

# The Slow Rhythm of Midodrine: A Peculiar Case of Profound Bradycardia

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## Abstract

Shock is a state of decreased organ perfusion that is life-threatening and requires emergent medical intervention [1]. As such, patients who present with shock are often managed in the critical care unit with intravenous fluid boluses and vasoactive agents. The ultimate goal is to prevent multi-system organ failure and to achieve a mean arterial pressure >65mmHg. Oral Midodrine has been hailed as an adjunctive therapy in critical care patients with refractory hypotension [2, 3, 4, 5]. However, Midodrine is only FDA approved, and remains the sole treatment for symptomatic orthostatic hypotension [6]. The mechanism of action is through alpha-1 adrenergic activation leading to an increase in vascular tone [2, 3, 4, 5]. Midodrine does not stimulate cardiac beta adrenergic receptors, however its use can result in profound bradycardia [6]. We present a case of a 53 year old patient in hypovolemic shock, refractory to fluid resuscitation who developed profound bradycardia after the initiation of Midodrine. This case highlights an overlooked and potentially dangerous side effect of a commonly used, off-label indication for this medication.

## Objective

The objective of this case report is to highlight the effect of Midodrine on the cardiovascular system.

## Introduction

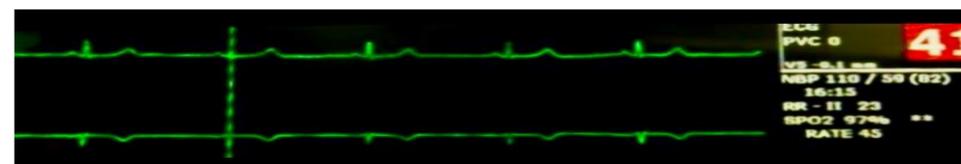
Midodrine is a short-acting vasopressor approved by the FDA in 1996 for orthostatic hypotension. It belongs to the drug class alpha-1-receptor agonist which increases vascular tone and raises blood pressure. Midodrine is historically used to treat patients with symptomatic low blood pressure when a patient moves from sitting to standing, known as orthostatic hypotension. Midodrine is also proved to be a safe way to prevent a drop in blood pressure inpatients during dialysis sessions because it maintains vascular tone. More recently, Midodrine has been used in the ICU setting to maintain patients' mean arterial blood pressure when they are being weaned off other vasopressors. It has also been used in adjunct with other vasopressors, or alone..

## Hospital Course

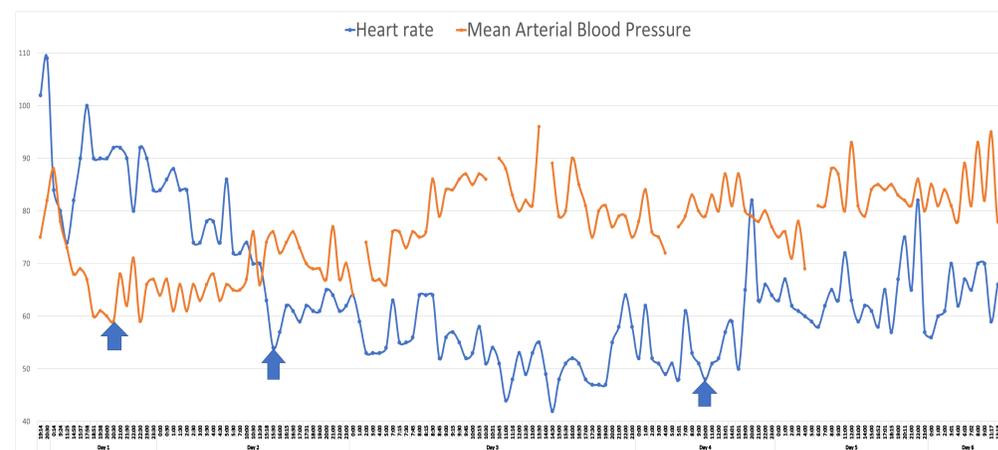
The patient is a 53 year old female with a history of Crohn's disease (diagnosed at 18 y/o) who presented with nausea, non-bilious emesis and concerns for high output ostomy. On presentation she reported left lower quadrant abdominal pain that was 8 to 10/10 in severity, intermittent, sharp in quality and non-radiating. She also reported 300-500 mL in her ileostomy bag every hour, which has increased from her usual 250mL. She also reported a reduced appetite over the past 4 days with a 7 pound weight loss prior to arrival. The patient denied recent GI illness, smoking, alcohol, or recreational drug abuse. She also denies any extra-intestinal manifestations such as a rash, blurry vision, muscle/joint pain, chest pain, palpitations or back pain.

Initial vitals were stable with pulse ranging 76 to 104 beats per minute and blood pressure from 107/56 to 142/88 mmHg. CBC was unremarkable, CMP was remarkable for acute renal injury, hypokalemia and hypomagnesemia. The patient was admitted for an acute gastroenteritis and subsequently developed hypovolemic shock.

The intriguing part about the case was reflected in the patient's response to Midodrine. As noted above, the patient was in hypovolemic shock with initial blood pressure readings as low as 80/50 mmHg and heart rates between 90 to 110 beats per minute. After the initiation of Midodrine, the patient's blood pressure improved to 110/60 mmHg, however her pulse rate remained within the range of 39 to 60 beats per minute on telemetry (Figure 1). The patient was not on any atrioventricular nodal blocking agents and was asymptomatic.



**Figure 1:** Telemetry strip showing profound sinus bradycardia and normal P-R interval. There was no evidence of pauses, heart block or P-QRS dissociation on telemetry or electrocardiography.



**Figure 2:** A graphic representation of mean arterial blood pressure (blue line) versus heart rate (orange line) in the setting of Midodrine administration. The X axis (Day and time) represents the real time recordings by nursing staff. The first arrow represents the first time of Midodrine administration. The second arrow represents the initial drop of heart rate and the last arrow represents the discontinuation of Midodrine.

## Discussion

In Critical Care and Progressive Care patients, our goals in correcting hypotension include providing volume support and/or pressure support. In refractory hypotension cases where volume resuscitation does not improve hypotension, we must focus on providing pressure support. Midodrine is a typical first-line agent in providing pressure support through its effects as an agonist on alpha-1 adrenergic receptors. Of note, Midodrine's mechanism of action can be compared to that of phenylephrine, epinephrine and also norepinephrine which predominantly acts as an agonist on alpha-1 adrenergic receptors. Although phenylephrine, epinephrine and norepinephrine are common vasopressor agents used in the setting of Critical Care and Anesthesia, Midodrine is not. Due to Midodrine's nature as an oral medication that is commonly used outside of Critical Care and Anesthesia, the effect of reflex bradycardia often seen in vasopressor agents used in Critical Care and Anesthesia can be overlooked. The significance of this is that reflex bradycardia from Midodrine administration can worsen hypotension and increase the requirement for further vasopressor agent support. This ultimately prolongs the course of treatment needed in the Critical Care setting.

## Conclusion

Given the fact that Midodrine is frequently used off label in hypotensive patients, this case serves as a cautionary finding to not only avert excessive workup for bradycardia, but also alert clinicians to this underreported side effect. Midodrine should be stopped especially if the patient experiences symptomatic bradycardia or shows evidence of reduced cardiac output. As such, the case importantly highlights an overlooked and potentially dangerous side effect of a commonly used, off-label indication for Midodrine.

## References

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