Use of midodrine to discontinue intravenous vasopressors in intensive care unit patients

Akash Dev MBA, Ava Oliver BS, Anuya Alapati MD, Kenneth Nugent MD

ABSTRACT

Purpose: *Midodrine, an oral alpha-adrenergic agonist, has been used off-label in critically ill patients to facilitate discontinuation of intravenous (IV) vasopressors. The proposed benefits include earlier liberation from vasopressors and expedited ICU discharge. However, existing evidence has been inconsistent.*

Methods: *We searched PubMed using the MeSH terms "midodrine" and "vasoconstrictor agents" with filters for clinical studies in adults (≥19 years). Studies in patients with cirrhosis were excluded.*

Results: *Seven clinical studies were identified: three randomized controlled trials (RCTs), three retrospective studies, and one case-control study. Two RCTs with 62 and 132 patients found no difference in vasopressor duration or ICU length of stay with midodrine. One RCT demonstrated reduced vasopressor use and costs. Retrospective and case-control studies suggested limited or adjunctive benefits. Bradycardia was the most consistent adverse effect, reported in up to 15% of patients.*

Conclusions: *Evidence regarding midodrine's efficacy in facilitating IV vasopressor discontinuation is inconsistent. While some studies suggest potential benefit, most trials demonstrate no significant impact on vasopressor duration or ICU length of stay. Safety concerns, particularly bradycardia, warrant caution. Large, multicenter RCTs are needed before midodrine can be recommended as standard practice in ICU vasopressor management.*

INTRODUCTION

Hypotension, defined as mean arterial pressure (MAP) <65 mmHg, is a frequent and serious complication in critically ill patients and is associated with increased morbidity and mortality.[1,2] Intravenous vasopressors such as norepinephrine, phenylephrine, epinephrine, and vasopressin are cornerstone therapies to restore perfusion.[3] However, prolonged vasopressor use carries risks, including arrhythmias, ischemia, acute kidney injury, and increased ICU costs.[4]

Midodrine, an oral direct alpha-adrenergic agonist, is FDA-approved for orthostatic hypotension. Its active metabolite, desglymidodrine, increases systemic vascular resistance by stimulating peripheral alpha-1 adrenergic receptors.[7–10] Beyond orthostatic hypotension, midodrine has been used off-label in conditions such as postural orthostatic tachycardia syndrome, vasovagal syncope, dysautonomia, stress urinary incontinence, and heart failure.[11–13]

In the ICU, midodrine has gained interest as an adjunct therapy to facilitate vasopressor weaning, potentially reducing ICU length of stay, lowering costs, and improving resource use.[5,6] This review evaluates current evidence regarding midodrine's role in vasopressor discontinuation, focusing on efficacy, safety, and clinical outcomes.

Corresponding author: **Akash Dev**
Contact Information: Akash.Dev@ttuhsc.edu
DOI: 10.12746/swjm.v13i57.1577

METHODS

A PubMed search was performed using the MeSH terms "midodrine" and "vasoconstrictor agents." Filters

Table 1. Midodrine Effect on Vasopressor Weaning, ICU Length of Stay, and Mortality

