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Review of adjunctive midodrine to facilitate weaning intravenous vasopressors in critically ill patients

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Review of adjunctive midodrine to facilitate weaning intravenous vasopressors in critically ill patients

Baptist Health South Florida

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Disclosure Statement

The following contributors have nothing to disclose regarding any financial or nonfinancial relationships with the products described, reviewed, or evaluated in this presentation:

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Presentation Objectives

Review the impact of adjunctive midodrine utilization to facilitate weaning intravenous (IV) vasopressors in a community hospital

Background

- IV vasopressors are utilized as mainstay therapy for shock in ICU
- Adverse effects:
  - Tachycardia
  - Local tissue necrosis
  - Gangrene if extravasation occurs
  - Bradycardia
  - Dysrhythmia
- Midodrine is an oral alpha-1 adrenergic agonist used as adjunctive therapy to wean off IV vasopressors
  - Decreases in ICU LOS and IV vasopressor rate

VanValkinburgh D, Hashmi MF. Inotropes And Vasopressors. [Updated 2019 Oct 24]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020 Jan.

Supporting Literature

Study	Objective	Study Design	Results
2013 – Levine AR, et al	Midodrine was evaluated as adjunctive therapy to wean vasopressors	• Prospective, observational study • Starting: 10 mg TID; Max: 40 mg TID • 20 patients included; 14 weaned in 24 hrs	Decreased vasopressor rate after initiating midodrine: -0.62 ± 1.40 mcg/min/hr compared to -2.20 ± 2.45 mcg/min/hr during the first four doses of midodrine (p=0.012)
2016 – Whitson MR, et al	Evaluate the duration of vasopressor and ICU LOS with adjunctive midodrine therapy	• Retrospective, single-center, observational study • 140 patients: vasopressor alone • 135 patients: vasopressor + midodrine • Starting dose: 10 mg TID; Max: 20 mg TID	• Decreased vasopressor duration: 8 days (vasopressor only) vs. 2.9 days (vasopressor + midodrine) (p<0.001) • Decreased ICU LOS: 9.4 days (vasopressor only) vs. 7.5 days (vasopressor + midodrine) (p=0.017)
2019 – Rizvi, et al	Incidence of midodrine continuation upon ICU and hospital discharge and associated risks	• Single-center retrospective study • 1,010 patients included	• ICU discharge: 67% (672/1,010) • Hospital discharge: 34% (311/1,010) • 50% also prescribed antihypertensives • Shorter ICU LOS (7.5 ± 8.9 vs 10.6 ± 13.4 days) and reduced risk of in-hospital mortality (HR, 0.47 [95% CI, 0.32-0.70]; p < 0.001)

Research Purpose

To assess how adjunctive midodrine is being utilized in our institution to wean off vasopressors

To determine whether patients are being transitioned off midodirne when it is no longer warranted

Research Setting

- Baptist Hospital of Miami
  - Non-profit community hospital
  - 728-bed
  - 40-bed ICU

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Study Design

Approved by Baptist Hospital of Miami IRB	• Single center, biphasic study
Phase I: Retrospective Chart Review	• Up to 100 patients between October 2018 - September 2019
Phase II: Prospective Chart Review	• Up to 100 patients between March - April 2020 • Pharmacist interventions

Study Population

Inclusion

- Adults 18 years of age and older
- ICU admission
- Midodrine prescribed during admission in conjunction with IV vasopressor

Exclusion

- Midodrine is a pre-admission medication
- Pregnancy

Study Outcomes

Primary

- Time to vasopressor discontinuation after midodrine initiation
- Percentage of patients transitioned off of midodrine at ICU and hospital discharge

Secondary

- Time from midodrine initiation to ICU discharge determination
- ICU LOS
- Time on vasopressor prior to initiation of midodrine
- Pharmacy interventions in phase II
- Duration of midodrine use

