Effect of the Initial Maintenance Dose of Droxidopa on Treatment Persistence in Patients With Neurogenic Orthostatic Hypotension

American Autonomic Society
2020 Virtual
November 6–7, 2020

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KEY POINTS

- Real-world use of droxidopa for the treatment of neurogenic orthostatic hypotension (nOH) was examined.
- Using clinical practice data, the relationships between droxidopa dosage, titration schedule, and treatment persistence were examined.
- The analyses revealed that patients are often not titrated consistent with the droxidopa product label recommendations (ie, customized titration).
- Customized titration schedules may lead to the use of lower daily maintenance dosages of droxidopa and less treatment persistence.
- When using droxidopa, prescribers should consider whether patients might benefit from higher doses and faster titrations to avoid suboptimal dosing, which can lead to poor clinical outcomes.

INTRODUCTION

- Droxidopa is approved to treat the symptoms of nOH and requires titration to an individualized optimally effective dose **(Figure 1)**.[1]
- If the titration is stopped because of lack of tolerability (eg, occurrence of supine hypertension), maintenance treatment should commence at the previous titration dose assuming it provided reasonable efficacy.

FIGURE 1 - Recommended Titration of Droxidopa[1]

TID=3 times daily.

- It is critical to rapidly identify the optimal dose to reduce patients' nOH symptom burden and improve their physical function.[2-4]

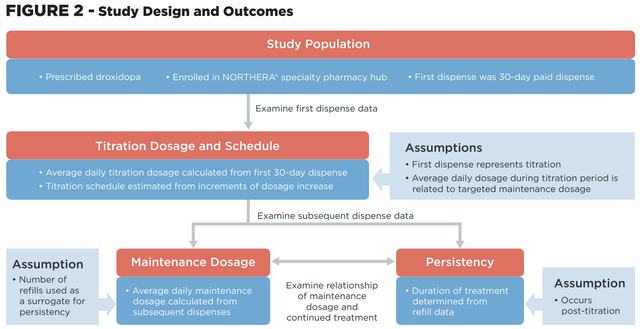
OBJECTIVE

To examine titration schedules, daily dosages, and treatment persistence of droxidopa in patients with nOH treated in clinical practice settings

METHODS

- Using patient-level data from the central NORTHERA® specialty pharmacy hub, outcomes related to titration dosage and schedule, maintenance dosage, and persistence were examined **(Figure 2)**.

FIGURE 2 - Study Design and Outcomes



RESULTS

DROXIDOPA TITRATION SCHEDULE AND DOSAGE

- 53% of patients were titrated using a custom schedule (ie, not per the droxidopa labeling recommendation; **Figure 3**).
- Patients custom titrated received substantially lower daily titration dosages of droxidopa vs those titrated consistent with the droxidopa label **(Figure 4)**.
  - Patients titrated per the droxidopa label received dosages more consistent with optimized dosages in the clinical trials.[5-8]
- 52% of patients titrated with custom schedules received ≤300 mg of droxidopa/day; in the clinical trials, 65% of patients received >900 mg droxidopa/day[9] **(Figure 5)**.

FIGURE 3 - Percentage of Patients by Titration Schedule

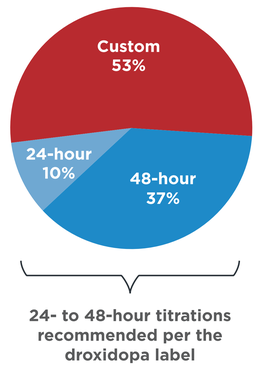
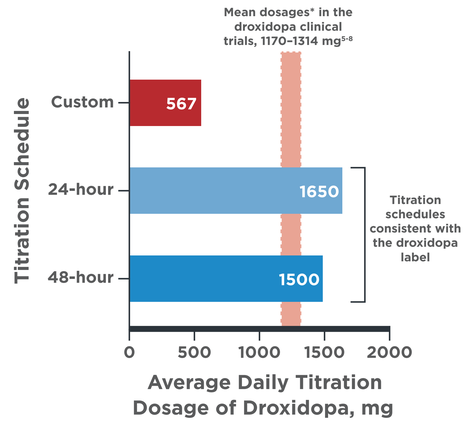
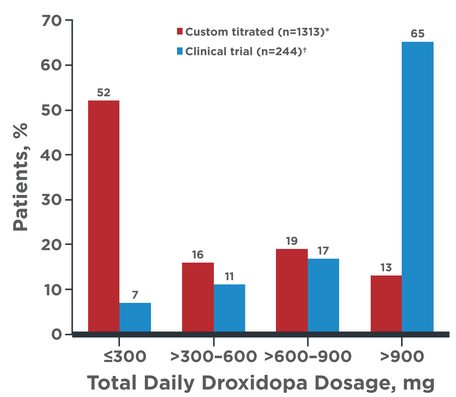


FIGURE 4 - Average Daily Titration Dosage by Titration Schedule



*Optimized dosage.

