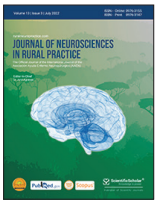
ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

https://ruralneuropractice.com

Journal of Neurosciences in Rural Practice

Article in Press



Original Article

Effect of motor, non-motor clinical features including sleep quality, and prescription pattern on adherence to antiparkinsonian medications in Parkinson's disease

Subhash Samanta[1], Niraj Kumar[2], M. Kanimozhi[1], Manisha Bisht[1], Ravi Gupta[3]

Departments of [1]Pharmacology, [2]Neurology, [3]Psychiatry, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.

ABSTRACT

Objectives: Adherence to antiparkinsonian medications (APMs) may significantly influence Parkinson's disease (PD) outcome. The present study assesses the role of motor and non-motor features, and prescription patterns on adherence.

Materials and Methods: This observational and cross-sectional study included 50 PD patients taking APMs for ≥24 months. Demographic data, PD characteristics, treatment, and follow-up history were collected. Patients following up at least once in six months were considered as regular, else were labeled irregular. Montreal cognitive assessment, patient health questionnaire-4, Pittsburgh sleep quality (SQ) index, Epworth sleepiness scale, global quality of life (GQOL) scale, and Morisky Green Levine medication adherence scale (MGL-MAS) were used to evaluate cognition, depressive and anxiety features, SQ, excessive daytime sleepiness (EDS), quality of life (QOL), and APMs adherence, respectively.

Results: Nearly half (46%) of the PD patients reported high adherence (MGL-MAS = 0). Most of the clinical characteristics were comparable between those with medium/low and high adherence, except for a larger proportion of patients in the medium/low adherence group belonging to Hoehn–Yahr stage >2 ($P = 0.02$). A comparable proportion of patients in both groups reported poor SQ ($P = 0.52$) and EDS ($P = 0.32$). In comparison to the high adherence group, a significantly lower median GQOL score was observed in the medium/low adherence group (median [interquartile range] = 65 [50–70] vs. 80 [70–85]; $P < 0.001$). The APMs prescription and follow-up patterns were comparable between both groups.

Conclusion: More than half the PD patients reported medium-to-low adherence. While motor severity and depressive symptoms were associated with medium-to-low adherence, poor SQ was comparable in both groups. Those with medium-to-low adherence reported poor QOL.

Keywords: Parkinson's disease, Antiparkinsonian medications, Prescription pattern, Sleep quality, Depression

INTRODUCTION

Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder affecting approximately 1% of individuals above the age of 60 years and 3–4% above 80 years.[1] The current treatment options in PD patients focus on either improving the dopaminergic deficit or reducing the cholinergic overactivity.[1] In addition to the dopaminergic agents including levodopa–carbidopa and dopamine agonists, catecholamine-o-methyl-transferase inhibitors and monoamine oxidase-B inhibitors may be used. Anticholinergics including trihexyphenidyl are used, especially for alleviating tremor.[1] To manage levodopa-induced dyskinesias, amantadine is used because of multiple modes of action.[1]

In addition to disease behavior and efficacy of antiparkinsonian medications (APMs), adherence to APMs also affects the success of pharmacotherapy in PD. Some studies have assessed the prevalence and factors affecting adherence to APMs in PD,[2-11] with only a single study from India.[8] PD duration, cognitive status, mood disorders including depression, poor follow-up compliance, and APMs-related adverse events have been reported to influence adherence to APMs.[2,4,5,8] However, in one of these studies, a diagnosis of depression and cognition was not made using standardized methods.[4] Even in two of these studies,[6,7] cognition was assessed using a mini-mental status examination, which has lesser sensitivity than Montreal Cognitive Assessment (MoCA) in diagnosing impaired cognition, due to two issues –

***Corresponding author:** Niraj Kumar, Department of Neurology, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.
drnirajkumarsingh@gmail.com

Received: 18 November 2023 **Accepted:** 22 April 2024 **Epub ahead of print:** 17 May 2024 **Published:** XXXX **DOI:** 10.25259/JNRP_585_2023
Supplementary material available on: https://doi.org/10.25259/JNRP_585_2023

ceiling effect and lack of identification of heterogeneity in cognitive functions.[12] We could find only a single study, which provided reliable evidence regarding the effect of cognition (using MoCA) on treatment adherence among PD patients.[13]

