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

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INTRODUCTION

- Sepsis is most recently defined by the Sepsis-3 guidelines as potentially fatal organ dysfunction resulting from the body's reaction to an infection. Organ dysfunction is measured by a SOFA (Sequential [Sepsis-Related] Organ Failure Assessment) Score change of ≥ 2 [1]
- Septic shock is diagnosed when sepsis is present, vasopressors are necessary to achieve a MAP of ≥65, and serum lactate is measured to be > 2 mmol/L after fluids were properly administered [1]
- Patients with septic shock and left ventricular (LV) dysfunction have been shown to have worse outcomes than septic shock patients without LV dysfunction, such as increased incidence of mortality [2]
- 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, resulting in conclusions not able to be drawn for this population [3, 4]

PURPOSE

The purpose of this study was to 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:** Patients included were at least 18 years old, admitted to the ICU, met the Sepsis-3 definition of septic shock, had a LV ejection fraction less than 40%, and received continuous infusions of norepinephrine and vasopressin as the final vasopressors discontinued
- **Exclusion:** Patients were excluded if they were transitioned to palliative care, if norepinephrine and vasopressin were discontinued simultaneously, if the patient expired within 48 hours of ICU admission, or if the patient was pregnant
- **Primary objective:** the occurrence of clinically significant hypotension, defined as re-initiation of norepinephrine or vasopressin after discontinuation, MAP < 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 used for clinically significant hypotension, ICU, and hospital mortality. T-test used for ICU and hospital lengths of stay, cumulative doses, and duration of vasopressors. For a 40% difference to be seen based off previous studies, each group would need to contain 31 patients
- This project was part of the health system's Medication Use Evaluation and Improvement Program, which has been reviewed by the Institutional Review Board and determined not to be human research

RESULTS

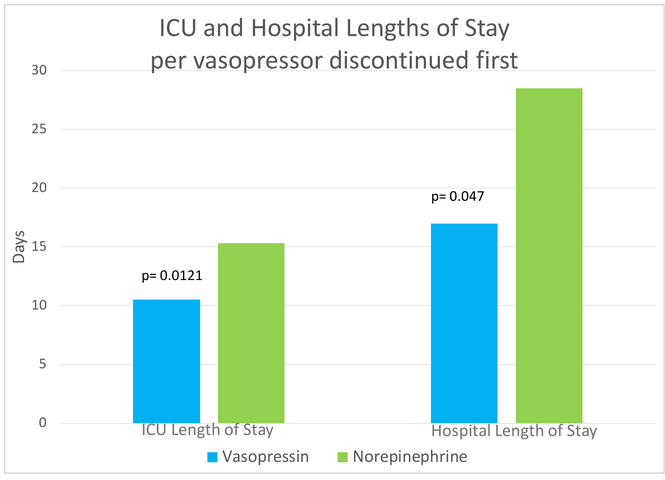
Table 1. Demographics

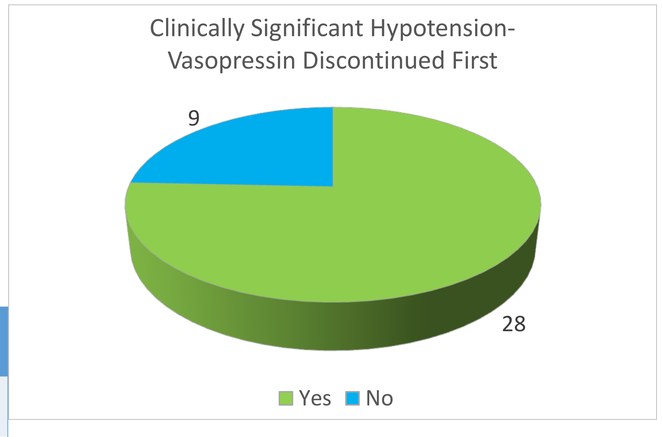
Vasopressor Discontinued First Groups	Vasopressin (n=37)	Norepinephrine (n=41)
Age - years, mean ± SD	60.2 ± 12.3	62.1 ± 14.9
Height - cm, mean ± SD	175.4 ± 10.9	169.6 ± 11.6
Admission weight – kg, mean ± SD	89.1 ± 26.4	82 ± 24
Male, n (%)	25 (67.6)	25 (61)
Ejection Fraction - %, mean ± SD	27.8 ± 9.4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

SD = standard deviation
n = population size

Table 2. Patient Outcomes

Vasopressor Discontinued First Groups	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
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





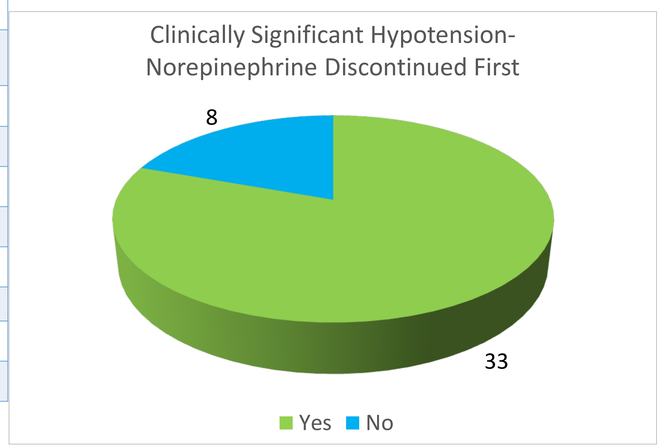


Table 3. Other Medications

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

DISCUSSION

- Although fewer patients experienced clinically significant hypotension when vasopressin was discontinued first, this primary outcome was not statistically significant. This indicates that there is no difference in events of clinically significant hypotension when norepinephrine and vasopressin are the last vasopressors in patients with septic shock and left ventricular dysfunction
- ICU and hospital mortality rates were not statistically significant between the two groups
- Discontinuing vasopressin first resulted in significantly 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, compared to those without ventricular dysfunction, and the significance of the results may differ between the groups
- Although these results indicate that there is no difference in clinically significant hypotension when discontinuing norepinephrine and vasopressin, it may be beneficial in patients with sepsis and LV dysfunction to discontinue vasopressin before norepinephrine as these results illustrated shorter ICU and hospital lengths of stay

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

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DISCLOSURES

The authors have no conflicts of interest to disclose