

Single-centre open label exploratory phase IIb pilot study of exogenous oral Melatonin for the treatment of Nocturia in adults with Parkinson's disease

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Objective

- To evaluate the effect of melatonin on nocturia in Parkinson's disease

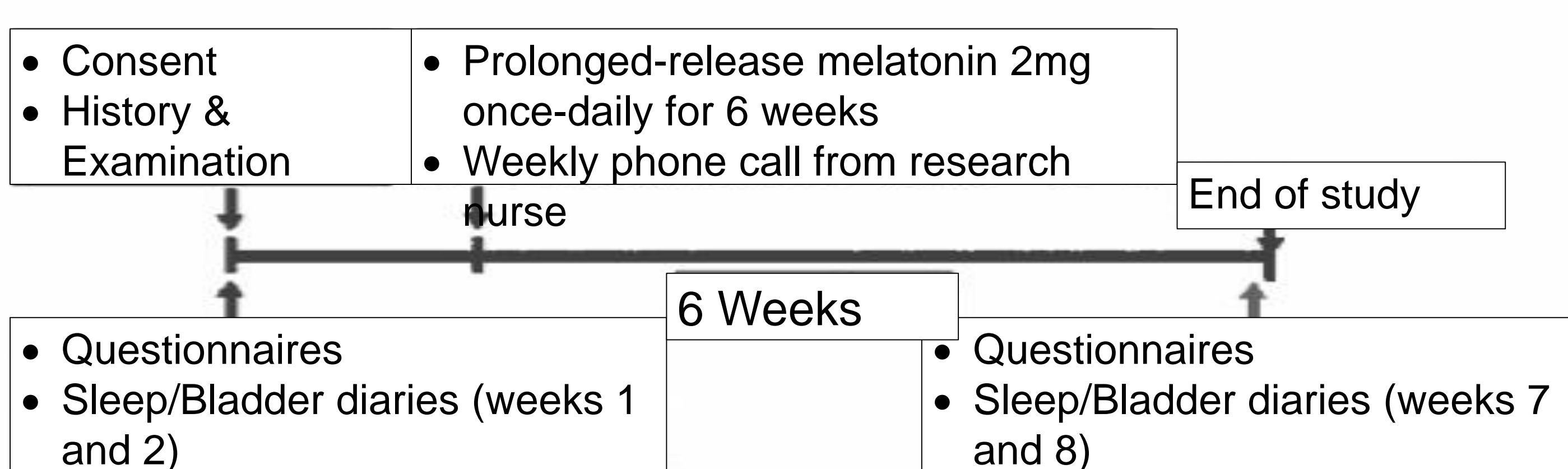
Background

- Nocturia is one of the commonest non motor symptoms in Parkinson's disease (PD), and has a highly significant negative impact on quality of life, affecting both the patients and their carers. It has been demonstrated that nocturia could be due to increased production of urine at night due to impaired circadian rhythm. We aimed to improve circadian regulation with melatonin with the aim to control symptoms and disability related to nocturia.

Methods

- This was an open label clinical trial of sustained-release Melatonin 2mg once daily for 6 weeks in patients with PD. We included over 18 year old patients reporting nocturia based on to NMSQuest item 9 –“Getting up regularly at night to pass urine” two or more times at night. Clinical examination and urodynamics were done at the beginning of the study. We excluded patients on Z drugs or clonazepam, cognitive decline (MOCA score <26), REM sleep behaviour disorder. Male patients found to have enlarged prostate, patients with urinary infection, significant retention on bladder scan, or bladder outflow obstruction on urodynamics were excluded.
- Assessments included urinary symptoms and quality of life questionnaires, bladder and sleep diaries Data of awakenings and quality of sleep was recorded using wrist accelerometer worn two weeks prior to starting melatonin, and during treatment.
- The primary analysis of “bother related to nocturia” compared the endpoints before (week 0) and whilst on treatment (week 6).
- Secondary outcomes were 1) Mean number of nocturia episodes per night 2) Nocturnal voided volumes 3) Lower urinary tract symptoms 4) Sleep disturbances and quality of sleep 5) Quality of life 6) Sleep disturbance in partners/carers 7) Safety

Study Timeline



Results

- 27 patients were recruited, however, only 18 completed the entire trial. Patients were eliminated because of lack of interest, logistical problems, failure to meet exclusion criteria and on one occasion due to failed urodynamic testing. 10 males and 8 females completed the study, which is representative as both males and females are affected by the disease, yet is 1.5 times more prevalent in males (Moisen et al, 2015). The mean age of participants in this study was 67.72, with a Standard Deviation (SD) of 7.18. The mean Hoehn and Yahr (H&Y) score for the severity of Parkinson's was 2.29, with a standard deviation of 0.47, which is an average PD severity score. Because of the significant improvement, five participants asked their GPs to continue taking melatonin after the trial.

Outcome Measure:	Mean Before	Mean After	Mean difference (After-Before)	P-Value:
ICIQ-N	3.83	3.00	-0.83	0.01346*
Nocturia-Related Bother	5.33	3.94	-1.38	0.06931
USP	9.56	8.84	-0.61	0.5688
OAB	7.44	6.67	-0.78	0.1946
SFQ	1.58	1.29	0.26	0.1156

Table 1 The Wilcoxon Ranked Test Sum test statistics for outcome measures of bladder symptoms from the ICIQ-N, USP and SF-Qualiveen.

Outcome Measure:	Mean Before	Mean After	P-Value:
Nocturnal Polyuria index	0.46	0.40	0.145
Mean frequency of nighttime voids	3.0	1.755	0.02524*

Table 2 The outcome measures of Nocturnal Polyuria index and frequency of nighttime voids calculated from the FVC.

Outcome Measure:	T-Value:	Degrees of Freedom:	P-Value:	95% Confidence Intervals:	Means of the differences:
Mean Sleep Onset (Minutes)	2.124	17	0.04865*	0.06285189 18.81492589	9.438889
Mean Number of Awakenings	3.9295	17	0.00108**	0.2647275 0.8786058	0.5716667
Mean Duration Awakenings (Minutes)	1.6416	15	0.1215	-1.1.125199 8.666449	3.770625
Mean Hours of Sleep (Hours)	-1.1989	17	0.247	-0.6700265 0.1844709	-0.2427778
Total PSQI Score	3.277	17	0.004445**	0.9300042 4.2922181	2.611111
Total PDSS Score	-0.8025	17	0.4333	-15.725725 7.059058	-4.333333
PDSS Question 8	-2.5978	17	0.01876*	-1.7114760 -0.1774129	-0.9444444

Table 3. The outcome measures of sleep quality from the sleep diary, PSQI and PDSS.

Conclusion

- In this open label phase IIb study, Melatonin was safe and reduced the mean frequency of voids and improves nocturia in PD. A significant benefit in sleep outcomes was observed. A larger multicenter phase III study can help consolidate these findings and possibly uncover a potential benefit in bladder symptom scores.

Grant reference: K-1303