Nearly 98% of patients with PD report some form of sleep dysfunction, making it one of the most common non-motor features of the disease.[14] Sleep quality (SQ) affects cognition, mood, energy, and initiative which are important for adherence to APMs. While poor SQ has been observed to affect medication adherence in patients with chronic neurological disorders including epilepsy,[15,16] similar assessment in patients with PD is lacking.[2,4,5,10,13] We hypothesized that poor SQ would reduce the APM's adherence in PD patients. Simultaneously, we also studied the role of non-motor and motor features of PD (depression, anxiety, daytime sleepiness, and quality of life), pill burden of APMs, and regularity of follow-up on medication adherence among PD patients.

MATERIALS AND METHODS

Consecutive patients visiting the movement disorders clinic and diagnosed with PD were included in this single-center, observational, and cross-sectional study that spanned from October 2020 to April 2022, following Institute Ethical Committee approval.

Inclusion and exclusion criteria

Patients aged ≥18 years on APMs for at least the past 24 months were included after taking written informed consent. The diagnosis of PD was made by a neurologist with a specialization in movement disorder (NK) using the United Kingdom PD Society brain bank criteria.[17] Exclusion criteria included pregnancy, Parkinson-plus syndromes (including multiple system atrophy, progressive supranuclear palsy, and cortico-basal degeneration), dementia with Lewy body disease, and secondary parkinsonism (e.g., drug/toxin-induced and vascular).

Assessment of PD and treatment variables

Collected data comprised PD onset age, presentation age, and disease phenotype (tremor dominant, postural instability/gait difficulty, or indeterminate type).[18] The severity of motor and non-motor symptoms (NMSs) was assessed using the movement disorders society-unified PD rating scale (MDS-UPDRS)-III (motor) score in "off" state,[19] and MDS-NMS rating scale, respectively.[20] The severity of PD was assessed using the Hoehn–Yahr stage.[21] Details of therapy, namely, name and dose of APMs were noted from the prescription, and levodopa equivalent daily dose (LEDD) was calculated.[22]

Assessment of cognitive status

Cognition status was assessed using the MoCA score.[23] The cutoff score of 24 was used in this study, as at this score, MoCA has shown approximately 81% sensitivity as well as specificity to detect mild cognitive impairment with area under the curve at 0.84.[24]

Pill burden

Since levodopa–carbidopa plasma concentration exceeds the "on" threshold for nearly 3 h,[25] the optimal prescription pattern for levodopa-carbidopa combination pill is 3–4 times per day. Pill burden was divided into two groups: One with ≤4 pills per day and the second with >4 pills per day.

Morisky green levine medication adherence scale (MGL-MAS)

Adherence to APMs was measured using MGL-MAS. This scale has four self-reported items where items are scored as no (=0) or yes (=1), making the range of total score between 0 and 4. While a total score of 0 suggests high adherence, a score of 1–2 and 3–4 suggests medium and low adherence to treatment, respectively.[26]

Evaluation of depressive and anxiety symptoms

Patient Health Questionnaire-4 evaluates participants on four items, the first two for anxiety and the remaining two for depressive symptoms. Each item is scored on a four-point Likert scale, varying from 0 (no such symptom) to 3 (symptom present almost every day).[27] A total score of ≥3 for the first two items suggests anxiety and the same score for the remaining two items indicates depression.

Assessment of excessive daytime sleepiness (EDS)

The propensity to fall asleep during daytime can be measured by an Epworth Sleepiness Scale (ESS) that assesses chances to fall asleep (EDS) when involved in eight separate acts. These items are rated from 0 to 3, with 0 meaning no dozing and 3 indicating a high chance of sleepiness. The total score ranges from 0 to 24.[28] A cutoff score of more than 10 indicates EDS. We used a validated Hindi version of this scale.[29]

Assessment of SQ

Self-reported, 19-item questionnaire-Pittsburgh SQ Index (PSQI) was used for assessing the quality of sleep of participants. It shows the quality of sleep over the past 1 month.[30] Besides the global score, PSQI provides scores on seven sub-scales: (1) duration of sleep, (2) disturbance during sleep, (3) sleep latency, (4) disturbance in daytime functioning, (5) sleep efficiency, (6) overall SQ, and (7) use

of medications to induce or maintain sleep. The score of each component varies from 0 to 3, with 3 indicating the highest disturbance. Global score is calculated by adding scores of seven subscales (score range 0–21). A cutoff of 5 of the global PSQI score has been found to differentiate between good sleepers from poor sleepers (>5 indicating poor SQ).[30]

