Critical Care Pearls for the General Hospital Pharmacist: A Focus on Prophylactic Medications

Jessica Papke, PharmD PGY-1 Pharmacy Practice Resident Memorial Hospital of South Bend South Bend, Indiana



A webinar for HealthTrust members June 4, 2018



## Disclosures

- This program may contain the mention of drugs or brands presented in a case study or comparative format using evidence-based research. Such examples are intended for educational and informational purposes and should not be perceived as an endorsement of any particular supplier, brand or drug.
- The presenter has no financial relationships with any commercial interests pertinent to this presentation.

## **Pharmacist Objectives**

- Recall the FAST HUG mnemonic for treating patients in an intensive care unit (ICU).
- Identify and recommend therapies for patients who require venous thromboembolism (VTE) prophylaxis in an ICU.
- Recommend therapies for patients who require stress ulcer prophylaxis (SUP) in an ICU.

## Pharmacy Technician Objectives

- Recall the FAST HUG mnemonic for treating patients in an intensive care unit (ICU).
- Identify the different products used for venous thromboembolism (VTE) prophylaxis in an ICU.
- Define the two different classes of medications used for stress ulcer prophylaxis (SUP) in an ICU.



#### Checklists

#### FAST HUG Mnemonic

#### **VTE Prophylaxis**

#### Stress Ulcer Prophylaxis

Why is this important?



### **Causes of Death**





Sources: Kochanek KD et al. Mortality in the United States 2016. Hyattsville, MD: National Center for Health Statistics. 2017. Makary MA, Daniel M. Medical error-the third leading cause of death in the US. BMJ. 2016 May 3;353:i2139.

### **Causes of Death**





Sources: Kochanek KD et al. Mortality in the United States 2016. Hyattsville, MD: National Center for Health Statistics. 2017. Makary MA, Daniel M. Medical error-the third leading cause of death in the US. BMJ. 2016 May 3;353:i2139.

#### Consider...

 What strategies come to mind when you think about improving patient safety and decreasing the rate of mortality due to medical errors?

# The Benefit of Checklists



# Do you use checklists in your life?









THE NEW YORK TIMES BESTSELLER

#### THE CHECKLIST MANIFESTO

HOW TO GET THINGS RIGHT

PICADOR

ATUL GAWANDE BESTSELLING AUTHOR OF BETTER AND COMPLICATIONS

The Checklist Manifesto: How to Get **Things Right** 

**Atul Gawanda** 

Source: https://www.amazon.com/Checklist-Manifesto-How-Things-Right/dp/0312430000



#### SURGICAL SAFETY CHECKLIST (FIRST EDITION)

#### Before induction of anaesthesia **DEFERSION Before skin incision DEFERSION Before patient leaves operating room**

#### SIGN IN



#### TIME OUT

- CONFIRM ALL TEAM MEMBERS HAVE INTRODUCED THEMSELVES BY NAME AND
- SURGEON, ANAESTHESIA PROFESSIONAL AND NURSE VERBALLY CONFIRM

#### ANTICIPATED CRITICAL EVENTS

- SURGEON REVIEWS: WHAT ARE THE CRITICAL OR UNEXPECTED STEPS. OPERATIVE DURATION, ANTICIPATED BLOOD LOSS?
- ANAESTHESIA TEAM REVIEWS: ARE THERE ANY PATIENT-SPECIFIC CONCERNS?
- NURSING TEAM REVIEWS: HAS STERILITY (INCLUDING INDICATOR RESULTS) BEEN CONFIRMED? ARE THERE EQUIPMENT ISSUES OR ANY CONCERNS?
  - HAS ANTIBIOTIC PROPHYLAXIS BEEN GIVEN WITHIN THE LAST 60 MINUTES? NOT APPLICABLE

IS ESSENTIAL IMAGING DISPLAYED?