Author, Year	Trial Design # of Patients	Midodrine Dose (Frequency)	Time on VP Prior to M	Time to Wean VP	ICU Length of Stay	Mortality	Author Conclusion
Wood 2023[14]	Case control 19 M 42 C	20 mg (every 8 h)	3.9 d* M 1.2 d C	26 hr* M 24 hr C	7 d* M 6 d C	NR***	Limited efficacy
Poveromo 2016[6]	Retrospective 94 M 94 C	2.5–10 mg (every 4 to 12 h)	1.6 d* M	1.2 d* M C NR***	5.5 d* M 5.0 d C	8 M (8.5%) 21 C (22%)	Possible adjunctive therapy
Whitson 2016[15]	Retrospective 135 M 140 C	10–40 mg (every 8 h)	NR***	2.9 d** M 3.8 d C	7.5 d** M 9.4 d C	31 M (23%) 36 C (26%)	May reduce vasopressor time
Rizvi 2018[16]	Retrospective uncontrolled 1,119 ICU patients	5–30 mg (every 8 h)	NR***	NR***	NR***	NR***	48% of patients were weaned off IV VP with midodrine. 15.4% of patients developed bradycardia
Costa-Pinto 2022[17]	RCT 32 M 30 C	10 mg (every 8 h)	>24 hours	16.5 hr* M 19.0 hr C	2 d* M 2.4 d C	1 M (3%)	No efficacy
El Adly 2022[15]	RCT 30 M 30 C	10 mg (every 8 h)	3.8 d* M 5.8 d C Total time	1.08 d* M 3.27 d C	12 d** M 12 d C	13 M (43%) 22 C (73%)	Reduced vasopressor time and costs
Santer 2020[18]	RCT 66 M 66 C	20 mg (every 8 h)	>24 hr	23.5 hr* M 22.5 hr C	6 d* M 6 d C	NR***	No efficacy Risk for bradycardia

IV-Intravenous; VP-Vasopressor; M-midodrine; C-control; RCT- randomized controlled trial; *- median; **- mean; ***

were applied to include clinical studies in adult patients (≥19 years). Studies in patients with cirrhosis were excluded due to differing pathophysiology. Titles and abstracts were screened, followed by full-text review of eligible articles. Reference lists of included studies were reviewed for additional citations.

Criteria for inclusion included clinical research (RCTs, cohort studies, case-control studies, case series), use of midodrine for therapeutic purposes in ICU patients, and outcomes related to vasopressor discontinuation, hemodynamics, or ICU stay. Exclusion criteria included pediatric patients, patients with cirrhosis or hepatic disease, and preclinical studies, editorials, reviews, or conference abstracts.

Results

Seven clinical studies met inclusion criteria (Table 1). These included three RCTs, three retrospective studies, and one case-control study.

Efficacy: Two RCTs (n = 62 and n = 132) found no reduction in vasopressor duration or ICU stay with midodrine.[17,18] One RCT (n = 60) reported shorter vasopressor duration and lower costs.[5] Retrospective

and case-control studies reported mixed results, with some suggesting modest reductions in vasopressor duration.[6,14,15]

Safety: Bradycardia was the most notable adverse effect. In one large retrospective cohort (n = 1,119), bradycardia occurred in 15.4% of patients.[16]

ICU length of stay: No consistent benefit was observed across studies. Variability in ICU discharge protocols may account for differences.

Limitations: Small sample sizes, heterogeneous populations, non-standardized dosing regimens, and single-center designs limited generalizability.

Discussion

This review highlights significant variability in study results evaluating midodrine for vasopressor weaning in the ICU. Only one RCT demonstrated a clear reduction in vasopressor duration and cost, whereas other randomized trials showed no benefit. Observational studies provided mixed conclusions, often limited by retrospective design and lack of standardized protocols.

Safety concerns, particularly bradycardia, must be considered in critically ill patients who are already hemodynamically unstable. In addition, inconsistent dosing strategies and heterogeneous patient populations complicate interpretation of outcomes.

The lack of reproducibility across similar RCTs underscores the need for larger multicenter trials with standardized protocols. Until such evidence is available, midodrine should not be adopted as routine therapy for vasopressor weaning.

Conclusion

Midodrine has been studied as an adjunctive therapy to facilitate IV vasopressor discontinuation in critically ill patients. Current evidence does not consistently demonstrate reductions in vasopressor duration, ICU length of stay, or mortality. Safety concerns, particularly bradycardia, further limit its widespread use. At present, midodrine should be considered investigational for this purpose, and routine use cannot be recommended. Large, well-designed multicenter RCTs are required to determine its role in ICU practice.

