INTRODUCTION

• Patients with schizophrenia are known to experience disruptions in the 24-hour sleep-wake cycle (SWC), including lower daytime physical activity levels and a range of problems in nighttime sleep quality.

• Assessment of sleep and activity in patients with schizophrenia can be challenging for researchers.

• Self-reported measures are limited by recall bias and the effects of medication.

• Sleep lab assessments may be costly and may not represent patients’ real-world sleep behavior.

• Wearable digital devices can provide an alternative means for assessing motor activity and sleep quality in patients with schizophrenia.

• However, there is a paucity of data on the feasibility of longitudinal assessment of SWC in schizophrenia outpatients.

• Actigraphy findings have not previously been reported for randomized controlled trials (RCTs) in this population.

• Actigraphy was included as an exploratory endpoint in the 25-week, prospective ALPINE (Aripiprazole Lauroxil and Paliperidone palmitate: Initiation Effectiveness) study.

• ALPINE was primarily designed to evaluate safety and effectiveness of the long-acting injectable (LAI) antipsychotic aripiprazole lauroxil (AL, ARISTADA) for treatment of schizophrenia using a 1-day initiation regimen and a 2-month dose interval.

• Paliperidone palmitate (PP; MEWA SYSTEM 7X, EXPLORATORY) was included as an active control.

• Significant improvements from baseline in Positive and Negative Syndrome Scale (PANSS) total scores were observed in the AL and PP treatment groups.

• Actigraphy data were collected in two 14-day cycles, with cycle 1 starting at week 3 and cycle 2 at week 9.

OBJECTIVES

• To evaluate the feasibility and utility of wrist actigraphy to measure key activity and sleep parameters in a randomized, double-blind clinical trial in recently stabilized outpatients with schizophrenia.

• To describe sleep-wake cycle in patients with schizophrenia receiving LAI antipsychotic treatment.

METHODS

Patients

• ALPINE enrolled adults (age 18–65 years) with an acute exacerbation of schizophrenia, diagnosed according to DSM-5 criteria, requiring hospitalization.

Study Design

• Patients were enrolled and randomized as inpatients during an acute exacerbation of schizophrenia, were discharged after 2 weeks if clinically stable, and were followed as outpatients for the remainder of the 25 weeks.

• AL was initiated using a 1-day regimen and patients were instructed to wear the device continuously on the non-dominant wrist.

• PAL was initiated using a 14-day regimen and patients were instructed to wear the device continuously on the non-dominant wrist.

• ALPINE Actigraphy Population

• Out of 145 patients who received the wrist actigraphy device, 126 (87%) provided valid actigraphy data from weeks 1 to 9.

RESULTS

ALPINE Actigraphy Population

• Out of 145 patients who received the wrist actigraphy device, 126 (87%) provided valid actigraphy data from weeks 1 to 9.

• A total of 113 patients provided s1 data of valid data in cycle 1; 81 patients provided s1 data of valid data in cycle 2.

• Assessments were performed using ActiGraph GT3X+ (ActiGraph, LLC) accelerometers and with on-board memory to store an entire collection period.

• Actigraphy devices were offered to patients on the first day of each cycle, and patients were instructed to wear the device continuously on the non-dominant hand.

• Upon return of the accelerometers to the study site, data were uploaded to a central data management system (Traf施FracX®, IQVIA) and manually reviewed for completeness.

• Actigraphy measures assessed for each 24-hour period included the following parameters, which are defined in more detail in Table 1.

1. Sleep and rest: total sleep time, sleep and light rest duration and sleep duration during rest, sleep onset latencies, wake after sleep onset (number and duration), and sleep efficiency.

2. Activity: circadian rhythm amplitude, period, and mesor (midline-estimating statistic of rhythm; average activity over 24 hours), hours of peak activity, and activity level during the peak hour.

Statistical Analysis

• Actigraphy measures were determined for each 24-hour period, and patient averages were calculated for each cycle; data were summarized by treatment group using descriptive statistics.

• Periods of non-wear greater than 2 hours occurring at any point during the 24-hour period were labeled as non-valid data; such 24-hour periods were excluded from further analysis.

• Each patient had up to 28 discrete collection days over the course of the two 14-day cycles; having 1 complete day was sufficient for inclusion in the actigraphy analysis.

• Summary statistics were generated for PANSS total score and PANSS Positive, Negative, and General Psychopathology subscale scores for week 3 (onset of actigraphy cycle 1) and week 9 (onset of actigraphy cycle 2).

• Statistical analyses were performed for each cycle and for period averages to evaluate periods of non-wear.

LIMITATIONS

• Baseline actigraphy was not collected prior to randomization in this study; therefore, comparisons between treatment groups should be avoided.

• Results may be limited because of possible selection bias; participation was voluntary and not all patients opted to participate or to wear the device continuously as instructed.

CONCLUSIONS

• Results from this exploratory analysis of data collected in an RCT demonstrate the feasibility of actigraphic monitoring in stabilized patients with schizophrenia in an ambulatory setting.

• Results from patients with schizophrenia receiving treatment with LAI antipsychotics may be particularly valuable for measuring SWC because all patients are known to be on stable treatment; therefore, any variability observed in results is not due to inconsistent treatment.

• The actigraphy results are consistent with published sleep and activity data, which have demonstrated longer total sleep times and lower average activity levels in patients with schizophrenia compared with the general population (1,2) and are thus in line with expectations for a recently discharged, stabilized cohort of schizophrenia outpatients.

• Data from this analysis can provide valuable input for future guidance of actigraphy studies in schizophrenia.

DISCLOSURES

1. RP, DJ, and VM are employees of Alkermes, Inc., and own stock/options in the company.

REFERENCES


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