

Caring for Critically Ill Complex Populations: Neurologically Injured, History of Substance Abuse or Obese Patients

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Conflicts of Interest

- None

Learning Objectives-Pharmacists

1. Describe infrequently encountered critically ill patient populations in an ICU: Neurologically Injured, History of Substance Abuse or Obese patients.
2. Identify risk factors for complications for these critically ill special populations.
3. Define pharmacokinetic and pharmacodynamic alterations in these specific patient populations.
4. Outline interventions for critical care pharmacists for these special patient populations.

Learning Objectives-Technicians

1. Identify infrequently encountered critically ill patient populations in an ICU: Neurologically Injured, History of Substance Abuse or Obese patients.
2. List risk factors for complications for these critically ill special populations.
3. State pharmacokinetic and pharmacodynamic alterations in these specific populations.
4. Specify alternate therapies for these special patient populations.



NEUROLOGICAL INJURY & THE ICU

Question

Have you encountered any “neuro” patients in your ICU patient population in the past 30 days?

- a) Yes
- b) No

Question

If yes, approximately how many “neuro” patients do you typically need to verify medications for in your hospital ICU setting daily?

- a) <5 per day
- b) 5 – 10 per day
- c) >10 patients daily

Neurologically Injured Patients in the ICU

- Stroke
 - Ischemic (87%)
 - Hemorrhagic (13%)
- Vascular abnormalities → hemorrhagic stroke
- Traumatic Brain Injury

Ischemic Stroke - Management

- TPA
 - Alteplase
 - Tenecteplase
- Mechanical thrombectomy



Or BOTH

TPA = tissue plasminogen activator

Post Ischemic Stroke -Management

- Post thrombectomy and/or TPA
 - Bleeding – neurological exam q15 mins during and until 2 hours post procedure (or infusion), q30 mins x 6 hours and then QD
 - Maintain BP \leq 180/ 105 mmHg during and up to 24 hours after the procedure
 - Intravenous Therapy
 - Nicardipine/Clevidipine
 - Labetalol
 - Hydralazine



Resume home anti-hypertensives

Seizures Prophylaxis

- Early vs. Late onset
- Can occur for both Hemorrhagic and Ischemic Stroke
- Seizure prophylaxis
 - Moderate - Severe Traumatic Brain Injury = GCS < 8
 - ≤ 7 days

NCS GUIDELINES

Guidelines for Seizure Prophylaxis in Adults Hospitalized with Moderate–Severe Traumatic Brain Injury: A Clinical Practice Guideline for Health Care Professionals from the Neurocritical Care Society



Jennifer A. Frontera^{1,11*†} , Emily J. Gilmore^{2†}, Emily L. Johnson³, DaiWai Olson⁴, Appaji Rayi⁵, Eljim Tesoro⁶, Jamie Ullman⁷, Yuhong Yuan⁸, Sahar F. Zafar⁹ and Shaun Rowe¹⁰

Glasgow Coma Scale		
BEHAVIOR	RESPONSE	SCORE
Eye opening response	Spontaneously	4
	To speech	3
	To pain	2
	No response	1
Best verbal response	Oriented to time, place, and person	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No response	1
Best motor response	Obeys commands	6
	Moves to localized pain	5
	Flexion withdrawal from pain	4
	Abnormal flexion (decorticate)	3
	Abnormal extension (decerebrate)	2
	No response	1
Total score:	<i>Best response</i>	15
	<i>Comatose client</i>	8 or less
	<i>Totally unresponsive</i>	3

TBI Classification based on GCS

Mild: 13 – 15

Moderate: 9 – 12

Severe: 3 – 8

Moderate to Severe TBI?

“we defined moderate – severe TBI as injury with acute radiographic abnormalities (e.g., subarachnoid hemorrhage, subdural or epidural hematoma, contusion, intracerebral hemorrhage, intraventricular hemorrhage, skull fracture) requiring hospitalization.”