Global quality of life (GQOL) scale

The GQOL scale is a self-rated scale. It has a single item, which can be scored on a scale of 0–100 (0 = no quality of life to 100 = perfect quality of life). Thus, better quality of life is indicated by higher scores. Participants were requested to indicate any number between 0 and 100 that best represents their quality of life.[31]

Regularity of follow-up

From the treatment chart, follow-up patterns for the past one year were assessed. Patients who visited the movement disorder clinic as per the follow-up schedule of our center (at least once in six months) were considered "regular" in follow-up, else were labeled "irregular."

Comorbid disorders

Associated comorbidities including hypertension and/or diabetes mellitus were also diagnosed based on medical records and/or clinical examination.

Statistical analysis

The Statistical Package for Social Sciences v 28.0 was used to analyze the data. The normal distribution of quantitative/continuous variables was assessed using the Shapiro–Wilk test. While normally distributed quantitative variables were depicted as mean with standard deviation (SD), non-parametric quantitative variables were presented as median with interquartile range (IQR). A between-groups comparison of normally distributed quantitative variable was done using an independent sample *t*-test, and the Mann–Whitney U-test was employed for non-parametrically distributed variables. Qualitative/categorical variables were presented as percentages and proportions. Qualitative variables were compared using Chi-square and Fisher's Exact tests, as applicable. $P < 0{\cdot}05$ (two-tailed) was considered statistically significant.

RESULTS

Demographic, clinical characteristics, and prescription pattern of APMs in PD patients

Fifty of the 112 screened PD patients fulfilled the inclusion and exclusion criteria [Supplementary Figure 1]. Of the 50 PD patients, 31 (62%) were male. The average onset age of PD was 53 ± 9.92 years, and the mean age at assessment was 59.18 ± 9.94 years. One-third of patients belonged to the young onset PD group. Two-thirds of patients had tremor-onset PD. While nearly half the patients (46%) were prescribed only levodopa–carbidopa monotherapy, 28% of

Table 1: Demographic and clinical characteristics of the patients with PD.

Variables	PD patients (*n*=50)
Age at onset of PD (in years):*Mean (±SD)	53±9.92
Age at assessment (in years):*Mean (±SD)	59.18±9.94
Male gender: *n* (%)	31 (62)
Comorbidities – HT and/or DM: *n* (%)	19 (38)
PD characteristics	
Disease duration (in months):#Median (IQR)	57.5 (36–99)
YOPD: *n* (%)	17 (34)
PD subtypes:$	
Tremor-dominant PD: *n* (%)	33 (66)
Postural instability and gait disorder: *n* (%)	16 (32)
MDS-UPDRS-III score:#Median (IQR)	38.5 (27–44)
MDS-NMS score:#Median (IQR)	59.5 (31–90)
Hoehn–Yahr stage >2: *n* (%)	12 (24)
Anxiety: *n* (%)	15 (30)
Depression: *n* (%)	16 (32)
EDS (ESS>10): *n* (%)	4 (8)
Poor sleep quality (PSQI >5): *n* (%)	28 (56)
Cognitive impairment (MoCA <26):@ *n* (%)	10/44 (22.7)
Type of APMs prescribed:	
Levodopa–carbidopa: *n* (%)	50 (100)
Pramipexole: *n* (%)	14 (28)
Ropinirole: *n* (%)	4 (8)
Anticholinergic: *n* (%)	10 (20)
Rasagiline: *n* (%)	8 (16)
Amantadine: *n* (%)	5 (10)
Entacapone: *n* (%)	4 (8)
Combination of APMs prescribed	
Levodopa–carbidopa only: *n* (%)	23 (46)
2 APMs: *n* (%)	13 (26)
>2 APMs: *n* (%)	14 (28)
LEDD (mg):# Median (IQR)	525 (400–862.5)
High pill burden: *n* (%)	31 (62)
Regular follow-up: *n* (%)	44 (88)
Global Quality of Life Scale score: #Median (IQR)	70 (63.75–80)