NOT APPLICABLE

#### SIGN OUT

NURSE VERBALLY CONFIRMS WITH THE TEAM:

- THE NAME OF THE PROCEDURE RECORDED
- THAT INSTRUMENT, SPONGE AND NEEDLE COUNTS ARE CORRECT (OR NOT APPLICABLE)
- HOW THE SPECIMEN IS LABELLED (INCLUDING PATIENT NAME)
- WHETHER THERE ARE ANY EQUIPMENT PROBLEMS TO BE ADDRESSED
- SURGEON, ANAESTHESIA PROFESSIONAL AND NURSE REVIEW THE KEY CONCERNS FOR RECOVERY AND MANAGEMENT **OF THIS PATIENT**

THIS CHECKLIST IS NOT INTENDED TO BE COMPREHENSIVE, ADDITIONS AND MODIFICATIONS TO FIT LOCAL PRACTICE ARE ENCOURAGED.

Source: Haynes AB et al. Safe Surgery Saves Lives Study Group. A surgical safety checklist to reduce morbidity and mortality in a global population. N Engl J Med. 2009 Jan 29;360(5):491-9.

#### A Good Checklist Is:

Short and quick
 Practical
 Focus on top mistakes
 Physically available



# Give your patients a FAST HUG everyday!

# FAST HUG

#### What: Mnemonic

Who: <u>All</u> critically ill patients

When: 2005

Where: Intensive care units (ICU)

Why: Improve patient safety and care!

## Feeding

- 25–30 kcal/kg/day
- Start feedings within 24–48 hours
- Enteral feedings preferred over parenteral feeding
- High dose protein (1.2–2 g/kg/day)



Sources: Vincent JL. Give your patient a fast hug (at least) once a day. Crit Care Med. 2005 Jun;33(6):1225-9

1ξ McClave SA et al., Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically III Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr. 2009 May-Jun;33(3):277-316.



- Affects psychology and physiology recovery
- Difficult to assess
  - Behavioral Pain Scale (BPS)
  - Critical Care Pain Observation Tool (CPOT)
- Continuous may be more effective than as needed
  - IV opioids recommended as first line agent
- Monitor for side effects

Sources: Vincent JL. Give your patient a fast hug (at least) once a day. Crit Care Med. 2005 Jun;33(6):1225-9 Barr J et al., Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. Crit Care Med. 2013 Jan;41(1):263-306.



- Titrated to the individual
- Caution with over sedation
  - Richmond Agitation and Sedation Scale (RASS)
  - Sedation-agitation Scale (SAS)
- Non-benzodiazepines preferred over benzodiazepines in mechanically ventilated patients

Sources: Vincent JL. Give your patient a fast hug (at least) once a day. Crit Care Med. 2005 Jun;33(6):1225-9 Barr J et al., Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. Crit Care Med. 2013 Jan;41(1):263-306.

## hromboembolic Prophylaxis

- Considered high risk for VTE
- Without it, 13–31% will develop VTE
- Initiate within 24 hours of admission
- More to come...



Sources: Vincent JL. Give your patient a fast hug (at least) once a day. Crit Care Med. 2005 Jun;33(6):1225-9 Ho KM, Chavan S, Pilcher D. Omission of early thromboprophylaxis and mortality in critically ill patients: a multicenter registry study. Chest. 2011 Dec;140(6):1436-46. Assessment Question 1: Which of the following should be used for VTE prophylaxis in ICU patients?

- A) Low molecular weight heparin (LMWH)
- B) Unfractionated Heparin (UFH)
- C) Aspirin
- D) A & B

Assessment Response 1: Which of the following should be used for VTE prophylaxis in ICU patients?