Data Collection

Demographics (age, gender, weight)	Dialysis status and urine output	APACHE IV score	Type of shock	Vasopressor starting rate, rate at midodrine initiation (mcg/kg/hr)
Average rate of vasopressor 24 hrs before midodrine initiation	Vasopressor duration before midodrine initiation	Duration of vasopressor with midodrine	Duration of vasopressor	Initial and maximum midodrine dose/frequency
Average daily dose of midodrine and average vasopressor rate (mcg/kg/hr)	Mechanical ventilation and hydrocortisone utilization	ICU LOS	Reinstitution of vasopressor after discontinuation	Medication that counteracts midodrine (HR, BP, both)
	Midodrine continued post ICU or post hospital discharge	Type of pharmacy intervention		

APACHE: acute physiology and chronic health evaluation

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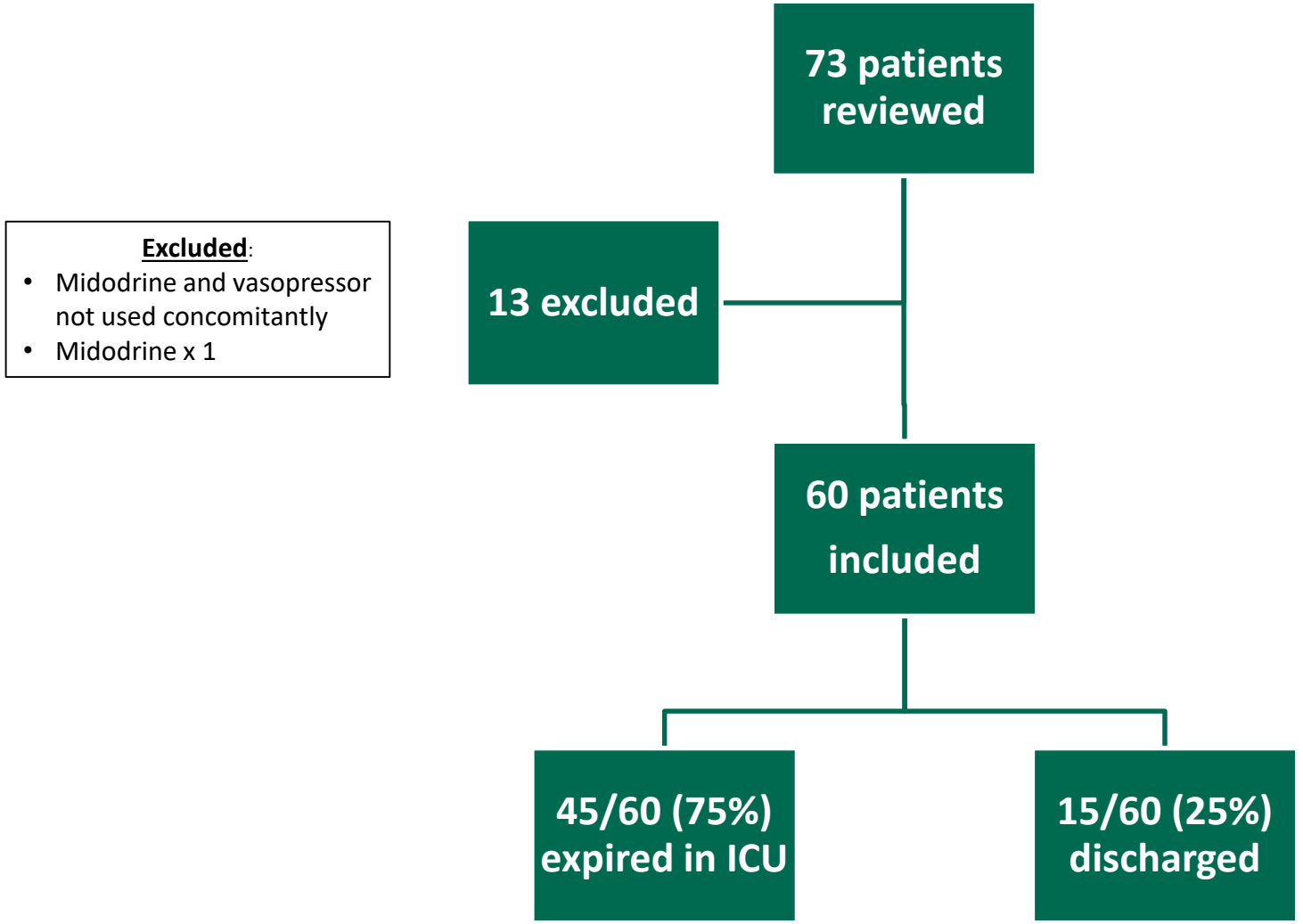
Subject Selection – Phase I