*Normal distribution, #Non-parametric distribution, $One patient had indeterminate subtype of PD, @Six patients MoCA could not be done as they were illiterate, EDS: Excessive daytime sleepiness, ESS: Epworth sleepiness scale, DM: Diabetes mellitus, HT: Hypertension, IQR: Interquartile range, LEDD: Levodopa equivalent daily dose, MDS-NMS: Movement disorders society-non-motor rating scale, MDS-UPDRS: Movement disorders society-unified Parkinson disease rating scale, MoCA: Montreal cognitive assessment scale score, PD: Parkinson's disease; PSQI: Pittsburgh sleep quality index, SD: Standard deviation, YOPD: Young onset Parkinson's disease, APMs: Antiparkinsonian medications

patients were on >2 APMs. The median GQOL scale score was 70 for the entire cohort of patients. The remaining demographic and clinical characteristics of the participants are depicted in Table 1.

Comparison of demographic and clinical characteristics of patients with high adherence versus those with medium/low adherence to APMs

Among the 50 recruited PD patients, nearly half (46%) patients reported high adherence (MGL-MAS = 0) to APMs. The majority of demographic and clinical features in the two groups were comparable [Table 2]. Medium/low adherence was associated with greater severity of PD (Hoehn–Yahr stage >2; medium/low adherence vs. high adherence = 37% vs. 8.7%; $P = 0.02$). Although, depressive symptoms were noted in a much higher proportion of patients in the medium/low adherence as compared to the group having high adherence, but did not reach statistical significance (44.4% vs. 17.4%; $P = 0.06$). Patients in the medium/low adherence group had poorer life quality than those in the high adherence group (median [IQR] = 65 [50–70] vs. 80 [70–85]; $P < 0.001$). However, poor SQ ($P = 0.52$) and EDS ($P = 0.22$) did not affect adherence to medication.

Table 2: Comparison of demographic, clinical, treatment characteristics, and follow-up patterns of patients with and without high adherence to APMs.

Variables	High adherence (*n*=23)	Medium/low adherence (*n*=27)	*P*-value	df	Test value
Age at onset of PD (in years):* Mean (SD)	55.09 (10.04)	51.22 (9.65)	0.17	48	C.I=−9.47–1.74
Age at assessment (in years):* Mean (SD)	60.30 (9.45)	58.22 (10.43)	0.46	48	C.I=−7.78–3.62
Male gender: *n* (%)	14 (60.9)	17 (63)	0.88	1	χ^2=0.02
Comorbidities – HT and/or DM: *n* (%)	9 (39.1)	10 (37)	0.88	1	χ^2=0.02
PD characteristics					
Disease duration (in months):# Median (IQR)	46 (36–84)	60 (36–120)	0.27	-	U=254
YOPD: *n* (%)	8 (34.8)	9 (33.3)	0.91	1	χ^2=0.01
PD subtypes$					
Tremor-dominant PD: *n* (%)	16 (69.6)	17 (63)	0.31	2	χ^2=2.36
Postural instability and gait disorder: *n* (%)	6 (26.1)	10 (37)			
MDS-UPDRS-III score#: Median (IQR)	38 (25–44)	40 (27–47)	0.94	-	U=314.5
MDS-NMS score#: Median (IQR)	52 (29–85)	79 (32–125)	0.16	-	U=239
Hoehn–Yahr stage >2: *n* (%)**	2 (8.7)	10 (37)	0.02	-	-
Anxiety: *n* (%)	8 (34.8)	7 (25.9)	0.49	1	χ^2=0.46
Depression: *n* (%)**	4 (17.4)	12 (44.4)	0.06	-	-
EDS (ESS>10): *n* (%)**	3 (13)	1 (3.7)	0.32	-	-
Poor sleep quality (PSQI >5): *n* (%)	14 (60.9)	14 (51.9)	0.52	1	χ^2=0.41
Cognitive impairment (MoCA <26):@ *n* (%)	3/21 (14.3)	7/23 (30.4)	0.74	1	χ^2=0.11
Global quality of life scale score:# Median (IQR)	80 (70-85)	65 (50-70)	<0.001	-	U=502.5
APMs prescribed					
Levodopa–carbidopa: *n* (%)	23 (100)	27 (100)	-	-	-
Dopamine agonist: *n* (%)	7 (30.4)	11 (40.7)	0.45	1	χ^2=0.57
Anticholinergic: *n* (%)**	4 (17.4)	6 (22.2)	0.74	-	-
MAOBI: *n* (%)**	3 (13)	5 (18.5)	0.71	-	-
Amantadine: *n* (%)**	1 (4.3)	4 (14.8)	0.36	-	-
COMTI: *n* (%)**	2 (8.7)	2 (7.4)	1.00	-	-
Combination of APMs prescribed					
Levodopa–carbidopa+COMTI: *n* (%)	12 (52.2)	12 (44.4)	0.59	1	χ^2=0.29
LD-carbidopa+other APMs: *n* (%)	11 (47.8)	15 (55.6)			
LEDD (mg)#: Median (IQR)	415 (400–725)	600 (400–900)	0.29	-	U=257
High pill burden (>4 pills per day): *n* (%)	12 (52.2)	19 (70.4)	0.18	1	χ^2=1.75
Regular follow-up: *n* (%)**	21 (91.3)	23 (85.2)	0.67	-	-

