<tr>
<td>Mag</td>
<td>2.3</td>
</tr>
</tbody>
</table>
Pathophysiology for Tumor Lysis Syndrome

- Cellular breakdown
  - Hyperphosphatemia
  - Calcium-phosphate unbalance
  - arrhythmias

- Neuromuscular irritability
- hyperkalemia

- Purine catabolism
  - Hyperuricemia
  - Precipitated uric acid crystals in renal tubules

- Acute renal failure
- ARF
## Metabolic Derangements

<table>
<thead>
<tr>
<th>Metabolic Parameter</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uric Acid (UA)</td>
<td>$x \geq 8 \text{ mg/dL or}$ 25% increase from baseline</td>
</tr>
<tr>
<td>Potassium</td>
<td>$x \geq 6.0 \text{ mEq/L or}$ 25% increase from baseline</td>
</tr>
<tr>
<td>Phosphorous</td>
<td>$x \geq 6.5 \text{ mg/dL (children)}$, $x \geq 4.5 \text{ mg/dL (adults), or}$ 25% increase from baseline</td>
</tr>
<tr>
<td>Calcium</td>
<td>$x \leq 7.0 \text{ mg/dL or}$ 25% decrease from baseline</td>
</tr>
</tbody>
</table>
TLS: Risk Factors

Initiation of cytotoxic treatment:
- Chemo, XRT, glucocorticoids
- WBC > 50,000
- Baseline elevated uric acid
- Pre-treatment LDH 2x upper normal limit
- Impaired renal function
- Acidic urine
- Volume depletion

Tumor size > 10cm or Chemosensitive tumors:
- Lymphomas
- Leukemia (ALL)
- Breast
- Small cell lung
- CRC
- GI stromal
- Germ cell tumor
Tumor Lysis Treatment: Treat underlying electrolyte abnormality

<table>
<thead>
<tr>
<th>PROBLEM</th>
<th>INTERVENTION</th>
<th>DOSAGES</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal insufficiency and hypovolemia</td>
<td>Intravenous fluids</td>
<td>Normal saline, 3 L/daily</td>
<td>Use with caution if decreased systolic function</td>
</tr>
<tr>
<td></td>
<td>Dialysis</td>
<td></td>
<td>For fluid-unresponsive oliguric renal failure or patients with CHF</td>
</tr>
<tr>
<td>Hyperuricemia</td>
<td>Allopurinol</td>
<td>100 mg/m² per dose orally every 8 h (maximum daily dose: 800 mg)</td>
<td>Drug-drug interactions with 6-MP and azathioprine; only effective for prophylaxis</td>
</tr>
<tr>
<td></td>
<td>Rasburicase</td>
<td>0.15-0.2 mg/kg/d iv</td>
<td>Contraindicated in pregnancy and G6PD deficiency; costly</td>
</tr>
<tr>
<td>Hyperphosphatemia</td>
<td>Minimize phosphate intake</td>
<td>Minimal consumption of dairy and bread products</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Phosphate binders (aluminum hydroxide or aluminum carbonate)</td>
<td>30 mL orally every 6 h</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dialysis</td>
<td></td>
<td>If no response to oral therapy</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>Insulin (regular)</td>
<td>10 U iv</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dextrose</td>
<td>50 mL of 50% dextrose iv push, then infuse 50-75 mL of 10% dextrose over 1 h</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Albuterol</td>
<td>20 mg nebulized</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dialysis</td>
<td></td>
<td>If no response to other therapy</td>
</tr>
<tr>
<td></td>
<td>Calcium gluconate</td>
<td>1000 mg iv</td>
<td>If hyperkalemic EKG changes are noted</td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>Calcium gluconate</td>
<td>1000 mg iv (no faster than 200 mg/min)</td>
<td>Use with caution in severe hyperphosphatemia</td>
</tr>
</tbody>
</table>
Case Study: Hypercalcemia

SC- 55 year-old man with abdominal/liver mesothelioma most recently received liver directed therapy

