Adverse Events and Patient Satisfaction: Dopamine Agonist and Levodopa Use for RLS

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Background

- Restless Legs Syndrome (RLS) is a neurologic disorder characterized by a strong urge to move the legs. Symptoms tend to intensify at night, and sleep disruptions can substantially impact quality of life.[1]
- Dopaminergic treatments (DTs) include agonists (FDA approved) and levodopa. Efficacy of these treatments is well-established in clinical trials;[2,3] however, outside clinical trials, less is known about treatment issues experienced by RLS patients.
- Treatment-related symptom augmentation and early morning rebound (EMR) are complications of long-term dopaminergic treatment that impact patient health outcomes.[3-6]
- Rates of augmentation among RLS patients on DTs are difficult to assess and compare in the current literature due to varying methods of assessment.[3-6]
- No standard exists for patient-reported assessments of augmentation to date to help estimate augmentation and its impact in community samples.

Objectives

- The aim of the study was to:
  - First, develop a method for identifying augmentation using a patient-reported assessment, and
  - Second, gauge the prevalence of augmentation and other complications and their impact in a community sample.

Methods

Study Procedures

- A 20-minute online survey was completed by 266 RLS patients currently treated with DTs. Subjects were referred by a primary care physician or neurologist.

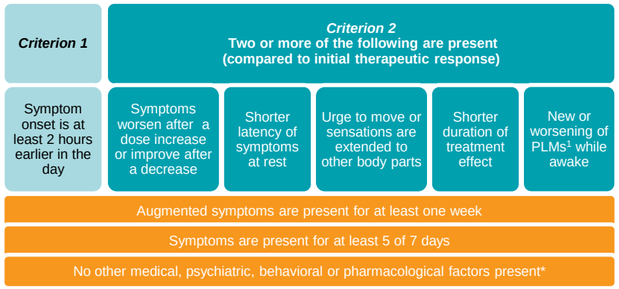
Assessments of Patient Outcomes

- Treatment satisfaction was assessed using a 7-point scale: 1 "not satisfied" to 7 "totally satisfied."
- RLS severity was measured with the IRLS scale.[7] Scale is 0-40, with 40 indicating most severe.
- Quality of life impact was assessed using the RLS-QOL scale.[8] Scale is 0-100, with 100 indicating best quality of life.
- Sleep impact was determined by the MOS sleep scale. Scale is 0-100, with 100 indicating greatest sleep impact. (© the RAND Corporation)

Determining Augmentation and Early Morning Rebound

- The methods for assessing augmentation and EMR were determined by clinical experts (authors Allen, Ondo and Ball) with expertise in diagnosing treatment complications in RLS.
- EMR was defined as symptom re-emergence in the morning (12:00am to 10:00am) followed by a symptom-free period, with no other changes in the nature of symptoms.[6]
- Augmentation of RLS symptoms at any time while on current treatment was assessed using NIH guidelines, which require criterion 1 or 2 and all confirmations to be met to definitively conclude augmentation (Figure 1).

Figure 1: NIH Guidelines for Augmentation[4]

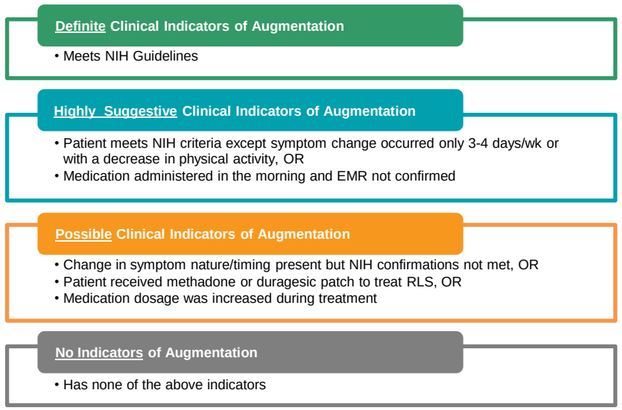


[1] Periodic limb movements

*Medical, psychiatric, behavioral and pharmacologic factors considered to be alternate explanations for augmentation are: a significant decrease in physical activity, introduction of antihistamines, SSRIs or SNRIs, 3+ blood donations in a year, substantial blood loss, or iron deficiency/anaemia.