*Normal distribution, #Non-parametric distribution, $One patient had indeterminate subtype of PD, @Six patients were illiterate and MoCA could not be done, **Fisher's exact test, APMs: Antiparkinsonian medications, C.I: Confidence interval, COMTI: Catechol-o-methyl transferase inhibitor, df: Degrees of freedom, DM: Diabetes mellitus, EDS: Excessive daytime sleepiness, ESS: Epworth sleepiness scale, HT: Hypertension, IQR: Interquartile range, LEDD: Levodopa equivalent daily dose, MAOBI: Monoamine oxidase B inhibitor, MDS-NMS: Movement disorders society-non-motor rating scale, MDS-UPDRS: Movement disorders society-unified Parkinson's disease rating scale, MoCA: Montreal cognitive assessment scale score, PD: Parkinson's disease, PSQI: Pittsburgh sleep quality index, SD: Standard deviation, YOPD: Young-onset Parkinson's disease

Comparison of treatment characteristics and follow-up pattern of patients with and without high adherence to APMs

A comparison of treatment characteristics including prescription pattern and follow-up pattern of patients in high versus medium/low adherence group is shown in Table 2. Levodopa–carbidopa combination (n = 50; 100%) was the most commonly prescribed drug. The prescription pattern of APMs, LEDD, pill burden, and follow-up pattern was comparable between both groups.

Comparison of clinical and treatment-related variables between patients with and without poor quality of sleep

Comparison of clinical and treatment-related variables of PD patients with and without poor SQ are depicted in Supplementary Table 1. While majority of the characteristics were comparable in those with and without poor quality of sleep, except that a significantly higher proportion of patients with poor quality of sleep reported depressive symptoms (P = 0.02).

DISCUSSION

More than half the PD patients (54%) in this study reported medium/low adherence to APMs. While the majority of other characteristics including demographic, disease-related, and APMs prescription patterns were comparable in both groups, a significantly higher proportion of patients in the medium/low adherence group belonged to Hoehn–Yahr stage >2. A much higher proportion of PD patients in the medium/low adherence group reported depressive symptoms, although not significant. The SQ and EDS were not associated with adherence to APMs. The median GQOL score in patients with medium/low adherence was significantly lower than those in the high adherence group. Levodopa–carbidopa monotherapy was most commonly prescribed (46%).

Lack of adherence to APMs is a significant problem in PD[32,33] as it influences the therapeutic response,[4,9] thereby affecting the life quality of patients and care providers. It also affects the decision-making regarding modifications in APMs dosage and frequency. In our study, 54% of PD patients reported medium/low adherence to APMs, similar to that reported in prior studies, which observed medium/low adherence in 56.8–61% of PD patients.[8,9,11] While one of these studies used an 8-item Morisky MAS, a self-reported assessment scale,[8] the second assessed medication possession ratio,[9] and the third study utilized an electronic microprocessor-monitoring to detect the opening of the pill container.[11] In a review comprising nine studies, the non-adherence rate varied between 10% and 67%.[33] The wide variability of the non-adherence rate was related to differences in the assessment methods such as the use of a visual analog scale, self-reporting by patients, counting the pills while refilling in the pharmacy, and electronically monitoring of opening the pill container.[33]