A) Low molecular weight heparin (LMWH)

B) Unfractionated Heparin (UFH)

C) Aspirin

D) A or B



- Head at minimum 30–45°
- Decrease aspiration/pneumonia



Sources: Vincent JL. Give your patient a fast hug (at least) once a day. Crit Care Med. 2005 Jun;33(6):1225-9 Metheny NA, Frantz RA. Head-of-bed elevation in critically ill patients: a review. Crit Care Nurse. 2013 Jun;33(3):53-66; Image: https://www.topregisterednurse.com/fowlers-position/

# Ulcer Prophylaxis

- Not for routine use
- Several possible treatment options
- More to come...





Sources: Vincent JL. Give your patient a fast hug (at least) once a day. Crit Care Med. 2005 Jun;33(6):1225-9 NICE-SUGAR Study Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group and the Canadian Critical Care Trials Group, Intensive versus conventional glucose control in critically ill patients with traumatic brain injury: long-term follow-up of a subgroup of patients from the NICE-SUGAR study. Intensive Care Med. 2015 Jun;41(6):1037-47.

26



Sources: Vincent JL. Give your patient a fast hug (at least) once a day. Crit Care Med. 2005 Jun;33(6):1225-9 NICE-SUGAR Study Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group and the Canadian Critical Care Trials Group, Intensive versus conventional glucose control in critically ill patients with traumatic brain injury: long-term follow-up of a subgroup of patients from the NICE-SUGAR study. Intensive Care Med. 2015 Jun;41(6):1037-47.

## **VTE Prophylaxis**



### Why does it matter?

- Centers for Medicare and Medicaid Services (CMS) Measure
  - Second most common medical complication of postoperative patients
  - Second most common cause of excess length of stay
  - Third most common cause of excess mortality and excess charges



## Who should receive it? **CHEST Guidelines**

- Critically ill patients should receive pharmacologic prophylaxis
- No validated risk assessment score in critically ill patients
- Patient with a high risk of bleeding should receive mechanical prophylaxis rather than go without prophylaxis



30

### Who shouldn't receive it?

- 80% of critically ill patients will have minor or major bleeding
  - One in five major bleed when not on medication
- Patients at a high risk of bleeding should receive mechanical prophylaxis
- Patients on comfort measures
- Patients with VTE on admission

Sources: Kahn SR et al., Prevention of VTE in nonsurgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):e195S-e226S.

Arnold DM et al., Bleeding during critical illness: a prospective cohort study using a new measurement tool. Clin Invest Med. 2007;30(2):E93-102.

#### What medication should be used?

- No clear conclusion for choosing of one pharmacologic medication over another
- Recommendation: LMWH or UFH



### Dosing of Enoxaparin (LMWH)

- 40 mg SubQ daily
- BMI >40 kg/m<sup>2</sup> appropriate to increase dose by 30% CrCl < 30 mL/minute: 30 mg SubQ daily</li>
- Knee or hip replacement: 30 mg SubQ BID



### **Dosing of Heparin**

- 5,000 units SubQ TID or BID
- No renal adjustments



### Monitoring

- Platelet count every 2–3 days starting at day four for heparin-induced-thrombocytopenia (HIT)
  - Platelets <150 x 10<sup>9</sup> /L OR 30–50% decrease from baseline
- Signs and symptoms of bleeding



#### BID or TID?

 No recommendation on frequency of UFH in guidelines



Source: King CS et al., Twice vs three times daily heparin dosing for thromboembolism prophylaxis in the general medical population: A metaanalysis. Chest. 2007 Feb;131(2):507-16.

- King et al. meta-analysis (February 2007)
- 12 studies included (1,664 TID vs. 6,314 BID)
- No difference in the overall rate (per 1,000 patient-days) of VTE (BID, 5.4; vs. TID, 3.5; p 0.87=)
- Risk for major bleeding was significantly increased with TID heparin (BID, 0.35; vs. TID, 0.96; p < 0.001)



- Wein et al. meta-analysis (July 2007)
- Thirty-six studies included
- UFH TID was more effective in preventing DVT than a BID dosing regimen (RR 0.27; versus RR 0.52; 95% CI 0.28–0.96)