- Due to the patient-reported nature of the study, other clinical indicators were assessed to develop an augmentation likelihood scale for those not satisfying the NIH criteria (Figure 2).

Figure 2: Likelihood of Augmentation Scale



Results

Table 1: Subject Characteristics

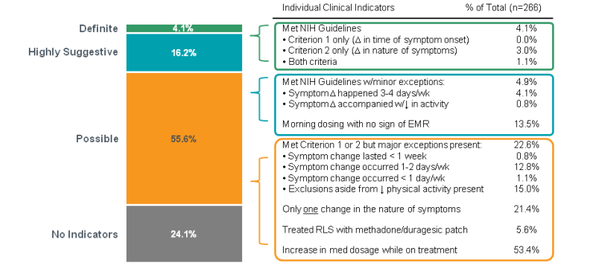
Total RLS Patients (n=266)	
Gender	66.2% Female
Age - mean (SD)	57.6 years (13.1)
Hispanic	3.0%
Race – Caucasian	85.0%
African American	3.0%
Other or decline to answer	12.0%
Years since RLS symptom onset - mean (SD)	9.6 years (12.0)
Years since RLS diagnosis - mean (SD)	4.3 years (5.1)
RLS severity (IRLS global score) - mean (SD)	18.1 (9.2)

- The subject demographics (Table 1) are indicative of RLS as reported in the literature; predominantly female, Caucasian, and older.

Table 2: RLS Treatment Characteristics

Total RLS Patients (n=266)	
Current physician primarily responsible for managing RLS	
Neurologist	32.3%
Primary care physician (Family Practitioner/Internist/General Practitioner)	66.5%
Other type of physician	5.6%
Current primary RLS treatment	
Dopamine agonist	91.7%
Levodopa	8.3%
Frequency of medication administration	
Once daily	67.3%
More than once per day	27.1%
Duration of current primary treatment - mean (SD)	2.7 years (2.4)
Switched from other dopaminergic med to current med	36.8%

Figure 3: Distribution of Subjects across Likelihood of Augmentation Scale



Note: Clinical indicator frequencies do not correspond with classification group frequencies due to overlap.

- 76% of subjects reported at least one possible clinical indicator of augmentation.
  - 4% met all NIH indicators for augmentation.
  - 20% reported definite or highly suggestive indicators.
  - An additional 28% met at least part of the NIH guidelines.
  - Other indicators of augmentation were noted, such as morning dosing with no sign of EMR (14%) or an increase in medication dosage during treatment (53%).
- Approximately 10% of subjects reported patterns meeting the definition of EMR.
- Statistical results comparing patients experiencing EMR (n=26) versus no EMR (n=240) are not provided due to insufficient sample size for EMR group.

Table 3: Comparison of Treatment Satisfaction and Patient Reported Outcomes by Augmentation Likelihood

Mean (SD)	Definite/Highly Suggestive (n=54) (A)*	Possible (n=148) (B)*	No Clinical Indicators (n=64) (C)*
Treatment Satisfaction	4.0 (1.3)	4.6 (1.4) [A]	5.3 (1.1) [AB]
RLS-QOL Summary Score	63.9 (20.8)	76.9 (15.5) [A]	90.1 (10.6) [AB]
IRLS Summary Score	23.6 (8.4)	18.9 (8.8) [A]	12.0 (7.3) [AB]
Sleep Problems Index II	44.9 (18.6)	34.0 (18.2) [A]	24.1 (13.0) [AB]

*Significance testing conducted at p< 0.05. Significant differences denoted by A/B/C with letter(s) next to the significantly better score.

- Those reporting definite or highly suggestive clinical indicators of augmentation score significantly worse across all outcome measures than patients with possible or no clinical indicators.

Conclusions

- The data show a significant negative impact of augmentation on treatment satisfaction, sleep, and quality of life.
- Being able to recognize patients presenting with indications of augmentation and EMR is pivotal for treatment success and minimizing their impact on RLS patients.
- The development of a patient-reported augmentation scale would be of value.

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Disclosures

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