Effect of vasopressor discontinuation order on the incidence of hypotension in patients with septic shock and left ventricular dysfunction

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INTRODUCTION

- Patients with septic shock and left ventricular (LV) dysfunction have higher mortality than septic shock patients without LV dysfunction [1]
- Hammond et al. and Musallam et al. evaluated the sequence of discontinuing vasopressin and norepinephrine, and they found a decrease in clinically significant hypotension when norepinephrine was discontinued first. However, patients with LV dysfunction comprised only 18% and 26% of the total study population respectively, which makes it difficult to apply to this patient population [2, 3]

PURPOSE

Identify the impact of norepinephrine and vasopressin discontinuation order in septic shock patients with left ventricular dysfunction

METHODS

- **Design:** Single center retrospective chart review from January 2015 – June 2019
- **Inclusion**:
  - At least 18 years old
  - Admitted to the ICU
  - Met the Sepsis-3 definition of septic shock
  - LV ejection fraction less than 40%
  - Received continuous infusions of norepinephrine and vasopressin as the final vasopressors discontinued
- **Exclusion:**
  - Patients transitioned to palliative care
  - Norepinephrine and vasopressin discontinued simultaneously
  - Patients who expired within 48 hours of ICU admission
  - Patients who were pregnant
- **Primary objective:** the occurrence of clinically significant hypotension, defined as re-initiation of norepinephrine or vasopressin after discontinuation, mean arterial pressure < 60 mmHg after vasopressor discontinuation, administration of crystalloids of 500 mL or more after the first vasopressor was discontinued, or administration of 25 grams of albumin 5% after the first vasopressor was discontinued
- **Secondary objectives:** vasopressor infusion duration, hospital and ICU lengths of stay, and hospital mortality
- **Statistical analysis:**
  - Chi-squared test: clinically significant hypotension, ICU and hospital mortality
  - T-test: ICU and hospital lengths of stay, cumulative doses, duration of vasopressors, length of mechanical ventilation
  - Power: For a 40% difference to be seen based off previous studies, each group would need to contain 31 patients
- This research has been reviewed by the Institutional Review Board (IRB)

RESULTS

Table 1. Demographics

	Vasopressin (n=37)	Norepinephrine (n=41)
Age - years, mean ± SD	60.2 ± 12.3	62.1 ± 14.9
Height - cm, mean ± SD	175.4 ± 10.9	169.6 ± 11.6
Admission weight – kg, mean ± SD	89.1 ± 26.4	82 ± 24
Male, n (%)	25 (67.6)	25 (61)
Ejection Fraction - %, mean ± SD	27.8 ± 9.4	28.1 ± 9.6
SOFA Score – mean ± SD	9.5 ± 2.2	9.6 ± 2.7

SD = standard deviation cm = centimeters
SOFA = Sequential Organ Failure Assessment kg = kilograms
n = population size

Table 2. Patient Outcomes

	Vasopressin (n=37)	Norepinephrine (n=41)	P-value
Clinically Significant Hypotension, n (%)	28 (75.7)	33 (80.5)	0.61
ICU Mortality, n (%)	10 (27.1)	15 (36.6)	0.82
Hospital Mortality, n (%)	11 (29.7)	15 (36.6)	0.41
ICU Length of Stay - days, mean ± SD	10.5 ± 9.5	17 ± 12.55	0.0121
Hospital Length of Stay - days, mean ± SD	15.3 ± 17.9	28.5 ± 21.7	0.047
Length of MV - days, mean ± SD	9.4 ± 10.1	13.7 ± 10.9	0.0768
Norepinephrine			
Duration - hours, mean ± SD	67.5 ± 58.8	57.8 ± 45.8	0.038
Cumulative NE dose - mg, mean ± SD	151.6 ± 197.1	83.8 ± 140.7	0.083
Vasopressin			
Duration - hours, mean ± SD	34.3 ± 46.8	82.8 ± 50.2	0.0042
Cumulative VP dose - mg, mean ± SD	81.6 ± 141.9	141.3 ± 118.7	0.039

ICU = intensive care unit MV = mechanical ventilation
NE = norepinephrine VP = vasopressin