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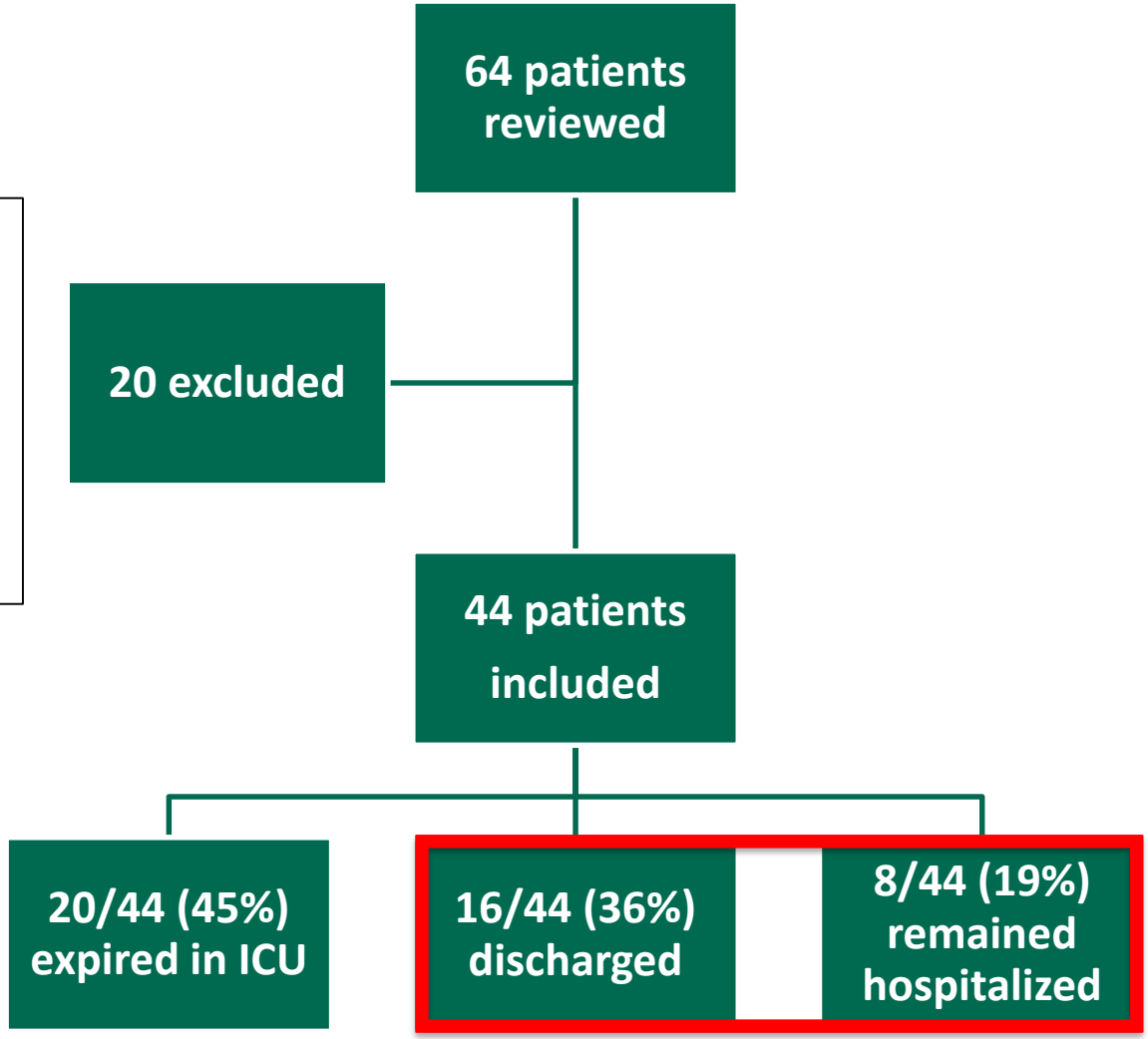
Subject Selection – Phase II

