Turk J Intensive Care 2025;23(4):335-337
DOI: 10.63729/TJIC.2025.678

CASE REPORT / *OLGU SUNUMU*

Use of midodrine for treatment of hypotension: a case report

Hipotansiyon tedavisi için midodrin kullanımı: bir olgu sunumu

Zeynep Öztürk Yalçın[1], Burçin Halaçlı[2], Kutay Demirkan[1], Arzu Topeli[2]

[1]*Department of Clinical Pharmacy, Faculty of Pharmacy, Hacettepe University, Ankara, Türkiye*
[2]*Division of Intensive Care Medicine, Department of Internal Medicine, Faculty of Medicine, Hacettepe University, Ankara, Türkiye*

ABSTRACT

Midodrine is an orally approved α-agonist increasingly utilized in intensive care units for the treatment of refractory hypotension with peripheral effects. The current case report presents the clinical manifestation of midodrine utilization in a female patient experiencing refractory hypotension. She was admitted to the intensive care unit of a university hospital due to confusion and suspicion of intoxication.

Due to the patient's hypotensive condition, vasopressor support (norepinephrine) was initiated to address shock of unidentified cause. Midodrine was recommended by the clinical pharmacist to the patient due to the persisting need for norepinephrine. This case report highlights that, based on the clinical judgement of the clinician, midodrine can be used during vasopressor weaning when no other specific cause of hypotension has been identified.

Keywords: midodrine, hypotension, vasopressors, intensive care unit

ÖZ

Midodrin, periferik etkili bir α-agonist olup, dirençli hipotansiyonun tedavisinde yoğun bakım ünitelerinde giderek daha sık kullanılan, oral yolla uygulanan onaylı bir ajandır. Bu olgu sunumunda, refrakter hipotansiyon gelişen kadın bir hastada midodrin tedavisinin klinik etkileri değerlendirilmiştir. Hasta, konfüzyon ve zehirlenme şüphesiyle bir üniversite hastanesinin yoğun bakım ünitesine kabul edilmiştir. Hipotansif durumu nedeniyle, etiyolojisi net olarak belirlenemeyen şoka yönelik vazopresör tedavi (norepinefrin) başlanmıştır. Norepinefrin gereksiniminin devam etmesi üzerine, klinik eczacı tarafından hastaya midodrin tedavisi önerilmiştir. Bu olgu, hipotansiyonun belirgin ve spesifik bir nedeninin saptanamadığı durumlarda, klinisyenin klinik yargısına dayanarak vazopresör tedavinin kesilme sürecinde midodrinin destekleyici bir seçenek olarak kullanılabileceğini ortaya koymaktadır.

Anahtar kelimeler: midodrin, hipotansiyon, vazopressörler, yoğun bakım ünitesi

Introduction

Patients admitted to intensive care unit (ICU) often require intravenous vasoactive drugs to maintain normotension or other clinically indicated blood pressure targets. In hypotensive patients without impairment of tissue oxygenation, there is a need for the use of oral agents that could facilitate weaning from intravenous vasopressors and assist in earlier discharge. Midodrine, an oral α_1-adrenergic agonist, received accelerated approval by the U.S. Food and Drug Administration (FDA) in 1996 for the treatment of symptomatic orthostatic hypotension (1).

In this case report, it was indicated that midodrine may be considered as an option during vasopressor weaning in an ICU patient when no other specific cause of refractory hypotension is identified.

✉ Zeynep Öztürk Yalçın • ozturkzeynep96@gmail.com

Received / Geliş tarihi: 06.12.2024 **Accepted / Kabul tarihi:** 17.07.2025 **Published / Yayın tarihi:** 26.12.2025