Presenting symptoms: nausea, fatigue, constipation, confusion

<table>
<thead>
<tr>
<th>CMP</th>
<th>Na</th>
</tr>
</thead>
<tbody>
<tr>
<td>K</td>
<td>4.2</td>
</tr>
<tr>
<td>Cl</td>
<td>95</td>
</tr>
<tr>
<td>CO2</td>
<td>27</td>
</tr>
<tr>
<td>BUN</td>
<td>15</td>
</tr>
<tr>
<td>Crt</td>
<td>0.85</td>
</tr>
<tr>
<td>Glucose</td>
<td>151</td>
</tr>
<tr>
<td>Ca</td>
<td>14</td>
</tr>
<tr>
<td>Total Protein</td>
<td>6.7</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.9</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>0.6</td>
</tr>
<tr>
<td>Alk Phos</td>
<td>271</td>
</tr>
<tr>
<td>AST</td>
<td>35</td>
</tr>
<tr>
<td>ALT</td>
<td>24</td>
</tr>
<tr>
<td>Phos</td>
<td>2.5</td>
</tr>
<tr>
<td>PTH</td>
<td>&lt;4</td>
</tr>
<tr>
<td>PTHrp</td>
<td>34 (0-0.2)</td>
</tr>
</tbody>
</table>
Hypercalcemia

Most common onc emergency; occurs in 10-20% of patients with cancer

90% of the time hypercalcemia is caused by

- **hyperparathyroidism** (long-standing asymptomatic)
- **malignancy** (higher Ca concentrations, symptomatic)

Normal Calcium

- 8.4-10.2 mg/dl

Hypercalemia:

- Serum Calcium > 10.3mg/dl
- Ionized Calcium >5.2mg/dl
Hypercalcemia Pathophysiology

Bone destruction from tumor invasion
  ◦ Tumors cells release osteoclast activating factor > bone breakdown > release of Ca

Tumor secretion of PTH (parathyroid hormone) & PTHrp
  ◦ Causes increased osteoclast activity
  ◦ Paraneoplastic phenomena
Cancers Associated with Hypercalcemia

*MULTIPLE MYELOMA

Any cancer with bony metastasis
- Breast cancer
- Lung cancer
- Head and neck cancers
- Renal cancer
  (potentiated by inability to excrete Ca)
- Lymphoma/leukemia
Clinical Manifestations

Ca <12 often asymptomatic

Ca 12-14 polyuria, polydipsia, anorexia, nausea, constipation, bradycardia

Ca >14 weakness, difficulty concentrating, confusion, stupor, coma, diaphragm paralysis, vent arrhythmias, asystole

Neuropsych: anxiety, depression, cognitive dysfunction, confusion, stupor, coma

GI: constipation, Nausea, anorexia (2/2 decreased smooth muscle tone and/or abnormal autonomic function)

Renal: polyuria (2/2 decreased concentrating ability of distal tubule), nephrolithiasis, acute and chronic renal insufficiency

CV: acute increase in Ca shortens myocardial action potential (shortens QT and lengthens ST)

MSK: weakness, bone pain
# Hypercalcemia Treatment

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>USUAL DOSAGE</th>
<th>POINTS TO REMEMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hydration:</strong> Correct volume depletion due to hypercalcemia induced urinary salt wasting and vomiting, improves renal clearance of Ca.</td>
<td>Normal Saline Rapid infusion 300-500cc/hr until euvolemic</td>
<td>Use caution in patients with heart failure</td>
</tr>
<tr>
<td>Furosemide</td>
<td>20-40mg IV every 12-24 hours</td>
<td>Only after adequate hydration</td>
</tr>
<tr>
<td><strong>Calcium Regulator:</strong> Increases Renal calcium excretion &amp; decreases bone resorption</td>
<td>Calcitonin 4-8 IU/kg SQ or IV every 12 hours</td>
<td>Tachyphylaxis occurs quickly, slow onset (lowers Ca 1-2 mg/dL within 4-6 hours of admni.</td>
</tr>
<tr>
<td><strong>Bisphosphonates:</strong> Anti-resorptive therapy</td>
<td>Pamidronate 60-90mg IV q3-4 week (infuse over 4-6 hours)</td>
<td>Adjust infusion time to creatinine clearance</td>
</tr>
<tr>
<td>Zometa (Zoledronic Acid)</td>
<td>4mg IV q4-6 weeks (infuse over 15 min)</td>
<td>Consider alternative treatment in pt. with renal failure</td>
</tr>
<tr>
<td>Xgeva (Denosumab)</td>
<td>120mg SQ q4week</td>
<td>Approved for the prevention of skeletal-related events from bone metastasis</td>
</tr>
<tr>
<td><strong>Dialysis</strong></td>
<td>Last resort</td>
<td>Using dialysate without calcium in it</td>
</tr>
</tbody>
</table>
Case Study: Spinal Cord Compression