Excluded:

- *13 patients:*
  - No vasopressors
  - Midodrine was a home medication
  - Midodrine and vasopressor not used concomitantly
  - Midodrine x 1
- *7 patients:*
  - Continuation of vasopressor and midodrine past study deadline



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Baseline Characteristics

Characteristics	Phase I (N=15)	Phase II (N=24)	p-value
Age, years (mean, SD)	69.3 ± 16.3	67.6 ± 15.2	p = 0.751
Gender – male, n (%)	12 (80)	15 (63)	p = 0.305
APACHE IV Score (mean, SD)	61.9 ± 18.1	43.4 ± 15.2	p = 0.002
Type of shock, n (%) Distributive Cardiogenic Hypovolemic	 11 (74) 2 (13) 2 (13)	 21 (88) 1 (4) 2 (8)	-
Dialysis, n (%)	7 (47)	8 (33)	p = 0.505
Hydrocortisone utilization, n (%)	6 (40)	5 (21)	p = 0.277
Mechanical ventilation, n (%)	12 (80)	22 (92)	p = 0.354

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Baseline Characteristics

Vasopressor Information	Phase I (N=15)	Phase II (N=24)	p-value
Vasopressor used, n (%) Norepinephrine Epinephrine Phenylephrine Vasopressin Dopamine	 14 (93) 1 (7) 3 (20) 6 (40) 2 (13)	 24 (100) 1 (4) 3 (13) 7 (29) 3 (13)	-
Midodrine initial dose, n (%) 5 mg TID 10 mg TID	 7 (47) 8 (53)	 9 (38) 15 (63)	p = 0.739
Vasopressor rate in ICU* (mcg/kg/min) (mean, SD)	9.6 ± 8.1	5.3 ± 3.4	p = 0.025
Vasopressor rate at midodrine initiation* (mcg/kg/min) (mean, SD) (mcg/min) (mean, SD)	8.6 ± 14.3 6.7 ± 11.0	3.5 ± 3.2 2.7 ± 2.6	p = 0.106 p = 0.096

*Norepinephrine equivalents

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Results: Primary Outcome

- Time to vasopressor discontinuation after midodrine initiation

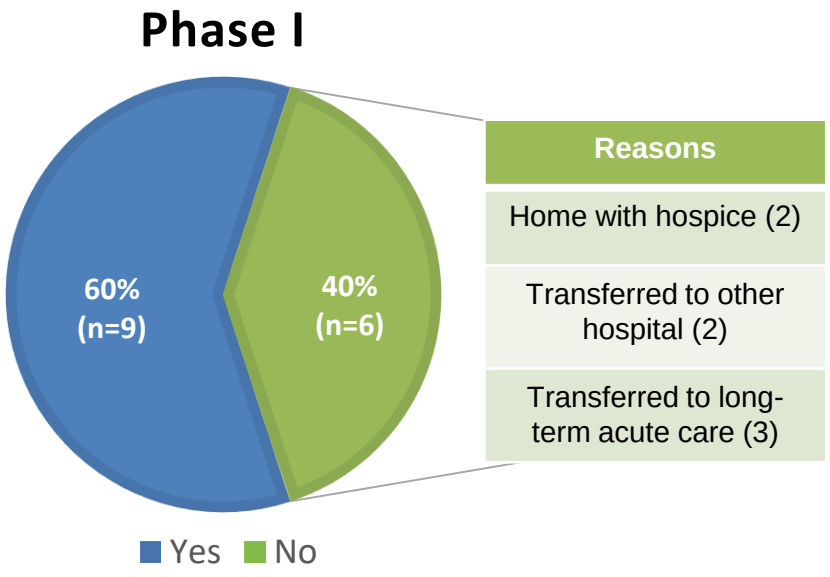
	Phase I (N=15)	Phase II (N=24)	p-value
Days (mean, SD)	3 ± 5.2	4 ± 2.8	p = 0.832

