

# A Comparison of Initial Monotherapy with Norepinephrine Versus Vasopressin for Resuscitation in Septic Shock

## BACKGROUND:

- Due to recent drug shortages, clinicians have had to identify alternatives to manage patients' disease states.
- Norepinephrine is recommended by the Surviving Sepsis Campaign guidelines as first-line therapy for the management of resuscitation in septic shock. However, due to norepinephrine's lack of availability, this study evaluated the clinical usefulness of vasopressin as an alternative vasopressor monotherapy.

## OBJECTIVE:

- To determine whether vasopressin was noninferior to norepinephrine as an initial vasoactive agent for the attainment of a goal MAP.

## METHODS:

- **Design:** Single site, retrospective noninferiority case-cohort
- **Study duration:** Data from May 2008 through September 2009 was utilized
- **Inclusion criteria:** Older than 18 years of age, received either vasopressin or norepinephrine monotherapy for a diagnosis of septic shock
- **Exclusion criteria:** Admitted to a cardiac or cardiac surgery service; did not have a 1:1 frequency match based on severity of illness ranges in the vasopressin treatment group
- **Primary outcome measure:** Proportion of patients who achieved a mean arterial pressure (MAP) goal  $\geq 65$  mm Hg within the first 6 hours of the initiation of treatment for septic shock
- **Secondary outcome measures:** Evaluate the impact of vasopressin therapy on sepsis-related outcomes, including time course of septic shock, all-cause mortality, ICU length of stay, and requirement for renal replacement therapy
- **Power:** The number of patients needed to achieve 80% power was calculated to be 66 patients per sample group. However, after inclusion and exclusion criteria were met, there were 65 patients per sample group. Post hoc analysis revealed 78% power to detect noninferiority based on the observed results.

## RESULTS:

- **Primary outcome measure:** The proportion of patients who achieved a goal MAP in the vasopressin group was 63% (95% CI 51% to 75%) and in the norepinephrine group was 67.7% (95% CI 56% to 79%). The absolute difference between groups was 4.7% (95% CI -21.2% to 12%).
- **Secondary outcome measures:** Median time to goal MAP achievement was similar between groups at 1 hour for vasopressin (IQR 1-1.25) and 1 hour for vasopressin (IQR 1-2) ( $p = 0.23$ ). No significant difference was noted between norepinephrine and vasopressin with regard to ICU length of stay (median 7 [IQR 3-15] and 7 [IQR 4-24])

days, respectively;  $p = 0.25$ ) or length of hospitalization (median 15 [IQR 7-31] and 15 [IQR = 8-34] days, respectively;  $p = 0.58$ ). No significant difference was noted between norepinephrine and vasopressin with regard to mortality (49.2% and 44.6%, respectively;  $p = 0.6$ ) or requirement for renal replacement therapy (32.3% and 29.2%, respectively;  $p = 0.7$ ).

- **Author's conclusion:** Both vasopressin- and norepinephrine-treated patients achieved a similar proportion of MAP within the first 6 hours of septic shock which is consistent with study results. They also state that while there are limitations of the retrospective study design, the data is useful for consideration of alternative vasopressors in the setting of drug shortages.

#### **STRENGTHS:**

- Appropriate dosages of vasopressin and norepinephrine given in each treatment group

#### **LIMITATIONS:**

- Single-center retrospective study design
- Potential for selection bias (exclusion of a large number of patients)
- Data collection from the electronic medical record was not blinded
- Calculation of severity of illness based upon Acute Physiology and Chronic Health Evaluation II (APACHE II) scores

#### **CONCLUSIONS:**

- In clinical practice, if norepinephrine or epinephrine is not available due to a drug shortage, vasopressin would be a suitable alternative for resuscitation in septic shock patients who meet the criteria described in this study (e.g., greater than 18 years of age, non-cardiac or cardiac surgery patients).
- Further prospective research is needed to better determine the usefulness of vasopressin in the treatment of septic shock. To improve the study design, comparison of adverse drug events between groups should be analyzed.

**Reference:** Daley MJ, Lat I, Mieux KD, Jennings HR, Hall JB, Kress JP. A Comparison for Initial Monotherapy with Norepinephrine Versus Vasopressin for Resuscitation in Septic Shock. *The Annals of Pharmacotherapy* 2013 March; 47:301-310.

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