Pharmacologic Management of Trauma and Surgical Patients

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IV FLUIDS

- Lactated ringers (LR) preferred over normal saline (NS) in surgical patients
  - LR cannot be run in same line as blood (incompatible)
  - Exception: NS or Plasma-Lyte preferred over LR in TBI patients
- NS is associated with worse outcomes including:
  - Hyperchloremic metabolic acidosis
  - Hyperkalemia
  - Postoperative infection
  - Increased blood transfusion
  - Decreased renal blood flow and renal injury
  - Mortality

	pH	mOsm/L	Na+ (mEq/L)	Cl- (mEq/L)	K+ (mEq/L)	Ca++ (mEq/L)	Lactate (mEq/L)	Acetate (mEq/L)	Gluconate (mEq/L)
NS	**5.6**	**308**	**154**	**154**	**-**	**-**	**-**	**-**	**-**
LR	**6.6**	**274**	**130**	**109**	**4**	**3**	**28**	**-**	**-**
Plasma-Lyte	**7.4**	**294**	**140**	**98**	**5**	**-**	**-**	**27**	**23**

**Hyperkalemia is NOT a contraindication to giving LR or Plasma-Lyte*

SURGICAL ANTIMICROBIAL PROPHYLAXIS

Open Extremity Fractures

Fracture Type	Classification	Antibiotic Coverage
Type I	Open with skin wound < 1 cm in length and clean	1st generation cephalosporin (cefazolin)
Type II	Open with laceration > 1 cm in length without extensive soft tissue damage, flaps, or avulsions	1st generation cephalosporin (cefazolin) ± aminoglycoside (gentamicin) once daily†
Type III	> 10 cm wound with extensive soft tissue injury or a traumatic amputation	1st generation cephalosporin (cefazolin) ± aminoglycoside (gentamicin) once daily†
Type IIIa	Adequate soft tissue coverage	
Type IIIb	Significant soft tissue loss with exposed bone requiring tissue transfer to achieve coverage	
Type IIIc	Vascular injury requiring repair for limb preservation	

*PCN allergy: may consider vancomycin in place of cephalosporin

†Aminoglycoside not routinely used – orthopedic surgeon discretion if dirty wound

High dose penicillin should be added if fecal or potential clostridial contamination (farm-related injury)

- Continue antibiotics for not longer than 24 hours after soft tissue coverage achieved
- Ciprofloxacin offers no advantage to cephalosporin/aminoglycoside regimen and may have detrimental effect on healing and higher infection rates in type III fractures

Penetrating Abdominal Trauma

- A single dose should be given preoperatively
- Absence of hollow viscous injury → no further administration
- Presence of hollow viscous injury → antibiotics continued for only 24 hours postoperatively

Antibiotic	Dose	Intraoperative Re-Dosing Interval*	
Piperacillin/tazobactam	3.375 g IV	CrCl > 40 mL/min	Q2H
		CrCl 20-40 mL/min	Q4H
		CrCl < 20 mL/min	Q6H
		Intermittent Dialysis	–
β-Lactam Allergy			
Ciprofloxacin + Metronidazole	400 mg IV + 500 mg IV	No re-dosing	

*Re-dosing should not exceed 4 doses; re-dosing should occur after every 1 L of blood

PAIN, SEDATION, AND DELIRIUM

Pain Management

Generic (Trade)	Dose	Onset	Duration	Hemodynamic Effect	Clinical Pearls
Fentanyl	IV: 25-100 mcg Q1-2 hr CI: 25-200 mcg/hr	30 sec	30-60 min	Relatively neutral, some bradycardia	Preferred agent for CI No active metabolites
Hydromorphone (Dilaudid®)	PO: 2-4 mg Q4-6 hr IV: 0.5-2 mg Q3-6 hr CI: 0.5-1 mg/hr	PO: 15-30 min IV: 5 min	PO: 3-5 hrs IV: 3-5 hrs	Neutral	Better PRN than fentanyl; longer acting
Morphine	PO: 15-30 mg Q4 hr (Q8-12 hr for SR) IV: 2-5 mg Q3-5 hr CI: 5-15 mg/hr	PO: 30 min IV: 5-10 min	PO: 3-4 hr IV: 3-4 hr	Circulatory depression	Active metabolite (renally excreted) Histamine release can cause itching/hypotension
Oxycodone (Oxycontin®)	PO: 5-15 mg Q4-6 hr	15-30 min	4-6 hr	Neutral	Preferred use as PRN when on scheduled APAP
Oxycodone/APAP (Percocet®)	PO: 1-2 tab (5/325 mg) Q4-6 hr	15-30 min	4-6 hr	Neutral	Preferred at discharge so patient receives APAP
Hydrocodone/APAP (Lortab®)	PO: 1-2 tab (5/325 mg) Q4-6 hr	60 min	4-6 hr	Neutral	Preferred at discharge so patient receives APAP
Ketorolac (Toradol®)	IV: 15 mg Q6 hr	30 min	4-6 hr	Neutral	MAX duration 5 days (longer use contraindicated) Increased risk of GI bleeds Contraindicated in advanced renal impairment, concomitant use of other NSAIDs
Acetaminophen (Tylenol®)	PO: 650-975 mg Q6-8 hr PR: 650 mg Q4-6 hr IV: 1000 mg Q6-8 hr	PO/PR: < 1 hr IV: 5-10 min	PO/PR: 4-6 hr IV: 4-6 hr	Neutral	Max of 4 g/day unless elderly or hepatic impairment (then use max 3 g/day)