72 year-old woman with metastatic breast cancer, on oral chemotherapy

Known bone mets

Presents with hip pain with radiculopathy after aggressive PT session, happened previously and symptoms resolved, xray showed facet arthropathy, scattered (known) metastatic foci

managed conservatively (NSAIDS, oxycodone, rest)

2 weeks later re-presented with worsening low back/right hip pain now with complete numbness of leg, and RLE weakness, no bowel bladder dysfunction
Spinal Cord Compression

Definition: spinal cord compromise secondary to the spread of cancer to the vertebral bodies followed by expansion into the spinal canal or ischemia of the spinal cord
- Direct invasion of tumor
- Retropulsion of bone fragments
Spinal Cord Compression Key Points

Primary tumors of spinal cord (astrocytoma, glioma)

Spinal cord metastasis (lymphoma)

Vertebral metastasis
- Breast cancer
- Lung cancer
- Prostate cancer

SCC should be on differential list in any patient with cancer complaining of back pain with neurologic deficits

If chronic, often patient will tolerate back pain and not report problems until there is a neurologic deficit
Spinal Cord Compression Management

Diagnostic Imaging: Spine MRI w/ & w/o contrast

Treatment:
- Steroids
- IV dexamethasone bolus followed by 4-8mg IV Q6

Neurosurgery
Radiation Therapy
Rehabilitation

Interventions are directed at preserving function
Case Study: Superior Vena Cava Syndrome

60 year-old man with lymphoma, completed chemotherapy and achieved a CR 8 months ago

Presents with upper extremity swelling, shortness of breath, has right upper chest port that has not been flushed for months

PE- development of collateral circulation visible on right upper chest

Figure 2. Venous Circulation Including the Superior Vena Cava
Superior Vena Cava Syndrome (SVCS): Compression of the SVC from tumor, enlarged LN or thrombosis

<table>
<thead>
<tr>
<th>Clinical Manifestations:</th>
<th>Symptoms:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea,</td>
<td>Cough</td>
</tr>
<tr>
<td>UE swelling</td>
<td>chest pain</td>
</tr>
<tr>
<td>Facial/periorbital edema</td>
<td>Hoarseness</td>
</tr>
<tr>
<td>Jugular venous distention</td>
<td>nasal stuffiness</td>
</tr>
<tr>
<td></td>
<td>Epistaxis</td>
</tr>
<tr>
<td></td>
<td>visible veins on chest/breast</td>
</tr>
<tr>
<td></td>
<td>breast swelling</td>
</tr>
</tbody>
</table>
Figure 1. Photographs of the patient showing the reduction in swelling of the face, neck and upper extremities (A) At initial presentation and (B) after treatment (hospital day 8).

www.nature.com
Treatment

ABCs (emergent/urgent)

Treat underlying disease
- XRT (radiation therapy)
- Chemotherapy
- Treatment of thrombosis
  - ??? Remove central line
- Steroids
- Stenting
- Surgery

Comfort measures: elevate HOB, avoid straining/Valsalva maneuver
Infusion Reactions: Hypersensitivity vs Anaphylactic

- **Anaphylaxis** - severe allergic reaction that may cause death
  - Platinum Drugs/Taxanes
- **Acute illness minutes to hours** after offending exposure
- 2 or more of the following
  - Involve of skin/mucosa (hives/angioedema)
  - Respiratory compromise (dyspnea, wheezing)
  - Reduced BP or syncope
  - GI symptoms (abd pain, diarrhea, emesis)

- **Hypersensitivity** - mild to severe symptoms
  - Flushing, rigors, shortness of breath, etc
  - cyclophosphamide, ixabepilone, bleomycin, L-asparaginase, monoclonal ab - Rituxan
Hypersensitivity Reaction Protocol

1. **STOP INFUSION** for Severe hypersensitivity reaction (difficulty breathing, face/throat/tongue swelling or syncope).