Table 3. Other Medications

Vasopressor and Steroid Use	Vasopressin discontinued first (n=37)	Norepinephrine discontinued first (n=41)
Phenylephrine, n (%)	3 (8.1)	0 (0)
Dopamine, n (%)	4 (10.8)	2 (4.9)
Epinephrine, n (%)	5 (13.5)	14 (34.1)
Milrinone Used, n (%)	7 (18.9)	9 (22)
Hydrocortisone Used, n (%)	13 (35.1)	18 (43.9)
Duration - days, mean ± SD	3.4 ± 8.5	2.5 ± 4.6

Figure 1

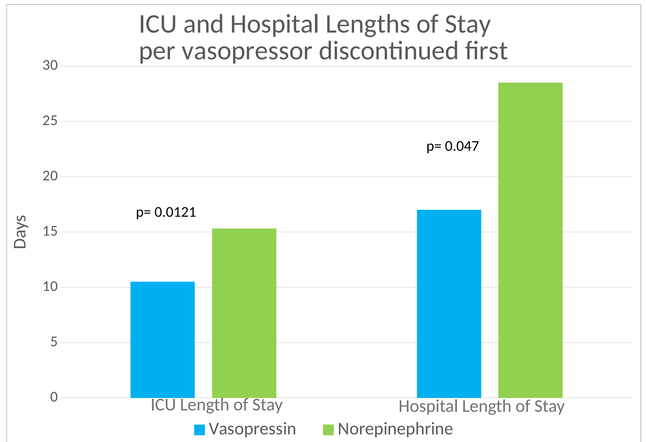


Figure 2

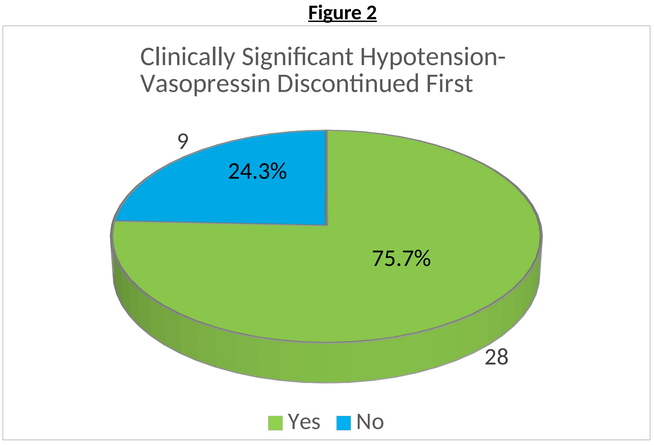
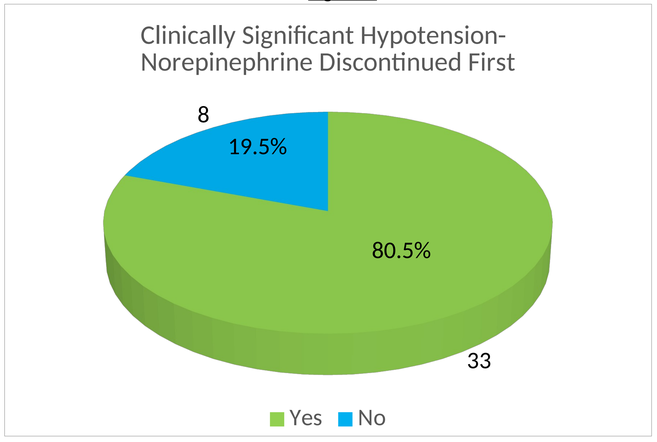


Figure 3



DISCUSSION

- Although fewer patients experienced clinically significant hypotension when vasopressin was discontinued first, this primary outcome was not statistically significant, indicating that these patients had no difference in events of clinically significant hypotension when norepinephrine and vasopressin were the last vasopressors
- ICU and hospital mortality were not different between the two groups
- Patients that had vasopressin discontinued first had shorter ICU and hospital lengths of stay

CLINICAL IMPLICATIONS

- Current literature and guideline recommendations regarding the proper sequence of vasopressor discontinuation in patients with LV dysfunction is limited
- Patients with LV dysfunction may experience worse outcomes, including clinically significant hypotension and risk of mortality, compared to those without left ventricular dysfunction, and the significance of these outcomes may vary on the different patient populations

NEXT STEPS

- Further studies with larger patient populations are needed to determine the relationship between norepinephrine and vasopressin discontinuation sequence and the occurrence of clinically significant hypotension in patients with LV dysfunction
- Combination of data with another site is currently ongoing and results from both sites are to be analyzed together
- Results from the study will be submitted for publication

REFERENCES

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DISCLOSURES

The authors have no conflicts of interest to disclose