FIGURE 5 - Daily Droxidopa Dosages in Patients Using Custom Titration Schedules* vs in the Clinical Trials†[9]

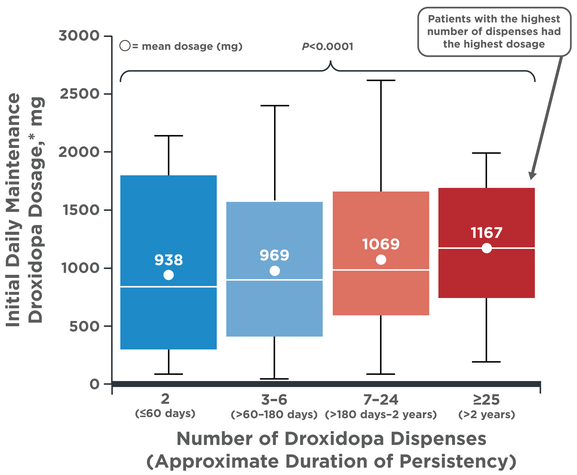


*Average dosage.
†Optimized dosage.

DROXIDOPA MAINTENANCE DOSAGE AND TREATMENT PERSISTENCE

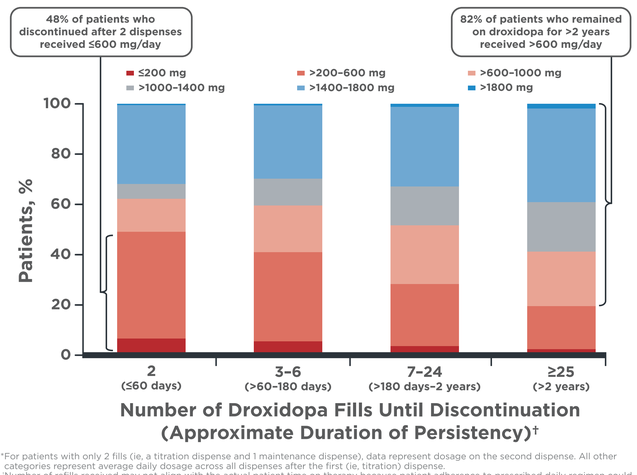
- There was a significant relationship between initial daily maintenance dosage of droxidopa and treatment persistence, as determined by number of dispenses ($P<0.0001$; **Figure 6**).
- Dosage level stratification by number of fills also supports a relationship between greater treatment persistence and higher average daily dosages **(Figure 7)**.

FIGURE 6 - Initial Daily Maintenance Dosage* by Number of Dispenses



*Calculated from total milligrams dispensed on second dispense/days supplied.

FIGURE 7 - Distribution of Average Daily Maintenance Dosage in Persistency Groupings*



*For patients with only 2 fills (ie, a titration dispense and 1 maintenance dispense), data represent dosage on the second dispense. All other categories represent average daily dosage across all dispenses after the first (ie, titration) dispense.
†Number of refills received may not align with the actual patient time on therapy because patient adherence to prescribed daily regimen could not be determined in the data. Discontinuation was defined as no prescription refill within 30 days of the expected run-out from the last fill.

LIMITATIONS

- The reasons for use of custom titration schedules could not be examined.
- Although daily titration and final maintenance dosage are likely strongly related, the relationship was not established in our analyses.
- Comparisons of outcomes between patients treated in clinical practice vs clinical trial settings may be limited due to differences in patient characteristics (eg, disease severity, demographics, comorbidities).

CONCLUSIONS

- More than 50% of patients treated with droxidopa in clinical practice settings are not titrated according to the 24- or 48-hour schedule recommended on the product label.
- Patients titrated using a customized schedule received lower daily dosages of droxidopa vs patients titrated per the product label or clinical trial populations.
- A relationship between higher maintenance dosages of droxidopa and greater treatment persistence was identified.
- Customized titration schedules may lead to the identification and use of lower daily maintenance dosages of droxidopa and less treatment persistence.
- Clinicians should ensure patients with nOH are efficiently titrated to a droxidopa dosage that allows for optimal symptomatic and functional improvement.

ACKNOWLEDGMENTS

The authors received medical writing and editorial assistance from ICON (North Wales, PA, USA), which was supported by Lundbeck.

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ETHICS

Institutional review board/patient consent was not required for these analyses of real-world evidence using aggregated anonymous patient prescription data.

DISCLOSURES

The data reported were derived from studies funded by Lundbeck. FA is a consultant for AbbVie, Acadia, Adamas, Amneal Pharmaceuticals, Kyowa Kirin, Lundbeck, Neurocrine, Sunovion, Teva, and US World Meds. LAH, SK, BP, and AF are employees of Lundbeck.