Implementation of a Vasopressin Initiation Policy in Septic Shock

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Background

- Septic shock is life-threatening and associated with high rates of mortality, accounting for 1 in 3 hospital deaths[1,2]
- The Surviving Sepsis Campaign recommends early management with fluid resuscitation and norepinephrine (NE) as the first-line vasopressor targeting a mean arterial pressure (MAP) of ≥ 65 mmHg[3]
- Vasopressin is recommended as additional support, but there is no consensus on when to initiate therapy[3]
- Some institutions found no difference in mortality or time to reach target MAP when starting vasopressin once NE exceeded 50 mcg/minute[4,5]
- At St. Joseph's Medical Center, a retrospective medication use evaluation (MUE) revealed the average rate of NE was 19 mcg/minute prior to starting vasopressin
  - Vasopressin has potential serious adverse effects and is associated with high medication costs
  - **A hospital policy to start vasopressin when NE exceeds 30 mcg/minute unless physician order specifies otherwise, was developed and approved by SJMC Critical Care and P&T committees**
  - Education was provided to intensivists, hospitalists, pharmacists, and nurses of the 4 intensive care units

Objectives

- To evaluate the safety and efficacy of implementing a vasopressin initiation policy
- Primary outcome: time to reach MAP ≥ 65 mmHg
- Secondary outcomes: dose of NE at the start of vasopressin, duration of NE at the start of vasopressin, duration of vasopressors, length of ICU stay, mortality, new onset arrhythmias

Methodology and Interventions

Figure 1: Inclusion and Exclusion Criteria

Inclusion	Exclusion
• Adult patients ≥ 18 years old admitted to the ICU at SJMC • Suspected sepsis or septic shock • Received NE and vasopressin concurrently	• Treatment for systemic shock not related to sepsis (e.g., cardiogenic, hemorrhagic) • Patients entered hospice or comfort care • Patients transferred out of SJMC to another facility • Received NE and/or vasopressin for ≤ 8 hours • Received vasopressin for cardiogenic surgery

Figure 2: Patient Selection

	Time period	Charts reviewed (patients admitted who received vasopressin)	Excluded	Total remaining
Pre-Intervention	July 2019 – September 2019	153	Cardiac surgery (N=53) Hospice/comfort care (N=47) Other (N=15)	38
Post-Intervention	December 2019 – February 2020	123	Cardiac surgery (N=47) Hospice/comfort care (N=34) Other (N=12)	30

Figure 3: Baseline Characteristics

Baseline Characteristic	Pre-Intervention (N=38)	Post-Intervention (N=30)	p-value
Age – years[1]	70 (58-77)	65 (55-79)	0.741
Weight – kg[1]	79.0 (69.0-97.9)	75.3 (63.6-95.3)	0.383
Gender • Male • Female	 26 (68%) 12 (32%)	 20 (67%) 10 (33%)	0.878
APACHE II[1]	22 (17.5-31)[2]	25 (20-32)[3]	0.189

[1]Median (interquartile range).
[2]Data available for N=36.
[3]Data available for N=29.
Abbreviations: APACHE, Acute Physiologic Chronic Health Evaluation.

Results

Figure 4: Primary Outcome

Primary outcome	Pre-Intervention (N=39)[1]	Post-Intervention (N=28)[2]	p-value
Time to reach target MAP (hours)[3]	1.3 (2.1-1.2)	1.8 (1.1-4.6)	0.948

[1]One patient met inclusion criteria twice during admission.
[2]Two patients did not reach the primary outcome.
[3]Median (interquartile range).
Abbreviations: MAP, mean arterial pressure.

Figure 5: Secondary Outcomes

Secondary outcomes	Pre-Intervention (N=39)[1]	Post-Intervention (N=30)	p-value
NE dose at vasopressin start (mcg/minute)[2]	17 (12.5-22.0)	27 (20.0-31.5)	**0.001**
NE duration at vasopressin start (hours)[2]	6.2 (1.8-11.1)	5.3 (3.0-10.3)	0.889
Total duration of NE (hours)[2]	46.1 (27.3-75.0)	45.4 (35.6-76.9)	0.663
Total duration of vasopressin (hours)[2]	21.9 (14.8-55.13)	25.5 (16.2-35.4)	0.624
Mortality – no. (%)	13 (34.2%)	16 (53.3%)	0.064
Total ICU length of stay (days)[2]	3.6 (2.3-9.6)	3.1 (2.1-11.8)	0.916
New onset arrhythmias – no. (%)	18 (47.4%)	15 (50.0%)	0.829

[1]One patient met inclusion criteria twice during admission.
[2]Median (interquartile range).
Abbreviations: NE, norepinephrine.

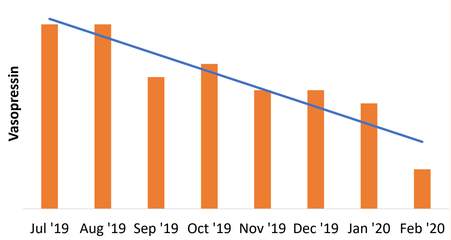
Figure 6: Subgroup Analysis

- Included patients from the post-intervention that followed the vasopressin initiation policy
- Compliance: 14 of 30 patients (46.7%)

	Post-intervention (N=14)	p-value
NE dose at vasopressin start (mcg/minute)[1]	32 (30-47.5)	**0.00002**
Time to reach target MAP (hours)[1]	1.8 (1.2-2.5)	0.856
Mortality	6 (42.9%)	0.299

[1]Median (interquartile range).
Abbreviations: NE, norepinephrine; MAP, mean arterial pressure.

Figure 7: Financial Impact



Discussion and Conclusions

- Implementing a vasopressin initiation policy did not result in a significant difference in time to reach target MAP
- Differences in mean duration of vasopressors and ICU length of stay, new onset arrhythmias were not significant
- Mortality was higher post-intervention, but not statistically significant
  - APACHE II scores were higher in the post-intervention group and had a higher estimated risk of mortality (40% pre versus 55% post)
- The NE dose at the start of vasopressin was significantly higher in the post-intervention group
- There were fewer vasopressin units purchased in the post-intervention period
- Further education is needed to help increase compliance to the vasopressin initiation policy

Limitations

- Small sample size and data collection period
- Adherence to the vasopressin initiation policy was not required
- Physicians' order set "favorites" were not updated – some vasopressin orders had comments to start vasopressin when NE was 10 to 15 mcg/minute
- Education to emergency room physicians and nursing staff was not personally provided by pharmacy

Future Directions

- Continue data collection of vasopressin use in septic shock
- Update the order set to include instructions not to start vasopressin until NE has reached a certain dosage
- Propose pharmacy approval of vasopressin compounding only after confirming NE has reached a certain dose

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