NCS Guidelines for Seizure Prophylaxis in Moderate to Severe TBI

	Recommendation	Level of recommendation, quality (certainty) of evidence
PICO 1	Should ASMs versus no ASMs be used in patients hospitalized for moderate–severe TBI with no history of clinical or electrographic seizures?	
Recommendation 1	The NCS guideline panel suggests that either prophylactic ASM (initiated during index hospitalization) or no ASM could be used in patients hospitalized with moderate–severe TBI	<u>Weak recommendation, low quality of evidence</u>
PICO 2	If an ASM is used, should levetiracetam or phenytoin/fosphenytoin be preferentially used for patients hospitalized with moderate–severe TBI with no history of clinical or electrographic seizures?	
Recommendation 2	If a prophylactic ASM is used in patients hospitalized with moderate–severe TBI, the NCS guideline panel suggests levetiracetam should be used rather than phenytoin/fosphenytoin for seizure prophylaxis	<u>Weak recommendation, very low quality of evidence</u>
PICO 3	If an ASM is used, should a long (> 7 days) versus short (≤ 7 days) duration of prophylaxis be used for patients hospitalized with moderate–severe TBI with no history of clinical or electrographic seizures?	
Recommendation 3	If a prophylactic ASM is used in patients hospitalized with moderate–severe TBI, the NCS guideline panel suggests a short duration of use (≤ 7 days) versus a longer duration of use (> 7 days)	<u>Weak recommendation, low quality of evidence</u>

Optimizing Levetiracetam

Dosing

- Loading dose- 750 – 1000 mg
- Maintenance Dose- *750 –1000 mg BID*

“associated with a two-fold increased odds of achieving target drug levels and a 68% lower odds of clinical or electrographic seizure compared to low-dosage LEV (500 mg BID)”
- *Avoid in patients with- depression, agitation, or other psychiatric features*
 - *Alternative-lacosamide*

Post Neurological Injury Seizure Management

- Limited clinical evidence
- One episode vs. multiple episodes
- Most experts → one anti-epileptic medication
- Duration
 - One episode → discontinue on discharge from hospital
 - >1 episode → 3 months
 - Late onset seizures → lifelong antiepileptics

Common drugs may influence motor recovery after stroke

Larry B. Goldstein, MD | [AUTHORS INFO & AFFILIATIONS](#)

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Phenytoin Exposure Is Associated With Functional and Cognitive Disability After Subarachnoid Hemorrhage

Andrew M. Naidech, MD, MSPH; Kurt T. Kreiter, PhD; Nazli Janjua, MD; Noeleen Ostapkovich, MS; Augusto Parra, MD, MPH; Christopher Commichau, MD; E. Sander Connolly, MD; Stephan A. Mayer, MD; Brian-Fred M. Fitzsimmons, MD

Hypertonic Saline

- Bolus
- Continuous infusion
- Various concentrations
 - 1.5%
 - 2%
 - 3%
 - 23.4% (30 ml bolus)
- Volume expander – can worsen heart failure

Peripheral vs. Central Line Administration

Saline Concentration (w/v NaCl)	Approx. Osmolarity (mOsm/L)	Description
0.9% (Normal Saline)	≈ 308 mOsm/L	Isotonic with plasma
1.5% Saline	≈ 512 mOsm/L	Mildly hypertonic
2% Saline	≈ 684 mOsm/L	Hypertonic
3% Saline	≈ 1026 mOsm/L	Strongly hypertonic; used for severe hyponatremia
23.5% Saline	≈ 8040 mOsm/L	Extremely hypertonic; used in small-volume, specialized clinical settings (e.g. intracranial pressure management)

Peripheral line Osmolarity limit <900 mOsm/L



**Emergency Neurological Life Support
Pharmacotherapy Protocol
Version 5.0**

Obtain BMP
Q8-6 hours

Concentration	Dose	Infusion duration
3%	5 ml/kg	5-20 min
5%	3 ml/kg	5-20 min
7.5%	2 ml/kg	5-20 min
23.4%	30 ml	10-20 min

Pediatric considerations:

Hypertonic saline 3%: 2-5 mL/kg over 10-20 min

Hypertonic saline 23.4%: 0.5 mL/kg (max dose: 30 mL)

Mannitol

- Frequently used for neurological emergencies
- Dose 0.5 – 1 g/kg
- Pearls
- Requires in-line filter (precipitates—crystal formation)— may require warming to dissolve crystals before administration
- May be given via peripheral access
- Duration of effect 90 min to 6 h
- Monitor trough osmolar gap (Goal < 20 mOsm/kg)

