

## September 2014 REBELCast Shownotes

**Topic #1:** The use of Non-Invasive Positive Pressure Ventilation in the pre-hospital treatment of patients with severe respiratory distress.

**Clinical Question:** In patients with undifferentiated respiratory distress, does the use of NIPPV in the pre-hospital setting reduce in-hospital mortality?

**OR:** Will starting NIPPV in the pre-hospital setting decrease the risk of my patient with respiratory distress dying in the hospital?

### Article

Mal S et al. Effect of Out-of-Hospital Noninvasive Positive-Pressure Support Ventilation in Adult Patients with Severe Respiratory Distress: A Systematic Review and Meta-Analysis. Ann of EM 2014; 63: 600-7.

**Background:** Severe respiratory distress is commonly seen in the pre-hospital setting. Unfortunately, pre-hospital personnel have limited tools to treat these patients. Dyspnea can result from a number of causes including asthma or COPD exacerbations, ADHF, myocardial infarction, pulmonary embolism and many more. Many of these patients will receive NIPPV upon arrival to the hospital. It is unclear if starting NIPPV in the field will benefit patients with severe respiratory distress.

### Details

- This study was a meta-analysis of 7 RCTs (n = 632) that compared the use of NIPPV to standard therapy in patients with severe respiratory distress.
- The meta-analysis looked at 2 main outcomes: death in-hospital and need for intubation and mechanical ventilation.
- The study found a statistically significant decrease for in-hospital mortality: RR = 0.58 (95% CI 0.35 – 0.95); NNT = 18
- The study found a statistically significant decrease in the need for intubation in the NIPPV group: RR = 0.37 (95% CI 0.24 – 0.58); NNT = 8

### Strengths

- 7 RCTs with 631 patients is impressive for a pre-hospital, critical care intervention.
- There was a low risk of bias in 5 out of 7 studies.
- Very few patients were lost to follow up (none in 4 studies, 3-4% in the other 3).
- Low heterogeneity across studies.

### Weaknesses

- Patients were not blinded to treatment (yes, sham NIPPV is possible).

- The majority of patients suffered from acute decompensated heart failure (ADHF) and 97% of patients had asthma, COPD or ADHF.
- External validity is not clear. 6 studies were performed in Europe where physicians are often part of the pre-hospital team.

**Clinical Bottom Line:** NIPPV should be considered in all patients with severe respiratory distress in the prehospital setting. It has the potential to prevent death in 5-6 patients who present with respiratory distress in the prehospital setting and prevent 12-13 intubations in this group.

**Topic #2:** Once-weekly Dalbavancin for skin infections.

**Clinical Question:** Is weekly dosing of Dalbavancin as effective as routine therapy for skin infections?

**Article:**

Boucher, HW et al. Once-Weekly Dalbavancin versus Daily Conventional Therapy for Skin Infection. N Engl J Med 2014; 370:2169-79.

**PMID:** 24897082

**Background:** Patients with extensive cellulitis or large abscesses often require hospital admission for intravenous antibiotics. This greatly adds to hospitals costs and the other associated risks of inpatient stays. Outpatient treatment of these patients is cost saving and increases patient satisfaction. But often, these patients will fail outpatient oral treatments. What if there was a treatment that was as effective as the usual once or twice daily treatment?

**What They Did:**

- Pooled analysis of DISCOVER 1 and DISCOVER 2 trials
- Inclusion criteria
  - Presence of cellulitis, major abscess, or wound infection, each associated with a minimum of 75 cm<sup>2</sup> of erythema.
  - Thought to require at least 3 days of IV therapy.
  - One or more signs of systemic infection (e.g., fever > 38 C, WBC > 12,000 cells/mm<sup>3</sup>, or > 10% bands)
  - At least two signs of local infection or than erythema
    - Purulent drainage or discharge
    - Fluctuance
    - Heat or localized warmth
    - Tenderness to palpation
    - Swelling or induration
- Exclusion criteria

- Patients who had received antibiotics within 14 days before randomization.
- 2 arms-total of 10-14 days of therapy
  - IV vancomycin (15 mg/kg) every 12 hours for at least three days with the option to switch to oral linezolid (600 mg) every 12 hours.
  - IV dalbavancin (1 g) on day one, followed by 500 mg IV on day 8 (IV or oral placebo given every 12 hours to complete treatment).
- Primary end point: measured at 48-72 hours, both cessation of infection-associated erythema and temperature of 37.6 C or lower at three consecutive measurements performed 6 hours apart.

### **Results:**

- 1303 patients included: 652 patients in dalbavancin group, 651 patients in vancomycin-linezolid group.
- 79.7% of dalbavancin group and 79.8% of vancomycin-linezolid group had successful outcome at 48-72 hours (95% CI -4.5 to 4.2).
- Most common reason for treatment failure: lack of complete resolution of skin warmth at infection site.
- Equivalent outcomes with MRSA infection
- Adverse effects: nausea (both groups, not statistically significant), diarrhea and pruritus (more in vancomycin-linezolid group,  $p=0.02$  and  $p=0.01$  respectively)

### **Limitations:**

- Sponsoring Drug Company collected the data, monitored study conduct, and performed statistical analysis.
- Subjective nature of some data points.

### **Conclusion:**

“Our results show that for the treatment of acute bacterial skin and skin-structure infection, the efficacy of dalbavancin administered once weekly was not inferior to that of a conventional twice-daily antibiotic regimen.”

### **Comments:**

- Study does show non-inferiority of dalbavancin making it an option for outpatient treatment of skin infections.
- First dose may be given in the ED with second dose at an infusion center.
- Be aware of the cost of a new IV drug, may be prohibitive.

### **Clinical Bottom Line:**

**IV dalbavancin is an alternative antibiotic for skin infections that can be dosed on a weekly basis. This potentially avoids a hospital admission, but as with other new medications, cost may be an issue. Other, non-drug company sponsored studies need to be conducted.**