Midodrine Drug Use Evaluation in Adult ICU Patients at a Community Teaching Hospital

Brianne Comstock, PharmD, Mindee Hite, PharmD, Kevin Silinskie, PharmD

Introduction

- Intravenous (IV) vasopressor use is associated with significant adverse events, requirement of placement and maintenance of a central venous catheter, and becomes a barrier to ICU discharge if the patient is otherwise medically ready
- Midodrine is an enteral peripherally-agent alpha-agonist often used to facilitate weaning off IV vasopressors
- A single-center retrospective cohort study in 2016 with 188 patients revealed that midodrine resulted in a significant reduction in IV vasopressor duration by 1.2 days, but did not result in a significant difference in hospital length of stay (LOS), ICU LOS, or ICU readmissions[1]
- More recently, 2 multi-center studies assessing the use of fixed-dose enteral midodrine as compared to placebo did not find a significant reduction in vasopressor duration, hospital LOS, or ICU LOS [2-3]
- This study aims to characterize the use of midodrine in adult ICU patients at RGH who are concurrently on vasopressor therapy by evaluating the effect of midodrine on duration of vasopressor therapy, incidence of bradycardia, and if midodrine is discontinued prior to discharge from the ICU and hospital

Methods

- Single center retrospective analysis between January 1, 2022 and June 30, 2022.
- Inclusion criteria: 18 years of age or older, admitted to an ICU, and initiated on midodrine at a frequency of TID or q8h while concurrently receiving continuous IV vasopressor therapy
- Exclusion criteria: history of end-stage renal disease on dialysis prior to admission, presumed or diagnosed hepatorenal syndrome, or active midodrine prescription prior to admission
- Primary and secondary objectives: duration of vasopressor therapy, incidence of bradycardia, and discontinuation of midodrine prior to discharge from the ICU
- Baseline comparisons performed using the chi-squared test for equal proportions with results reported as numbers, and percentages. Non-normally distributed will be compared using Wilcoxon rank sum tests and reported as medians and interquartile ranges

Results

Table 1. Baseline Demographics

Demographic	Control (n=30)	Midodrine (n=30)	P-value
Age (years)[a]	76 (61-80)	68 (62-76)	NS
Male gender[b]	22 (73)	21 (70)	NS
Weight (kg)[a]	82 (75-109)	87 (66-107)	NS
Height (cm)[a]	174 (165-178)	173 (168-178)	NS
BMI (kg/m^2)[a]	27.5 (25.2-33.6)	28.5 (22.9-36.0)	NS
Service			
Medical ICU[b]	13 (43)	26 (87)	<0.001
Surgical ICU[b]	9 (30)	0 (0)	0.002
Cardiac ICU[b]	5 (17)	3 (10)	NS
Cardiothoracic ICU[b]	3 (10)	1 (3)	NS
Etiology of Shock			
Hypovolemic[b]	3 (10)	6 (20)	NS
Cardiogenic[b]	10 (33)	4 (13)	NS
Septic[b]	14 (47)	18 (60)	NS
Distributive[b]	2 (7)	2 (7)	NS
Unknown Origin[b]	1 (3)	0 (0)	NS

[a] median (IQR), [b] n (%), NS = Not significant

- There was no difference in duration of IV vasopressor therapy for those that concomitantly received midodrine
- Midodrine did not reduce the incidence of IV vasopressor re-initiation
- Those who received midodrine experienced significantly more bradycardia
- 40% of patients started on midodrine during their admission who survived were continued on midodrine after discharge

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Discussion

- Patients in this analysis were more likely to be male, greater than 65 years old, and overweight
- The type of shock did not differ between groups, but majority presented with septic shock
- Midodrine was primarily used in medical ICU patients which is likely due local prescribing practices
- There was no difference in the duration of IV vasopressor therapy for those that concomitantly received midodrine compared to those that did not which is consistent with recently published literature
- The use of midodrine did not reduce the incidence of IV vasopressor re-initiation or readmission to the ICU
- More patients in the midodrine group experienced bradycardia compared to the control group
- Midodrine was mainly initiated in those receiving one IV vasopressor at a low dose, an appropriate scenario to attempt weaning of IV vasopressor
- In the midodrine group, 40% of patients discharged alive were prescribed midodrine to be continued beyond their admission which is likely unnecessary as their shock state is resolved at discharge

Results

Table 2. Primary and Secondary Outcomes

Outcome	Control (n = 30)	Midodrine (n = 30)	P-value
Duration of vasopressors (hours)[a]	63.4 (49.5-98)	67.5 (48.2-115)	NS
Re-initiation of vasopressors during ICU stay[b]	13 (43)	13 (43)	NS
Bradycardia (Heart Rate < 50 bpm)[b]	4 (13)	12 (40)	0.021
Required re-admission to ICU[b]	1 (3)	1 (3)	NS
Mortality during admission[b]	10 (33)	12 (40)	NS

Table 3. Midodrine Outcomes

Midodrine Outcomes	(n = 30)
Vasopressor dose at midodrine initiation (Norepinephrine equivalents mcg/kg/min)[a]	0.05 (0.03-0.12)
Number of vasopressors infusing at time of midodrine initiation[a]	1 (1-1)
Midodrine daily dose at initiation (mg)[a]	30 (30-30)
Midodrine average daily dose (mg)[a]	28.5 (20-40)
Midodrine maximum daily dose (mg)[a]	50 (30-60)
Transferred out of ICU on midodrine[b]	11 (37)
Discharged from hospital with midodrine prescription[b]	7 (23)
Discharged from hospital with midodrine prescription, corrected for mortality (n = 18)[b]	7 (40)
Total duration of midodrine (days)[a]	3.65 (2-10)
Duration of midodrine after vasopressor discontinuation (days)[a]	1.6 (0.8-8.4)
Reinitiation of midodrine during hospitalization[b]	5 (17)

Corresponding author:
brianne.comstock@rochesterregional.org
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