We observed poor quality of sleep and EDS in a comparable proportion of patients in both medium/low and high adherence groups. A previous study reported no significant difference in ESS score in PD patients (n = 54) with/without adequate medication adherence.[4] It may be difficult to interpret their result as they compared the mean (SD) of ESS score rather than the proportion of PD patients with EDS (ESS >10). While we hypothesized poor SQ to affect the APMs adherence, it was not observed in our cohort and this may be related to the low sample size. However, a significantly higher percentage of PD patients with poor quality of sleep reported depressive features (P = 0.02), and this may have influenced the APMs adherence as discussed in the subsequent paragraph. Poor SQ may affect cognition and emotional reactivity and induce physiological changes including reduced ACTH response, thereby precipitating depressive features.[34]

Previous studies have reported a significant association between depression and poor APMs adherence.[2,4,8] In the present study, a much higher proportion of patients in the medium/low adherence group reported depressive symptoms as compared to the high adherence group, although not statistically significant (P = 0.06), which may be due to the low sample size. Depression is commonly reported by PD patients, with one in every three PD patients having clinically bothersome depression.[35] Dopaminergic, noradrenergic, and serotonergic dysfunction in brainstem, limbic, and cortical areas have been implicated in causing depression symptoms in PD.[35] Patients suffering from depression may underappreciate the benefits of APMs, which may affect their adherence. Moreover, the lack of adherence may precipitate dopaminergic dysfunction, thereby, precipitating depression along with other Parkinsonian motor and NMSs.[32,33] Thus, maintaining adequate adherence may overcome this vicious cycle. While a single study has reported an association of other NMSs including constipation, anxiety, and falls with suboptimal adherence to APMs,[13] the proportion of patients with anxiety was comparable in both medium/low and high adherence groups in the present study. Moreover, the MDS-NMS scores were comparable in the two groups among our PD patients. Cognitive impairment and behavioral issues such as alcohol abuse have been reported to be associated with poor APMs adherence.[32,33] While the present study did not assess the behavioral issues, impaired cognition was seen in a comparable proportion of patients in both groups.

The worsening of parkinsonian symptoms due to poor adherence may result in a higher motor score. A multicentric European study involving 112 PD patients reported a significantly higher motor severity in the suboptimal

adherence group (median unified PD rating scale motor score [IQR] in the satisfactory adherence vs. suboptimal adherence groups = 19 [13–26] vs. 29 [20–41]; $P = 0.005$), although median Hoehn–Yahr stage was comparable in both groups.[5] While the MDS-UPDRS motor score was comparable in both groups, a significantly higher percentage of our patients in the medium/low adherence group belonged to the Hoehn–Yahr stage >2. It is likely that PD patients with higher motor severity have more motor fluctuations and dyskinesias and may develop a perception of reduced efficacy of APMs, thereby resulting in suboptimal adherence. By exacerbating Parkinsonian symptoms, poor adherence is likely to affect the quality of life in PD patients. The median GQOL score in our patients with medium/low adherence was significantly reduced than that in the high adherence group, similar to previous reports.[4,5]

Polypharmacy and use of multiple APMs may result in poor medication adherence in PD patients.[32,33] The treatment characteristics including prescription pattern of APMs, pill burden, LEDD, and follow-up pattern were comparable in both adherence groups in the present study. Levodopa–carbidopa monotherapy was the most commonly prescribed (46%) APM in our patients, with the remainder (54%) receiving two or more APMs. While previous studies reported poor adherence in those taking more APMs,[4,5] we did not find any association between high pill burden and medium/low adherence. Less number of patients in the present cohort ($n = 50$) as compared to the previous studies (54 and 112)[4,5] may be one of the reasons for the same. Moreover, higher age at assessment in the previous two studies (61.9 years and 65 years)[4,5] as compared to the present study (59.1 years) may be another contributory factor as older age (≥65) has been reported to be associated with suboptimal adherence to APMs.[33]