Case Report

A 54-year-old woman with a known diagnosis of schizophrenia was admitted to ICU of a university hospital with confusion and suspicion of intoxication. A suspicious box was found by relatives in the patient's residence. Box was submitted to Drug and Poison Information Unit (HIZBIB), but due to lack of necessary infrastructure, the sample could not be analyzed. Given the initial presentation and suspicion of intoxication; ethanol, methanol, and urine toxicology analyses were performed as part of the differential diagnosis. Toxicological screening revealed no abnormalities; both ethanol and methanol levels were negative. Cardiac evaluation, including transthoracic echocardiography, demonstrated preserved left ventricular systolic function, with an ejection fraction of approximately 60%. The patient's initial Glasgow Coma Score (GCS) was 14, which later deteriorated, requiring elective intubation. Following admission to the ICU, urinalysis revealed the presence of leukocyturia, a finding that prompted clinicians to consider the possibility of urosepsis as a potential diagnosis. Due to escalating vasopressor requirements, with norepinephrine titrated up to 0.87 mcg/kg/min, empirical antibiotic therapy was initiated with ampicillin-sulbactam, followed by piperacillin-tazobactam. No microbial growth was detected in urine or blood cultures. Despite adequate fluid resuscitation, the patient remained hemodynamically unstable. As a result, additional vasoactive agents—adrenaline and dobutamine—were introduced. Critical illness related corticosteroid insufficiency was not ruled out and methylprednisolone was also administered. Given a serum albumin level of 2.3 mg/dL, albumin replacement therapy was administered. However, due to progressive neurological deterioration and increasing vasopressor requirements, elective endotracheal intubation was performed. On ICU day 3, the patient was successfully extubated. Vasopressor requirement varied between 0.01-0.5 mcg/kg/min throughout the patient's hospitalization. Following improvement in clinical status and a decline in acute-phase reactants, antibiotic therapy was discontinued. Nevertheless, the patient remained hypotensive, necessitating ongoing vasopressor support. Midodrine was recommended by the clinical pharmacist to the patient due to the persisting need for norepinephrine and administered to the patient as 2*2.5 mg/day posology. While midodrine was given, 0.1 mcg/kg/min of norepinephrine was continued to the patient. 4 days after starting midodrine, the patient's norepinephrine requirement decreased to 0.03 mcg/kg/min. On the eighth day, the patient's norepinephrine was stopped and midodrine was increased to 2*5 mg/day. During this period, the patient did not need a vasopressor. On the fourteenth day, the dose of midodrine was reduced to 2*2.5 mg/day because the patient's blood pressure was within the normal range and the patient was transferred to ward, where midodrine treatment was was maintained at the same dose.

Discussion

Midodrine is an oral α_1-adrenergic agonist which undergoes enzymatic hydrolysis to form its active metabolite desglymidodrine. It exerts its sympathomimetic effect via activation of alpha adrenergic receptors in the blood vessels which causes an increase in venous return and blood pressure (2). FDA proposed to withdraw approval of midodrine because of lack of studies that verify the clinical benefit of the drug in August 2010. However, there were many studies declaring that midodrine is effective in the treatment of refractory hypotension. Anstey et al. showed that the rate of decline in vasopressor requirements increased after initiation of midodrine treatment. They hypothesize that midodrine administration is effective to wean intravenous vasopressors and shorten ICU and hospital length of stay (3). According to the results of another study carried out by Levine et al., midodrine treatment was associated with an improve in the magnitude of decline of the IV vasopressor dose (4). According to the MIDAS trial conducted by Santer et al. midodrine did not accelerate the discontinuation of intravenous vasopressors. The median time to vasopressor

discontinuation was 23.5 hours in the midodrine group compared to 22.5 hours in the placebo group, a difference that was not statistically significant (p=0.62). These findings do not support the routine off-label use of midodrine for facilitating weaning from intravenous vasopressors in critically ill patients. Therefore, in cases such as the one presented, where midodrine is considered for the management of persistent hypotension in the intensive care setting, it is essential to discuss the negative findings of the MIDAS trial. While earlier small-scale observational studies and case reports have suggested potential benefits, the results of this randomized controlled trial—providing a higher level of evidence—cast doubt on the clinical efficacy of midodrine in this context (5).

Our case report indicates that four days after initiating midodrine, the patient's requirement for norepinephrine was reduced. These findings imply that although the evidence supporting the use of midodrine in the treatment of refractory hypotension is limited and of low quality, midodrine may be used based on physicians' clinical judgement to wean patients from vasopressor therapy when another specific cause of hypotension cannot be identified (6).

Conclusion

In patients who remain hypotensive despite vasopressor therapy, there is limited and low-quality evidence to support the use of midodrine when weaning patients from vasopressors. It should be considered that midodrine may be used to wean hypotensive patients from vasopressor support when all other clinical causes have been ruled out (6).

Ethical approval

Written informed consent was obtained from the patient's sister for publication of the data in this case report.

Author contribution

Study conception and design: KD, AT, BH; analysis and interpretation of results: ZÖY; draft manuscript preparation: ZÖY, BH. The authors reviewed the results and approved the final version of the article.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

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