2. If loss of BP, pulse or consciousness: **CALL CODE STAT 1-2222**

3. For **SEVERE** reactions (difficulty breathing, face/throat/tongue swelling or syncope) **call a RRT (1-2222)** tell operator you need the RRT Team and Respiratory Therapy and immediately institute the following:
   - Obtain vital signs including continuous pulse oximetry
   - Place in supine position if hypotensive
   - Place on continuous pulse oximetry
   - Run oxygen at 10 liters/min per simple mask
   - Have crash cart at bedside, set up suction
   - Hang 1 liter normal saline wide open
   - Establish second IV site (18 gauge)
   - nebulizer

4. If difficulty breathing, face/throat, tongue swelling, syncope, and start algorithm:
   - Place patient on analyze mode of automatic external defibrillator
   - EpiPen 0.3 mg IM into thigh x 1
   - Diphenhydramine 50 mg IV x 1
   - Methylprednisolone 125 mg IV x 1
   - Albuterol 2.5 mg x1 via nebulizer
   - Famotidine 20 mg IV x 1

5. Document:
   - Second RN records name, dose, and time of every medication administered
   - Record BP, pulse, and O2 sat q’5 minutes

6. Re-assess:
   - If improving, continue to monitor
   - If worsening and physician not yet present, CALL CODE
   - After 1st EpiPen, if respiratory distress or hypotension persists for > 10 minutes, repeat EpiPen 0.3 mg IM x 1 into thigh

7. For MD consideration in cases of refractory anaphylaxis (MD should be present)
   - Repeat nebulizer(s) per MD if respiratory distress continues, consider racemic epinephrine 0.5 ml x 1 vial
Extravasation

Unintended leakage of chemotherapy drug into the extravascular space

Frequency: 0.1%-6% of peripheral IV infusions
  ◦ 1 million infusions/day= 1,000-60,000 extravasation events daily

Acute: swelling, redness, pain, tissue injury

Late: fibrosis, atrophy, local sensory disturbance, pain

Need Wound/Burn Clinic follow-up
Extravasation Example

Day 40 After Extravasation
Extravasation Example

Day 90 After Extravasation
Extravasation Example

Day 110 After Extravasation
# Example of Common Vesicants and Irritants

<table>
<thead>
<tr>
<th>VESICANT</th>
<th>COMMONLY USED TREATMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthracyclines</td>
<td>Dexrazoxane, topical DMSO, topical cooling</td>
</tr>
<tr>
<td>Daunorubicin, doxorubicin,</td>
<td></td>
</tr>
<tr>
<td>epirubicin, idarubicin,</td>
<td></td>
</tr>
<tr>
<td>mitomycin C</td>
<td></td>
</tr>
<tr>
<td>Vinca alkaloids</td>
<td>Topical warming, subcutaneous hyaluronidase</td>
</tr>
<tr>
<td>Vincristine, vinblastine,</td>
<td></td>
</tr>
<tr>
<td>vinorelbine</td>
<td></td>
</tr>
<tr>
<td>Mitomycin C</td>
<td>Topical cooling, topical DMSO</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IRRITANTS</th>
<th>COMMONLY USED TREATMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taxaneşs</td>
<td>Topical cooling, subcutaneous hyaluronidase</td>
</tr>
<tr>
<td>Docetaxel, paclitaxel</td>
<td></td>
</tr>
<tr>
<td>Platinumşs</td>
<td>Topical cooling, subcutaneous hyaluronidase</td>
</tr>
<tr>
<td>Carboplatin, cisplatin</td>
<td></td>
</tr>
<tr>
<td>Epipodophyllotoxins</td>
<td>Topical warming</td>
</tr>
<tr>
<td>Etoposide, teniposide</td>
<td></td>
</tr>
<tr>
<td>Topoisomerase I inhibitors</td>
<td>Topical cooling</td>
</tr>
<tr>
<td>Irinotecan, topotecan</td>
<td></td>
</tr>
</tbody>
</table>
References:

Mulitnational Association of Supportive Care in Cancer- MASCC Index
http://www.mascc.org/mascc-fn-risk-index-score


The Geriatric Patient: Equal Benefit from Equal Treatment. Cancer Control. 2001;8(2s). Lodovico Balducci, MD

UpToDate: use of G-CSF in adult patients with chemo-induced neutropenia

http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#site
http://www.eortc.be/services/doc/ctc/ (NCI toxicity grading criteria)
Questions???
TRANEXAMIC ACID IN TRAUMA: WHAT IS IT AND WHY DON’T WE USE IT?