Osmolar Gap

- Osmolar Gap = Measured Serum Osmolarity - Calculate Osmolarity
- Calculated Osmolarity = $2 \times [\text{Sodium (Na}^+)] + (\text{Glucose} / 18) + (\text{Blood Urea Nitrogen (BUN)} / 2.8)$
- Should be drawn as a trough
- Plasma osmolality of >320 mOsm/kg is not a contraindication of ongoing administration of mannitol
- An osmolar gap of >20 mOsm/kg indicates incomplete drug clearance between doses and increases risk of reverse osmotic shift and nephrotoxicity
- Pearl-OK to administer mannitol of osmolar gap <20 mOsm/kg

Patient Case

32 yr old male, admitted to the ICU post TBI

Patient has received 2 doses of mannitol in the past 24 hours

Patient has a new stat order for mannitol 1g/kg x 1 dose

Laboratory Parameters

Na	154 mEQ/L	BUN	29 mg/dL
K	4.5 mEQ/L	Cr	1.1 mg/dL
Cl	119 mEQ/L	Gluc	188 mg/dL
HCO ₃	18 mEQ/L		
Serum Osmolarity – 341 mOsm/L			

Patient Case

Calculated Osmolarity = $2 \times [\text{Sodium (Na}^+)] + (\text{Glucose} / 18) + (\text{Blood Urea Nitrogen (BUN)} / 2.8)$
Osmolar Gap = Measured Serum Osmolarity - Calculate Osmolarity

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HCO ₃	18 mEQ/L		
Serum Osmolarity – 341 mOsm/L			

1. Determined the Osmolar Gap for this patient?
2. Can this patient receive an additional dose of mannitol?

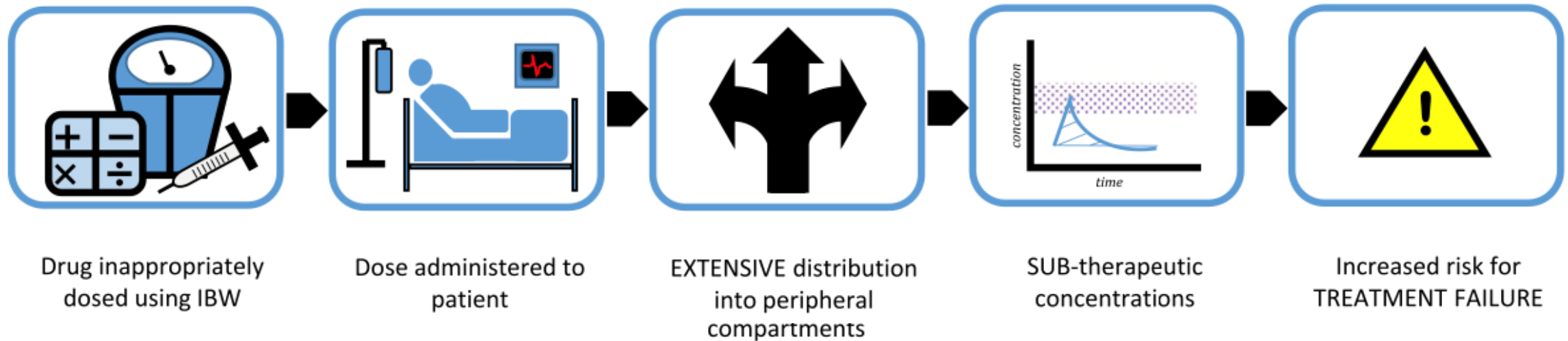
OBESITY & THE ICU



Obesity in America

- Obesity: BMI ≥ 30 kg/m²
 - ~ 40%
- Severe obesity: BMI ≥ 40 30 kg/m²
 - ~ 9.4%

Consequences of Incorrect Dosing



Commonly Use Equations for Weight in Drug Dosing

Weight measure	Equation
Body mass index (kg/m ²)	TBW/height (m) ²
Ideal body weight (kg)	Males: 50 kg + 2.3 kg/inch for height over 5 feet Females: 45.5 kg + 2.3 kg/inch for height over 5 feet
Lean body weight (kg)	Males: (9270 × TBW) / (6680 + 216 × BMI) Females: (9270 × TBW) / (8780 + 244 × BMI)
Adjusted body weight (kg)	CF (TBW – IBW) + IBW, where CF = correction factor (usually 0.4)

Obesity and Drug Dosing

“Designing dosing regimens in the critically ill obese patient requires a detailed understanding of the pharmacokinetic and pharmacodynamic profile of the medication and its impact on obesity coupled with critical illness on physiology and drug Pharmacokinetics...Because of the tremendous variability observed, an individualized dosing approach is preferred.”