This study has some limitations. First, it is a single-center and cross-sectional study with a low sample size, thereby limiting the generalizability of our results. However, we included only those patients who were on APMs for at least for past 24 months. Second, we did not take into consideration the adverse effects of APMs while assessing adherence. Since adverse events likely result in poor medication adherence early after initiating APMs, it is unlikely to have affected this study as all included patients were on APMs for the past 24 months. Third, the adherence in this study was assessed using a self-rated scale which is likely to result in underestimation. Fourth, we did not assess social and financial insecurity and educational status. While these factors have been linked to poor APMs adherence in developed countries,[32,33] the single Indian study to date failed to find such an association.[8] Fifth, we used a GQOL scale rather than PD specific QOL scale. However, this is the first study assessing the relation of adherence to APMs with a detailed non-motor evaluation using the MDS-NMS scale along with SQ and EDS assessment.

CONCLUSION

More than half the PD patients reported medium/low adherence to APMs. While the proportion of patients with poor SQ and EDS was comparable in both groups, higher motor severity of PD was more common in those with medium/low adherence. Although lacking statistical significance, a much higher percentage of PD patients in the medium/low adherence group reported depressive symptoms. PD patients with medium/low adherence reported poor quality of life.

Ethical approval

The research/study was approved by the Institutional Review Board at All India Institute of Medical Sciences, Rishikesh, number AIIMS/IEC/19/1277, dated November 29, 2019.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Rizek P, Kumar N, Jog MS. An update on the diagnosis and treatment of Parkinson disease. CMAJ 2016;188:1157-65.
2. Valldeoriola F, Coronell C, Pont C, Buongiorno MT, Cámara A, Gaig C, *et al*. Socio-demographic and clinical factors influencing the adherence to treatment in Parkinson's disease: The ADHESON study. Eur J Neurol 2011;18:980-7.
3. Kulkarni AS, Balkrishnan R, Anderson RT, Edin HM, Kirsch J, Stacy MA. Medication adherence and associated outcomes in Medicare health maintenance organization-enrolled older adults with Parkinson's disease. Mov Disord 2008;23:359-65.
4. Grosset KA, Bone I, Grosset DG. Suboptimal medication adherence in Parkinson's disease. Mov Disord 2005;20:1502-7.
5. Grosset D, Antonini A, Canesi M, Pezzoli G, Lees A, Shaw K, *et al*. Adherence to anti-Parkinson medication in a multicenter European study. Mov Disord 2009;24:826-32.
6. Wei YJ, Palumbo FB, Simoni-Wastila L, Shulman LM, Stuart B,