- Phung et al. meta-analysis
- 16 studies included (n = 27.667)
- Relative risk and 95% confidence intervals:
  - DVT 1.56 (0.64–4.33)
  - PE 1.67 (0.49–208.09)
  - Mortality1.17 (0.72–1.95)
  - Major bleeding 0.89 (0.08–7.05)



- ? Cost
- ? Nursing burden
- ? Bleeding risk
- ? Institutional policy
- ? Body weight

#### **VTE Dosing in Obese Patients**

- Do obese patients require different dosing strategies compared to non-obese patients?
- Standard dosing suboptimal in morbidly obese



Audience Poll: Does your hospital have a guideline/policy/protocol on dosing VTE prophylaxis in obese patients?

A) Yes

B) No

#### **Higher Doses in Obese Patients**

- Retrospective cohort (n = 3,928)
- General medicine
- Standard dose: heparin 5,000 units SubQ BID or TID OR enoxaparin 40 mg SubQ daily (n = 2,369)
- High dose: heparin 7,500 units SubQ TID OR enoxaparin 40 mg SubQ BID (n = 1,559)



# Higher Doses in Obese Patients (cont'd.)

- High-dose halved the odds of symptomatic VTE (odds ratio [OR] 0.52, 95%, [CI] 0.27-1.00; p = 0.05)
- High-dose did not increase bleeding (OR 0.84, 95% CI 0.66-1.07, p = 0.15)



## Enoxaparin Dosing in Obese Patients

- BMI > 50 kg/m<sup>2</sup>
  - 60 mg SubQ BID?
- BMI >40 kg/m<sup>2</sup>
  - 40 mg SubQ BID most validated in studies for patients
- BMI 35–40 kg/m<sup>2</sup>
  - 30 mg SubQ BID or 40 mg SubQ BID



Assessment Question 2: J.D. is a 67-year-old female on heparin 5,000 units BID for VTE prophylaxis. Her baseline platelets are  $413 \times 10^9$ /mm<sup>3</sup>. Which of the following platelet levels would indicate that she has potentially developed HIT?

- A) 500 x 10<sup>9</sup> mm<sup>3</sup>
- B) 120 x 10<sup>9</sup> mm<sup>3</sup>
- C) 319 x 10<sup>9</sup> mm<sup>3</sup>
- D) 189 x 10<sup>9</sup> mm<sup>3</sup>
- E) B and D

Assessment Response 2: J.D. is a 67-year-old female on heparin 5,000 units BID for VTE prophylaxis. Her baseline platelets are 413 x  $10^9$ /mm<sup>3</sup>. Which of the following platelet levels would indicate that she has potentially developed HIT?

- A) 500 x 10<sup>9</sup> mm<sup>3</sup>
- B) 120 x 10<sup>9</sup> mm<sup>3</sup>
- C) 319 x 10<sup>9</sup> mm<sup>3</sup>
- D) 189 x 10<sup>9</sup> mm<sup>3</sup>

#### E) B and D

#### **Direct Factor Xa Inhibitor**

- Betrixaban only direct-oral anticoagulant approved for VTE prophylaxis
- APEX trial betrixaban 80 mg daily versus enoxaparin 40 mg daily
  - CrCl <30 mL/min: betrixaban 40 mg daily and enoxaparin 20 mg daily

...continued



### APEX Trial (cont'd.)

49

- n = 3,759 betrixaban; n = 3,754 enoxaparin
- VTE rate reduced among subjects treated with 80 mg betrixaban vs. enoxaparin (4.87% vs. 7.06% RRR [0.13–0.44], P=.001)
- No difference in rate of VTE in 40 mg betrixaban vs. enoxaparin



#### **VTE Conclusions**

- LMWH or UFH appropriate for VTE prophylaxis in ICU patients
- No difference between BID or TID
- Higher doses appropriate in obese patients (BMI >35 kg/m<sup>2</sup>)

Stress Ulcer Prophylaxis



#### Guidelines



Sources: ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis. Am J Health Syst Pharm. 1999 Feb 15;56(4):347-79.

