Two-Year Longitudinal Data from the National Restless Legs Syndrome Opioid Registry

John Winkelman, MD, PhD[1,2], Benjamin Wipper, BA[1,2], Julia Purks, BS[3]
[1]Massachusetts General Hospital, [2]Harvard Medical School, [3]Larner College of Medicine at the University of Vermont

Background

Restless Legs Syndrome (RLS) is a sensory-motor neurological disorder characterized by an irresistible urge to move the legs that is often paired with leg discomfort. Low-dose opioid medications are frequently used in patients who have become refractory to first-line RLS treatments, particularly dopamine agonists. In the present work, we aim to collect longitudinal data on RLS treatment efficacy, dosage changes, and medication tolerability in a sample of patients using prescribed opioids for RLS. Here, we present data on the first two years of RLS treatment.

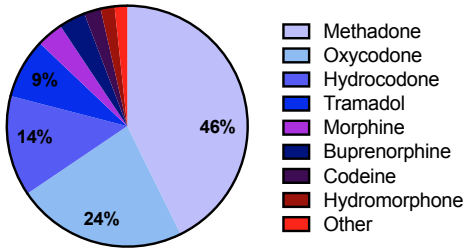
Methods

Inclusion to the registry required use of an opioid for diagnosed RLS and a previous therapeutic response to a dopamine agonist. Baseline information on initial and current opioid dosages, side effects, past and current RLS treatments, current RLS severity, psychiatric history and current symptoms, and opioid abuse risk factors was collected through a phone interview and online (REDCap) survey. Online follow-up surveys are performed every 6 months thereafter. All data is stored in a deidentified, secure online database. Recruitment for the registry occurred through the RLS Foundation, social media, and clinicians treating patients with RLS.

Baseline Data Overview

A total of 500 participants enrolled in the registry. Participants are 57% female, 72% aged 60 or older, and 98% white. Participants had been taking opioids for a median of 1-3 years upon entry into the registry. Half of participants were on opioid monotherapy. The most common side effects at registry entry were constipation (52% of subjects), drowsiness (24%), and itching (19%).

Opioids Used

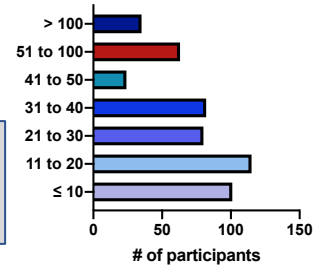


Median morphine milligram equivalents (MME) was 30.0 (methadone = 40.0, oxycodone = 22.5). Nearly half (47.8%) of participants were taking 25 MME or less daily and just 7.0% were taking 100 MME or higher.

MME Conversion Key:

30 MME = 7.5 mg methadone = 20 mg oxycodone = 30 mg hydrocodone = 300 mg tramadol

Baseline Daily MME

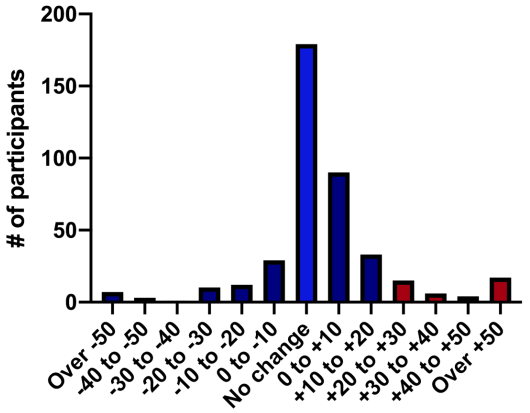


Two-Year Longitudinal Data Overview

Of 406 participants reaching two-year follow-up, 23 discontinued opioid treatment, 15 were lost to follow up, 5 passed away, and 2 withdrew (*96.0% retention rate among those who continued treatment with opioids for RLS*). International Restless Legs Syndrome Scale (IRLS), insomnia, and depression scores did not change from baseline to two years. There was a slight increase in anxiety scores. 11.1% added a dopamine agonist and/or an $\alpha_2\delta$ ligand during the follow-up period, whereas 8.1% removed such a medication. Individuals taking these non-opioid RLS medications (47.3% of participants) had higher two-year IRLS scores than those on opioid monotherapy (15.7 vs 11.5; $p < 0.0001$).

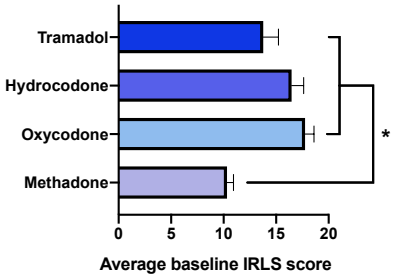
The median change in MME from baseline was 0. Roughly two-fifths of all participants (40.6%) increased their opioid dose at two years, and approximately half of those (54.5%) increased by ≤ 10 MME. Just 7.8% of all participants increased their opioid dose by > 25 MME. Predictors of large dose increases (≥ 40 MME; n = 24) were use of opioid medications for pain conditions in addition to RLS, discontinuation of non-opioid RLS medications since baseline, depression history, and male sex.

MME Changes from Baseline to Year Two

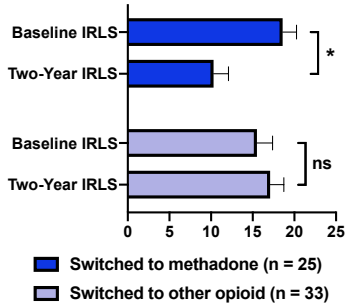


RLS Severity by Opioid Type

Baseline IRLS scores were significantly lower for participants taking methadone (10.3) than for participants who treated their RLS with oxycodone (17.7), hydrocodone (16.5), or tramadol (13.8).



Among those who switched to methadone during the follow-up period, two-year IRLS scores were significantly lower than at baseline (10.3 vs 18.7; $p = 0.0007$). However, this group did see a significant increase in daily MME. Registry participants who switched to other opioids had slightly worse RLS severity than at baseline (17.1 vs 15.1; $p = 0.6892$).



Conclusions

In this population, opioids are generally used at low doses with good efficacy. Approximately half of all participants use methadone, and nearly a quarter use oxycodone. At two-year follow-up, sleep quality and RLS symptom control were similar to baseline, and the majority of participants did not increase dose. Of the 40.6% of participants that increased dose, over half increased by a small amount (10 or less MME). Larger dose increases were accounted for by predictable factors. Participants using methadone had significantly lower IRLS scores. Longitudinal data collection will continue to grow knowledge on the safety and tolerability of opioids for RLS and may help in determining high-risk groups.