Beardsley R, *et al*. Antiparkinson drug use and adherence in medicare part D beneficiaries with Parkinson's disease. Clin Ther 2013;35:1513-25.e1.
7. Tarrants ML, Denarié MF, Castelli-Haley J, Millard J, Zhang D. Drug therapies for Parkinson's disease: A database analysis of patient compliance and persistence. Am J Geriatr Pharmacother 2010;8:374-83.
8. Aggarwal S, Paul G, Paul B, Mahendru D, Goyal S. Factors affecting adherence to pharmacotherapy in Parkinson's disease. Ann Indian Acad Neurol 2021;24:879-84.
9. Davis KL, Edin HM, Allen JK. Prevalence and cost of medication nonadherence in Parkinson's disease: Evidence from administrative claims data: Cost of Nonadherence in Parkinson's disease. Mov Disord 2010;25:474-80.
10. Elm JJ, Kamp C, Tilley BC, Guimaraes P, Fraser D, Deppen P, *et al*. Self-reported adherence versus pill count in Parkinson's disease: The NET-PD experience. Mov Disord 2007;22:822-7.
11. Leopold NA, Polansky M, Hurka MR. Drug adherence in Parkinson's disease. Mov Disord 2004;19:513-7.
12. Jia X, Wang Z, Huang F, Su C, Du W, Jiang H, *et al*. A comparison of the Mini-Mental State Examination (MMSE) with the Montreal Cognitive Assessment (MoCA) for mild cognitive impairment screening in Chinese middle-aged and older population: A cross-sectional study. BMC Psychiatry 2021;21:485.
13. Mendorf S, Witte OW, Zipprich H, Prell T. Association between nonmotor symptoms and nonadherence to medication in Parkinson's disease. Front Neurol 2020;11:551696.
14. Gros P, Videnovic A. Overview of sleep and circadian rhythm disorders in Parkinson disease. Clin Geriatr Med 2020;36:119-30.
15. Simie Tsega S, Yazew BG, Mekonnen K. Sleep quality and associated factors among adult patients with epilepsy attending follow-up care at referral hospitals in Amhara region, Ethiopia. PLoS One 2021;16:e0261386.
16. Bahar A, Budisasmita F, Wuysang AD, Bintang AK, Aulina S. The correlation of sleep quality toward the drug compliance of epilepsy patient. Med Clín Práct 2021;4:100204.
17. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: A clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992;55:181-4.
18. Stebbins GT, Goetz CG, Burn DJ, Jankovic J, Khoo TK, Tilley BC. How to identify tremor dominant and postural instability/gait difficulty groups with the movement disorder society unified Parkinson's disease rating scale: Comparison with the unified Parkinson's disease rating scale: PIGD and The MDS-UPDRS. Mov Disord 2013;28:668-70.
19. Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, *et al*. Movement disorder society-sponsored revision of the unified Parkinson's disease rating scale (MDS-UPDRS): Scale presentation and clinimetric testing results. Mov Disord 2008;23:2129-70.
20. Chaudhuri KR, Schrag A, Weintraub D, Rizos A, Rodriguez-Blazquez C, Mamikonyan E, *et al*. The movement disorder society nonmotor rating scale: Initial validation study. Mov Disord 2020;35:116-33.
21. Hoehn MM, Yahr MD. Parkinsonism: Onset, progression and mortality. Neurology 1967;17:427-42.
22. Schade S, Mollenhauer B, Trenkwalder C. Levodopa equivalent dose conversion factors: An updated proposal including opicapone and safinamide. Mov Disord Clin Pract 2020;7:343-5.
23. Nasreddine ZS, Phillips NA, Bedirian V, Charbonneau S, Whitehead V, Collin I, *et al*. The Montreal cognitive assessment, MoCA: A brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005;53:695-9.
24. Ciesielska N, Sokołowski R, Mazur E, Podhorecka M, Polak-Szabela A, Kędziora-Kornatowska K. Is the Montreal cognitive assessment (MoCA) test better suited than the Mini-Mental State Examination (MMSE) in mild cognitive impairment (MCI) detection among people aged over 60? Meta-analysis. Psychiatr Pol 2016;50:1039-52.
25. LeWitt PA. Levodopa therapy for Parkinson's disease: Pharmacokinetics and pharmacodynamics. Mov Disord 2015;30:64-72.
26. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care 1986;24:67-74.
27. Kroenke K, Spitzer RL, Williams JB, Löwe B. An ultra-brief screening scale for anxiety and depression: The PHQ-4. Psychosomatics 2009;50:613-21.
28. Johns MW. A new method for measuring daytime sleepiness: The Epworth sleepiness scale. Sleep 1991;14:540-5.
29. Kanabar K, Sharma SK, Sreenivas V, Biswas A, Soneja M. Validation of a Hindi version of the Epworth Sleepiness Scale (ESS) at AIIMS, New Delhi in sleep-disordered breathing. Sleep Breath 2016;20:1225-30.
30. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193-213.
31. Hyland ME, Sodergren SC. Development of a new type of global quality of life scale, and comparison of performance and preference for 12 global scales. Qual Life Res 1996;5:469-80.
32. Daley DJ, Myint PK, Gray RJ, Deane KH. Systematic review on factors associated with medication non-adherence in Parkinson's disease. Parkinsonism Relat Disord 2012;18:1053-61.
33. Malek N, Grosset DG. Medication adherence in patients with Parkinson's disease. CNS Drugs 2015;29:47-53.
34. O'Leary K, Bylsma LM, Rottenberg J. Why might poor sleep quality lead to depression? A role for emotion regulation. Cogn Emot 2017;31:1698-706.
35. Schapira AH, Chaudhuri KR, Jenner P. Non-motor features of Parkinson disease. Nat Rev Neurosci 2017;18:435-50.

How to cite this article: Samanta S, Kumar N, Kanimozhi M, Bisht M, Gupta R. Effect of motor, non-motor clinical features including sleep quality, and prescription pattern on adherence to antiparkinsonian medications in Parkinson's disease. J Neurosci Rural Pract. doi: 10.25259/JNRP_585_2023