Pearls for Obese Patients

Principle	Key Takeaways
Be consistent with weight measurements	Use the same scale and method each time; document whether weight is actual, estimated, or bed scale.
Don't change the dosing weight mid-therapy	Keep the same dosing weight throughout treatment to avoid calculation errors.
Monitor the patient, not just the numbers	Adjust doses based on clinical response and monitoring, not only pharmacokinetic estimates.
Expect variability	Drug distribution and clearance can be unpredictable in obese or critically ill patients—reassess frequently.
Know what drives the dose	Loading dose → depends on volume of distribution (Vd). Maintenance dose → depends on clearance (Cl).
Check risk vs. benefit	Higher doses increase toxicity risk, especially for narrow therapeutic window drugs.
Use tools wisely	Use validated dosing calculators or software; double-check weight units (kg vs lb).
Pick the right weight metric	Choosing the wrong weight (TBW, IBW, AdjBW) causes dosing errors. Hydrophilic drugs → IBW or AdjBW Lipophilic drugs → TBW If unsure → start with AdjBW and monitor.

Select Medications in Obese Patients

- Vasopressors
- Corticosteroids (based on indication)
 - Community acquired pneumonia and Shock – Hydrocortisone <400 mg /day
 - Acute Respiratory Distress Syndrome (ARDS) – Methylprednisolone 1 mg/kg (use IBW or AdjBW)
- Stress Ulcer Prophylaxis
- VTE Prophylaxis
 - Enoxaparin
 - BMI ≥ 40 kg/m² – 40 mg BID
 - BMI ≥ 50 kg/m² – 0.4–0.5 mg/ kg twice daily based on total body weight
 - Heparin –consider increasing dose to 7500 IU Q8H for BMI ≥ 50 kg/m²



PATIENTS WITH SUBSTANCE ABUSE DISORDER

Substance Use Disorder

- Significant impact on on critical illness and post-ICU outcomes
- Types of Substance Use Disorders
 - Alcohol withdrawal
 - Hallucinogen related disorder
 - Cocaine
 - Opioids

Identifying Substance Abuse Disorder in the ICU

- Patients → unable to communicate
- Families can be unaware
- Utox
- Consider detailed history if signs and symptoms of withdrawal

Withdrawal – Signs and Symptoms

Substance	Symptoms
Alcohol	Tremors. Sweating. Severe anxiety. Confusion. Seizures.
Opioids	Diarrhea and vomiting, thermoregulation disturbances, insomnia, muscle and joint pain, anxiety, and dysphoria
Cocaine	Fatigue, vivid dreams, sleep disturbance, increased appetite, agitation
3,4-Methylenedioxymethamphetamine (MDMA)	Serotonin depletion (depressed mood, fatigue)
Synthetic Cannabinoids	Craving, anxiety, tachycardia, hypertension, nausea, tremor, diaphoresis, and nightmares
Synthetic Cathinones “Bath salts”	Depression, anxiety, sleep disorder, paranoia, and cravings,

Pain Management in Patients with Opioid Use Disorder (OUD)

- Misconceptions
 - Medication used for OUD should cover the acute painful condition
 - Pain medications may result in relapse
 - Added opioids are likely to result in central nervous system (CNS) and respiratory depression,
 - Complaints of pain may constitute “drug-seeking” behavior
- Patients with Buprenorphine maintenance therapy
 - Discontinue buprenorphine during acute care
 - Transition to Methadone
 - Change to short acting Buprenorphine with additional opioids for pain
 - Keep maintenance therapy and add short acting opioids for pain management



Conclusion

- Evidence for special populations such as neurologically injured, obese and substance abuse disorder patient populations is always evolving
- Pharmacists and technicians should review key interventions for prevention of complication in these special patient populations
- Pharmacist and pharmacy technicians are key players for ensuring timely delivery of critical medications for these patients



QUESTIONS?