CI = continuous infusion; SR = sustained release

IV Acetaminophen is EXTREMELY expensive – please only use when oral or rectal administration is contraindicated!

Equivalent Analgesic Dosing

Opioid	IV	Oral
Codeine	**120 mg**	**200 mg**
Fentanyl	**0.1 mg (100 mcg)**	**N/A**
Hydrocodone	**N/A**	**30 mg**
Hydromorphone	**1.5 mg**	**7.5 mg**
Methadone	***Contact Pharmacy***	
Morphine	**10 mg**	**30 mg**
Oxycodone	**N/A**	**20 mg**

- Tolerance to one opioid does not mean tolerance to all opioids
- When converting from one to another, decrease dose ~25-50%
- Always have PRN agent available when titrating to account for difference in doses

Sedative Agents

Generic (Trade)	Dose	Onset	Duration	Hemodynamic Effect	Clinical Pearls
Propofol (Diprivan®)†	CI: 5-80 mcg/kg/min	30 sec	3-10 min	Bradycardia Hypotension	Provides 1.1 kcal/mL Doses > 80 mcg/kg/min associated with PRIS
Dexmedetomidine (Precedex®)†	CI: 0.3-1.5 mcg/kg/hr	5-10 min	60-120 min	Bradycardia Hypotension Rebound HTN	Lighter level of sedation Expensive (10x cost of propofol) No respiratory depression
Lorazepam (Ativan®)	PO: 2-4 mg Q4-6 hrs IV: 2-4 mg Q2-6 hrs	PO: 30-60 min IV: 5-20 min	6-8 hrs	Some hypotension	No active metabolite
Midazolam (Versed®)	IV: 2-5 mg Q1-2 hrs CI: 2-10 mg/hr	3-5 min	1.5-3 hrs	Some hypotension	Active metabolite Highly lipophilic – PK/PD become unpredictable after 48-72 hours

†Preferred sedatives; CI = continuous infusion; PRIS = propofol-related infusion syndrome

BENZODIAZEPINES ARE ASSOCIATED WITH PROLONGED MECHANICAL VENTILATION, INCREASED ICU LENGTH OF STAY, AND INCREASED INCIDENCE AND DURATION OF DELIRIUM – AVOID IF POSSIBLE!!!

- Goal RASS at RIH is -2 to 0 → MUST include titration parameters per The Joint Commission! Include **initial dose**, **goal clinical endpoint** (e.g. RASS or CPOT), **titration amount and frequency**, **maximum rate**.
    - *Propofol example: Initiate at 10 mcg/kg/min. Goal RASS: -2 to 0. If RASS above goal, may increase by 10 mcg/kg/min every 5 minutes to maintain goal RASS. If RASS below goal, stop infusion until RASS goal achieved, then resume at 50% of the previous rate. Maximum dose 80 mcg/kg/min.*

USE TICU/SICU SEDATION ORDER SET FOR PREBUILT ORDER ENTRY WITH TITRATION PARAMETERS.