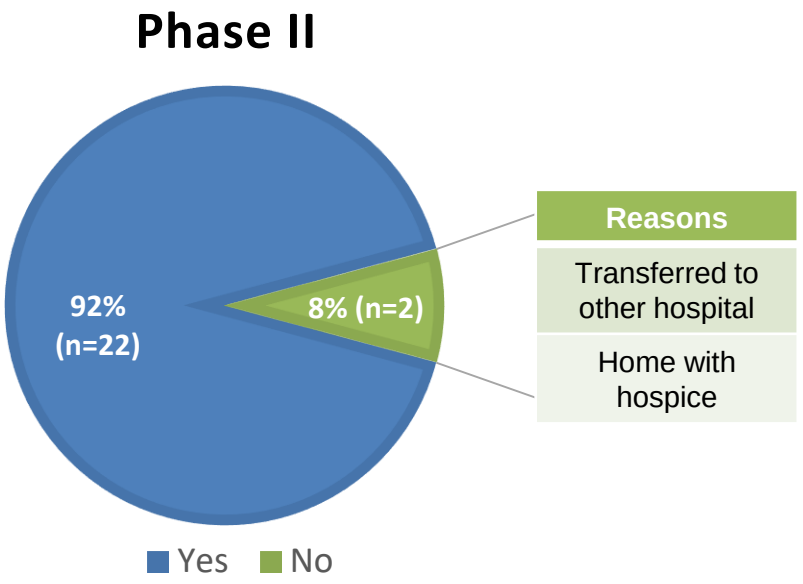
- Percentage of patients transitioned *off* of midodrine

	Phase I (N=15)	Phase II (N=24)	p-value
ICU Discharge, n (%)	6 (40)	19 (79)	p = 0.019
Hospital Discharge	9 (60)	22 (92)	p = 0.037

Results: Primary Outcome

Percentage of patients transitioned off of midodrine at *hospital discharge*





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Results: Secondary Outcome

Variable	Phase I (N=15)	Phase II (N=24)	p-value
Time from midodrine initiation to ICU discharge, days (mean, SD)	5 ± 6.7	12 ± 6.1	p = 0.002
ICU LOS, days (mean, SD)	12 ± 8.8	23 ± 11.9	p = 0.006
Time on vasopressor prior to initiation of midodrine, days (mean, SD)	5 ± 6.1	4 ± 2.8	p = 0.587
Midodrine duration, days (mean, SD)	12 ± 8.8	9 ± 8.3	p = 0.267
Pharmacy interventions in phase II, n Taper midodrine Discontinue midodrine	 - -	28 14 14	-

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Discussion

- Vasopressors were discontinued sooner in phase I (3 days) vs. phase II (4 days) after midodrine initiation
  - Average vasopressor duration was 8 days in both phases
- Patients in phase I were on vasopressors longer prior to midodrine initiation
  - Midodrine continued longer in phase I (12 days) vs. phase II (9 days)
- ICU LOS was shorter in phase I (12 days) vs. phase II (23 days)
  - Causes unrelated to vasopressor utilization
  - Mortality rate was higher in phase I (75%) vs. phase II (45%)
- Pharmacist involvement optimized midodrine therapy

Study Limitations

- Critically ill patients were included in phase I based on ICD-10 codes, which may have limited sample size
- Phase I was retrospective and pharmacist interventions were not calculated
- Limited sample size in phase II
- Phase II was conducted during COVID-19 pandemic

Conclusion

Midodrine was initiated later in phase I and continued for longer compared to phase II

Due to pharmacist interventions in phase II, inappropriate use of midodrine was reduced at ICU/hospital discharge

Future studies are necessary to solidify this correlation in our institution

Assessment Question

Which of the following is the role of midodrine in weaning off vasopressors?

A. Decrease blood pressure to maintain ACC/AHA blood pressure goal while in the ICU
B. Increase IV vasopressor rate to facilitate weaning
C. Increase adherence rates of anti-hypertensive medications once discharged
D. Decrease IV vasopressor rate, complications and ICU length of stay

Acknowledgements

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