Title:

Evaluation of midodrine use on clinical outcomes in septic shock

Purpose:

The purpose of this study was to evaluate the efficacy and safety of oral midodrine in weaning intravenous (IV) vasopressors in critically ill patients with septic shock. Despite the lack of a standard midodrine initiation guidance used in observational studies and the paucity of supportive evidence from meta-analysis and controlled trials, midodrine continues to be used in critical care settings. This study was thus designed to evaluate the use, efficacy, and safety of midodrine in clinical practice.

Methods:

This study was a retrospective chart review of patients admitted between January 2018 and December 2020 to the medical-surgical ICU and cardiac ICU of a 617-bed acute care, academic medical center. This study was approved by the Trinity Health of New England Institutional Review Board (IRB). Patients were included in the study if they were admitted to the medical-surgical ICU or cardiac ICU during the study period, received at least one IV vasopressor, had a diagnosis of septic shock, and were over the age of eighteen. Patients were excluded if they received midodrine without a vasopressor, received intermittent hemodialysis, were pregnant, were over the age of eighty-nine, or had a diagnosis of COVID-19. Patients were divided into two groups: those who received only vasopressors (the control group) and those who received vasopressors with adjunctive midodrine (midodrine group). The patients in the two treatment arms were case-matched based on Acute Physiology and Chronic Health Evaluation (APACHE) II scores. The primary outcome was ICU length of stay (LOS) in days. The secondary outcomes were hospital LOS (days), duration of vasopressor use (days), and mortality. For patients who received midodrine, the occurrence of bradycardia and hypertension were recorded. Chi-square analyses were used to compare categorical variables by treatment group. T-tests were used to compare age and APACHE II score. A Wilcoxon test was used to compare continuous variables. A statistically significant result was defined as having a *P-value* <0.05 level of significance.

Results:

Ultimately, 118 patients met the study criteria and were case-matched, with 59 patients in each treatment arm. There was no statistically significant difference between the two groups for demographic characteristics of gender, age, or APACHE II score. The following outcomes, in days, were significantly increased in the midodrine group vs the control group: median ICU LOS [9 vs 4.1 (*P*<0.01)], median hospital LOS [13.9 vs 8.3 (*P*<0.01)], and median duration of vasopressor use [5.3 vs 2.3 (*P* <0.01)]. There was no difference in hospital mortality between the groups (*P*= 0.57). Bradycardia was noted in 6 patients treated with midodrine. No patients treated with midodrine experienced hypertension.

Conclusions:

The study results indicate that the use of oral midodrine to wean IV vasopressors was significantly associated with an increased ICU LOS, increased hospital LOS, and increased duration of vasopressor use compared to the use of IV vasopressor alone. There was also a 10% incidence of bradycardia with midodrine initiation. Despite utilizing case matching to minimize confounding variables, the results of this study may reflect that in this institution, midodrine was being initiated as salvage therapy in patients who were not clinically improving, in addition to initiation as adjunct therapy in patients who were recovering from septic shock. This strategy of salvage therapy may not be associated with clinical benefits. Meanwhile, the benefits of midodrine initiation in patients demonstrating clinical improvement in the recovery phase of septic shock remain unclear. Lastly, further investigation can explore the use of midodrine as a vasopressor sparing agent in the early phase of sepsis (first 24 hours) rather than during the recovery phase.