Rhodes A et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med. 2017 Mar;43(3):304-377.

Guillamondegui OD et al. Stress Ulcer Prophylaxis. Chicago, IL: (EAST) 2008.

Madsen KR et al., Guideline for stress ulcer prophylaxis in the intensive care unit. Dan Med J. 2014 Mar;61(3):C4811.

#### Who should receive it?

- Large prospective cohort (n = 2,252) in ICU
- Respiratory failure (OR, 15.6)
  - Mechanical ventilation for  $\geq$  48 hours
- Coagulopathy (OR, 4.3)
  - Platelet count <50,000 /mm<sup>3</sup>
  - INR>1.5 without warfarin
  - PT>1.5 times the control value
  - PTT>2.0 times the control value



### Pharmacologic Agents for SUP

- Proton pump inhibitors (PPIs)
- Histamine 2 receptor antagonists (H2RAs)
- Antacids
- Sucralfate



#### PO Sucralfate vs. IV Ranitidine

- Randomized control trial (1998)
- Ranitidine IV 50 mg q8h (n = 596) vs. sucralfate
  PO 1g q6h (n = 604)
- Clinically important GI bleeding :1.7% ranitidine vs. 3.8% sucralfate (RR, 0.44; 95% CI 0.21-0.92; P=0.02)
- Ventilator-associated pneumonia (VAP) 19.1% ranitidine vs. 16.2% sucralfate group (RR 1.18; 95% CI, 0.92-1.51; P=0.19)



Source: Cook D et al., A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in patients requiring mechanical ventilation. Canadian Critical Care Trials Group. N Engl J Med. 1998 Mar 19;338(12):791-7.

### PPI vs. H2RA: Benefit

- Meta-analysis (2016)
  - PPI decrease risk of bleeding vs. H2RA (RR = 0.39 (05% CI 0.21-0.71)
  - No increase risk of nosocomial pneumonia
- Cohort study, mechanically ventilated (2014)
  - PPI (n = 21,873) vs. H2RA (n = 13,439)
  - PPI increased risk of bleeding vs. H2RA (RR 2.24; 95% CI, 1.81–2.76)

Sources: Marik PE et al,. Stress ulcer prophylaxis in the new millennium: a systematic review and meta-analysis. Crit Care Med. 2010 Nov;38(11):2222-8.

### PPI vs. H2RA: Risk

- Retrospective cohort, post-CABG (2013)
  - PPI (n = 11,382) vs. H2RA (n = 9,830)
  - Pneumonia increased in PPI vs. H2RA (RR 1.19, 95% CI 1.03–1.38)
- Cohort study, mechanically ventilated (2014)
  - PPI (n = 21,873) vs. (H2RA n = 13,439)
  - Pneumonia increased in PPI vs. H2RA (RR 1.2; 95% Cl, 1.03–1.41)
  - Clostridium difficile infection increased in PPI vs. H2RA (RR1.29; 95% CI, 1.04–1.64)

Sources: Bateman BT et al., Type of stress ulcer prophylaxis and risk of nosocomial pneumonia in cardiac surgical patients: cohort study. BMJ. 2013 Sep 19;347:f5416. 57 MacLaren R et al., Histamine-2 receptor antagonists vs proton pump inhibitors on gastrointestinal tract hemorrhage and infectious complications in the intensive care unit. JAMA Intern Med. 2014 Apr;174(4):564-74.

#### **SUP Conclusions**

- H2RA superior to sucralfate
- PPI as effective as H2RA; might be more effective
- H2RA might be safer than PPI

### Give your ICU patients a FAST HUG!

- Feeding
- Analgesia
- Sedation
- Thromboembolic Prophylaxis
- Head-of-bed
- Ulcer prophylaxis
- Glucose control