

LETTER TO THE EDITOR

Adjunctive Midodrine Therapy for Vasopressor-Dependent Shock in the ICU: A Closer Examination of Serious Adverse Effects

To the Editor:

The recent systematic review and meta-analysis by Kilcommons et al (1), published in a recent issue of *Critical Care Medicine*, presents a comprehensive synthesis of current literature regarding the efficacy of oral midodrine as an adjunct to IV vasopressor therapy in critically ill patients. While the study provides valuable clinical insights, the identification of bradycardia as the most frequently reported adverse event warrants further consideration.

In their discussion, bradycardia was consistently observed as the predominant complication associated with midodrine administration. Notably, three of the included studies reported a statistically significant increase in the incidence of bradycardia among patients treated with midodrine compared to those receiving placebo. As a result, the authors recommend cautious use of midodrine and advocate for vigilant cardiovascular monitoring in future clinical applications or investigations, particularly with regard to its potential to induce bradyarrhythmias (1).

However, a review of the existing literature suggests that this emphasis on bradycardia, while clinically pertinent, may represent only a subset of midodrine's broader adverse event profile. As an α -agonist, midodrine is associated with a diverse range of side effects involving multiple organ systems. In their comprehensive narrative review, Costa-Pinto et al (2) enumerate the wide array of commonly reported adverse events, including gastrointestinal symptoms (nausea, abdominal pain), genitourinary complications (urinary retention, dysuria), cardiovascular events (supine hypertension, bradycardia), and CNS manifestations (paresthesia, altered taste, or smell). According to their findings, up to 80% of patients undergoing midodrine therapy may exhibit at least one adverse event.

Of even greater clinical concern, several isolated case reports and observational studies have implicated midodrine in serious complications, such as Takotsubo cardiomyopathy (3), intracerebral hemorrhage (4), reversible cerebral vasoconstriction syndrome, myoclonic seizures, vascular ischemia, and ileus (2). The systematic review conducted by Puissant et al (5) corroborates these observations, highlighting the potential severity of midodrine-associated complications and emphasizes the need for vigilant patient monitoring to facilitate early detection.

Collectively, these findings underscore the importance of employing appropriate dosing strategies and cautious titration protocols when administering midodrine to mitigate the risk of both common and severe adverse events.

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