Management of Delirium

- Common complication in 20-80% of ICU patients
- Associated with increased morbidity and mortality
- Diagnosed via CAM-ICU
- Three types of delirium:

Hyperactive (< 2%)	Hypoactive (44%)	Mixed (54%)
• Agitation • Restlessness • Combative • Attempts to remove tubes/lines	• Quiet • Withdrawn • Flat affect • Lethargy • Decreased responsiveness • Difficult to assess	• Combination of hyper and hypoactive

Step 1: Identify and eliminate potentially contributing factors

- Sepsis
- Shock states
- Glycemic dysregulation
- Electrolyte abnormalities
- Hypoxia
- Dehydration
- Inadequate pain control
- Drug withdrawal
- Lack of continuation of home antipsychotics
- Environmental (sleep deprivation, immobilization, restraints)

Step 2: Implement and/or optimize non-pharmacologic therapy

- Frequent verbal reorientation
- Access to eyeglasses and hearing aids
- Head of bed elevation
- Early mobility, PT/OT when able
- Minimize restraint and foley catheter use
- Maintenance of sleep-wake cycle
- Minimize disturbances at night
- SAT/SBT at least daily

Step 3: Pharmacologic management

- Ensure appropriate pain management
- Discontinue deliriogenic medications (e.g. BZDs, anticholinergics)
- Resume home psychiatric medications
- Treat withdrawal
- Consider antipsychotics:
  - Quetiapine (Seroquel®) 50 mg PO BID to max 400 mg/day
  - Olanzapine (Zyprexa®) 5 mg PO daily to max 10 mg daily
  - Haloperidol (Haldol®) 5 mg IV Q6 hours

STRESS ULCER AND DEEP VENOUS THROMBOSIS PROPHYLAXIS

Indications for Stress Ulcer Prophylaxis

<table>
<tr><th>ASHP Therapeutic Guidelines</th><th>EAST Guidelines</th></tr>
<tr><td>In ICU patients with 1 major criteria:
Mechanical ventilation > 48 hours
Coagulopathy (unrelated to medication)
History of GI ulceration/bleed within 1 year
In ICU patients with 2 minor criteria:
Sepsis
ICU stay > 1 week
Occult or overt bleeding for ≥ 6 days
Corticosteroids (>250 mg hydrocortisone/day)
Special populations (treated as minor criteria):
Head injury with GCS ≤ 10
Thermal injury covering > 35% TBSA
Partial hepatectomy
Postoperative transplant patients
Multiple trauma with ISS ≥ 16
Spinal cord injury</td><td>In all ICU patients with:
Multiple trauma
Sepsis
Acute renal failure
ISS > 15
High dose steroids (>250 mg hydrocortisone/day or equivalent)
In all patients with:
Mechanical ventilation
Coagulopathy
Traumatic brain injury
Major burn injury</td></tr>
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Agents for Stress Ulcer Prophylaxis

- Histamine-2 receptor antagonist (H2RA) preferred over proton pump inhibitors (PPI)
- PPIs have a black box warning for risk of *C. difficile*
- Lack of superiority data of PPI over H2RA for SUP prophylaxis

Drug	Dose	Mechanism
Ranitidine (Zantac®)	IV: 50 mg Q8H PO: 150 mg BID	Histamine-2 receptor antagonist
Pantoprazole (Protonix®)	IV: 40 mg daily PO: 40 mg daily	Proton pump inhibitor
Lansoprazole (Prevacid®)	PO: 30 mg daily	Proton pump inhibitor *preferred for enteral administration

Prevention of VTE in Major Trauma

	CHEST Guidelines	EAST Guidelines
Agent	UFH, LMWH, or mechanical devices recommended over no pharmacologic intervention	LMWH preferred over URH in high risk trauma patients
Mechanical Prophylaxis	Add to pharmacologic prophylaxis in high risk trauma patients	SCDs have not been shown to be superior to no intervention; however, some benefit may be seen in head injury patients
IVC Filters	Not recommended	Considered in very high risk trauma patients: • Who cannot receive anticoagulation because of increased bleeding risk AND • Have injury patterns rendering them immobilized for a prolonged period of time
Doppler Ultrasound	Not recommended	Not recommended

VTE Prophylaxis and Treatment in Trauma Patients

	Prophylaxis	Treatment
Preferred	Enoxaparin 30 mg subQ Q12H	Enoxaparin 1 mg/kg subQ Q12H
Alternate	Heparin 5000 units subQ Q8H	Heparin high dose drip

- Enoxaparin (Lovenox®) BID dosing preferred in trauma patients with CrCl > 30 mL/min
  - Reduce to 30 mg Q24 hours if CrCl < 30 mL/min AND not receiving dialysis
- Heparin preferred for elderly patients with rib fractures and patients receiving dialysis
- Obesity VTE prophylaxis dosing: for patients **≥ 120 kg**:
  - Enoxaparin 40 mg subQ Q12H
  - Heparin 7500 units subQ Q8H