Laura MacCall, PharmD
PGY2 Pharmacy Resident, Emergency Medicine
Intermountain Medical Center
OBJECTIVES

- Describe the use of tranexamic acid (TXA) in trauma
- Explain the benefits and risks of TXA
- Identify barriers for use of TXA
Disclosures

- I have no relevant financial disclosures
- Off-label uses of TXA will be discussed
Tranexamic Acid (TXA)
Tranexamic Acid (TXA)

- 1 g IV x 1, then 1 g IV over 8 hours
- Give within 3 hours of injury for best result
<table>
<thead>
<tr>
<th>Hemostatic agent</th>
<th>Supply cost ($)</th>
<th>Cost per dose ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TXA 1 g</td>
<td>41</td>
<td>116</td>
</tr>
<tr>
<td>VIIa 2 mg</td>
<td>3800</td>
<td>5800</td>
</tr>
<tr>
<td>4-factor PCC 2500 units</td>
<td>3800</td>
<td>7200</td>
</tr>
<tr>
<td>3-factor PCC 2500 units</td>
<td>2200</td>
<td>3500</td>
</tr>
</tbody>
</table>
• 274 hospitals in 40 countries
• Use of TXA within 8 hours of injury
• Primary outcome: Death within 4 weeks of injury
• Significant reduction in all-cause mortality
• No increase in thrombotic events
• NNT= 67
MATTERS

• Military trial: retrospective
• 1 g TXA
• Primary outcome: death at 24 and 48 hours, in-hospital

• Results
  • Significant reduction in mortality at 48 hours and in-hospital
  • More thromboembolic events with TXA
  • NNT=7
TRANMAN
FUTURE DIRECTIONS

PATCH

Prehospital anti-fibrinolytics for traumatic coagulopathy and haemorrhage

CRASH 3

STAAMP

Study of tranexamic acid during air medical prehospital transport trial
CONCLUSION

ITLS believes that there is sufficient evidence to support the use of TXA in the management of traumatic hemorrhage, pursuant to system medical control approval. Following initial resuscitation including control of external bleeding and stabilization of airway, consideration should be given to administration of TXA during early stages of transport.
REAL WORLD

Cabarrus County, North Carolina
IHC UCR Massive Transfusion Protocol

Start Here
Draw Trauma Lab Panel A

Initiate Transfusion

Massive transfusion protocol needed?

If within 3 hours of injury
TXA 1 gram IV over 10 min.
Followed by TXA 1 gram IV
over 8 hours

Return unused blood products to transfusion.

Don't return blood products to transfusion

Done

Rapid TEG (R-TEG) Directed Transfusion

8.47 ± 1.88 seconds

Transfuse FFP

If Platelet count ≤ 40 x10^9/L

Transfuse cryoprecipitate

If Pt. develops DIC

Transfuse platelets

Return to R-TEG Directed Transfusion

Continue MTP

In case of massive hemorrhage

Consider DDAVP 0.3 mg/kg IV

Start here

Start here

Draw Trauma Lab Panel A

Done

Return unused blood products to transfusion.

Massive transfusion protocol needed?

If within 3 hours of injury
TXA 1 gram IV over 10 min.
Followed by TXA 1 gram IV
over 8 hours

Initiate Transfusion
So why don’t we use TXA?

- Inexpensive
- Easy to administer
- Relatively safe
- Saves lives!
ANY EVENT OF THIS SCALE IS UPSETTING. BUT WE HAVE A GREAT TEAM HERE AND EVERYONE HAS GIVEN THEIR BEST.

EARLY ADMINISTRATION OF THE CLOT STABILISER, TRANEXAMIC ACID, HAS HELPED. WE DON’T SEE ANYTHING NEAR AS MUCH COAGULOPATHY AS WE WOULD HAVE JUST A YEAR AGO.
TRANEXAMIC ACID IN TRAUMA: WHAT IS IT AND WHY DON’T WE USE IT?

Laura MacCall, PharmD
PGY2 Pharmacy Resident, Emergency Medicine
Intermountain Medical Center