

# WHAT'SUP?

*Nepean WTET summary 10/3/20*

## Background

- Pre the era of stress ulcer prophylaxis (SUP) significant upper GI bleeding (UGIB) was as common as 15% in ICU with high morbidity and mortality (M&M), necessitating at times drastic interventions such as partial/complete gastrectomy
- Pathophysiology;
  - Impaired splanchnic blood flow (eg shock) → impaired gastric (mucoid) protection
  - Acidic environment → propensity for erosions and ulceration
  - DIC → coagulopathy, may contribute to worsening bleeding risk
- SUP tries to reduce the M&M of UGIB associated with being critically ill and is to be considered separate from those with other risks for peptic ulcer disease (PUD) not related to being critically ill e.g. steroid use and previous PUD on regular PPI
- Those at risk in particular (though exact population still poorly defined);
  - Severe shock, trauma (spinal, burns, TBI), coagulopathy, likely need for invasive ventilation >48h (marker of sickness...)
  - This is NOT every ICU admission!

## Non-pharmacological strategies

- General; resuscitation and treatment of the underlying cause → optimise flow
- Feeding;
  - Absorbing feeds → adequate gastric perfusion and mucosal protection; no additional benefit from PPI in randomised controlled trials (RCT)
  - Even trophic feeds reduce stress ulceration and UGIB risk; but only small studies and unclear if adequate alone for those at high risk

## Pharmacological Agents

- Antacids (used to be given hourly!) → associated metabolic alkalosis; not used
- Sucralfate (thick paste that lines gastric mucosa protecting it from acidic environment) → obstruction and bezoars; not used
- Proton pump inhibitors (PPI) eg pantoprazole
  - Immunosuppressive; reduce natural killer cell activity and neutrophil bactericidal capacity
  - Major drug cause of acute interstitial nephritis
  - Increases incidence of ventilator associated pneumonia
  - Previously thought to increase C diff → but probably doesn't on recent studies
  - Most efficacious in reducing bleeding, but potential harm overall...
- Histamine 2 receptor blockers (H2RB) eg ranitidine
  - Needs renal dose adjustment
  - Cause of thrombocytopenia
  - Currently in short supply

## Key studies

- SUP-ICU
  - 2018; European; PPI vs placebo; blinded RCT, stratified multi-center trial
  - Approx 3300 patients (powered for a 5% mortality difference which is unrealistic and hence probably underpowered)
  - No difference in 90d mortality
  - Very broad inclusion (?diluted due to inclusion of non-high risk patients)
  - No difference in secondary outcome (composite) but reduced UGIB
- PEPTIC
  - 2020; One of the largest ICU trials (included Nepean!) approx. 27000pts
  - H2RB vs PPI in ventilated critically ill; randomised cluster crossover trial
  - Primary outcome 90d mortality; 18.3% in PPI, 17.5% H2RB (10% relative increase in mortality with PPIs!)
  - Less UGIB in PPI group; 5 per 1000 with 3 of these 5 needing transfusion and 2 needing endoscopy; NNT 1/200
  - Arguably 90d mortality is more important (we need to look beyond ICU stay) than UGIB from stress ulceration (which rarely leads to death)

## Summary

- SUP may not be as big a problem as it once was with advances in resuscitation and management of critically ill. Furthermore, a smaller proportion of high risk patients make up our ICU cohort with higher admission rate of 'less sick' patients means it is not relevant to many admissions
  - Await REVISE trial (comparing PPI to placebo) for high risk ICU patients!
- Currently consider SUP in high risk ICU patients (not all-comers)
- H2RB first line (in absence of specific indication for PPI) if NOT tolerating enteral feeds
- Review daily and STOP when no longer indicated (neither drugs are harmless agents)
- PPIs are absolutely indicated in TREATMENT of UGIB due to ulcerations of any cause

**PPI?**  
**Personalised Prescribing when Indicated**