Article citation: Dev A, Oliver A, Alapati A, et al. Use of midodrine to discontinue intravenous vasopressors in intensive care unit patients. The Southwest Journal of Medicine 2025;13(57):36–39
From: Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX (DA, OA, AA, KN)
Submitted: 9/01/2025
Accepted: 9/22/2025
Conflicts of interest: none

References

1. Schuurmans J, van Rossem BTB, Rellum SR, et al. Hypotension during intensive care stay and mortality and morbidity: a systematic review and meta-analysis. Intensive Care Med, 2024;50(4):516–25.
2. Schenk J, van der Ven WH, Schuurmans J, et al. Definition and incidence of hypotension in intensive care unit patients, an international survey of the European Society of Intensive Care Medicine. Journal of Critical Care, 2021;65:142–8.
3. VanValkinburgh D, Hashmi MF. Inotropes and vasopressors. StatPearls. 2024, StatPearls Publishing
4. Jentzer JC, Coons JC, Link CB, et al, Pharmacotherapy update on the use of vasopressors and inotropes in the intensive care unit. J Cardiovasc Pharmacol Ther, 2015;20(3):249–60.
5. Adly DHE, Bazan NS, Borolossy RME, et al. Midodrine improves clinical and economic outcomes in patients with septic shock: a randomized controlled clinical trial. Ir J Med Sci, 2022;191(6):2785–95.
6. Poveromo LB, Michalets EL, Sutherland SE. Midodrine for the weaning of vasopressor infusions. J Clin Pharm Ther, 2016;41(3):260–5.
7. Gilden JL. 112 – Midodrine and Other Sympathomimetics, in Primer on the Autonomic Nervous System (Second Edition), D. Robertson, et al., Editors. 2004, Academic Press: San Diego. p. 413–15.
8. McTavish D, Goa KL. Midodrine. A review of its pharmacological properties and therapeutic use in orthostatic

hypotension and secondary hypotensive disorders. Drugs, 1989;38(5):757–77.
9. Midodrine, in Meyler's Side Effects of Drugs: The International Encyclopedia of Adverse Drug Reactions and Interactions (Fifteenth Edition), J.K. Aronson, Editor. 2006, Elsevier: Amsterdam. p. 2343–4.
10. Taylor BN, Cassagnol M. Alpha-Adrenergic Receptors, in StatPearls. 2025, StatPearls Publishing.
11. Hajjiah A, Maadarani O, Bitar Z, et al. Use of Midodrine in Heart Failure: Two Case Reports and a Review of the Literature. Eur J Case Rep Intern Med, 2022;9(3):003246.
12. Ross AJ, Ocon AJ, Medow MS, et al. A double-blind placebo-controlled cross-over study of the vascular effects of midodrine in neuropathic compared with hyperadrenergic postural tachycardia syndrome. Clin Sci (Lond), 2014;126(4): 289–96.
13. Raj S, Sheldon R. Management of Postural Tachycardia Syndrome, Inappropriate Sinus Tachycardia and Vasovagal Syncope. Arrhythm Electrophysiol Rev, 2016;5(2):122–9.
14. Wood AJ, Rauniyar R, Jacques A, et al. Oral midodrine does not expedite liberation from protracted vasopressor infusions: A case-control study. Anaesth Intensive Care, 2023; 51(1):20–8.
15. Whitson MR, Mo E, Nabi T. Feasibility, Utility, and Safety of Midodrine During Recovery Phase From Septic Shock. Chest, 2016;149(6):1380–3.
16. Rizvi MS, Trivedi V, Nasim F, et al. Trends in Use of Midodrine in the ICU: A Single-Center Retrospective Case Series. Crit Care Med, 2018;46(7):e628–e633.
17. Costa-Pinto R, Bellomo R. Randomised-control trials do not support midodrine as an intravenous vasopressor weaning strategy. J Crit Care, 2022;72:153996.
18. Santer P, Anstey MH, Patrocinio MD, et al. Effect of midodrine versus placebo on time to vasopressor discontinuation in patients with persistent hypotension in the intensive care unit (MIDAS): an international randomised clinical trial. Intensive Care Med, 2020;46(10):1884–93.