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Sleep quality, REM sleep behavior disorder and daytime sleepiness in adults with and without Parkinson's

Calidad de sueño, trastorno conductual del sueño MOR y somnolencia diurna en adultos con y sin Parkinson

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Abstract

In Parkinson's disease (PD), poor sleep quality and sleep disorders are central part of the non-motor symptoms. The aim was to compare sleep quality (SQ), REM sleep behavior disorder (RBD) and excessive daytime sleepiness (EDS) among adults with and without Parkinson's disease (PD). A second objective was to know the relationship of SQ and RBD with EDS in patients with PD. Method. Sixty adults (38% women, mean age 66.7±8.11 years), 50% with PD diagnosis and 50% healthy controls, Instruments: Epworth Sleepiness Scale, Sleep Quality Pittsburgh Index and REM Behavioral Disorder Sleep Questionnaire, which was designed for this study. Results. Differences were found in SQ (PD = 9.90 ±4.47 *vs* Control group = 7.23 ±4.71, t = 2.25, p = .028), and the percentage of cases with symptoms of RBD (PD = 30%, control group = 6.7%, ji2 = 5.455, p = .020). No differences were found in EDS (PD = 7.43 ±5.46 *vs* Control group = 6.50 ±5.28, t = .673, p = .504). According to the linear regression analysis, the increase in EDS was not associated with SQ, EDS was only associated with RBD. Conclusion, the PD group presents a poor sleep quality and a higher prevalence of RBD symptoms. EDS did not differ between adults with and without PD. However, RBD was associated with an increase in EDS in the PD group.

Keywords: *sleep quality, rem behavior disorder, excessive daytime sleepiness, parkinson's disease.*

Resumen

En la enfermedad de Parkinson (EP), la mala calidad del sueño y los trastornos del sueño son una parte central de los síntomas no motores. El objetivo fue comparar la calidad del sueño (CS), el trastorno conductual del sueño MOR (TCS-MOR) y la somnolencia diurna excesiva (SDE) entre adultos con y sin enfermedad de Parkinson (EP). Un segundo objetivo fue conocer la relación de la CS y el TCS-MOR con la SDE en pacientes con EP. Método. Sesenta adultos (38% mujeres, edad promedio de 66.7 ± 8.11 años), 50% con diagnóstico de EP y 50% controles sanos. Instrumentos: Escala de Somnolencia de Epworth (ESE), Índice de Calidad de Sueño de Pittsburgh (ICSP) y Cuestionario del Trastorno Conductual del Sueño MOR, que fue diseñado para este estudio. Resultados. Se encontraron diferencias en la CS (EP = 9.90 ± 4.47 *vs* grupo control = 7.23 ± 4.71, t = 2.25, p = .028), y el porcentaje de casos con síntomas de TCS-MOR (EP = 30%, grupo control = 6.7%, ji2 = 5.455, p = 0.020). No se encontraron diferencias en SDE (EP = 7.43 ± 5.46 frente al grupo de control = 6.50 ±5.28, t = .673, p = .504). Con base en el análisis de regresión lineal, el aumento de SDE no se asoció con la CS, pero si se asoció con el TCS-MOR. En conclusión, el grupo con EP presenta una mala calidad de sueño y una mayor prevalencia de síntomas del TCS-MOR. La SDE no difiere entre adultos con y sin EP; sin embargo, el TCS-MOR se asoció con un aumento de SDE en el grupo con EP.

Palabras clave: *calidad de sueño, enfermedad de parkinson, trastorno conductual del sueño MOR, somnolencia diurna excesiva*.

Introduction

Parkinson's disease (PD) is a neurodegenerative movement disorder. It is estimated to occur in 0.3% of the population and increases to 1% in people over 60 years. Mexico has reported similar data, with a prevalence of the .28%.[1] Its main symptoms include tremor, stiffness, impaired balance[2], but also non-motor symptoms such as depression, anxiety and importantly sleep disorders.[3] These disorders may be present between 8 and 28%[4] in patients with PD, however, up to 90% of PD patients may complain of a sleep problem.[5] Complaints about poor sleep quality (SQ) are very frequent in PD patients. SQ in PD patients can be affected by different sleep disturbances include: REM sleep behavior disorder (RBD), insomnia, nocturia, restless leg syndrome, periodic limb movements, breathing sleep disorder, excessive daytime sleepiness (EDS) and circadian rhythm disorders[6], but the most characteristic ones are RBD and EDS.

RBD is the most characteristic alteration in PD patients. RBD is characterized by nocturnal complex motor behavior due to a loss of muscular atonia during REM sleep stage. RBD consists of acting out the dream, often accompanied by dreams of violent content, in which the patient is confronted, attacked or chased by animals or unknown persons.[7] In general population, the presence of the RBD is less than 1% and may reach 2% in the adult population.[8] In PD patients, it is estimated that the RBD is present between 15 and 60%, the combined prevalence of RBD in PD was 42.3%.[9]

Nevertheless, the EDS is considered a clinical manifestation of PD. The EDS is characterized by the inability to stay awake in boring or monotonous situations. It is considered that may be present in 50% of patients with PD[10] affecting its daytime function[11]. Higher ratings in Epworth Sleepiness Scale (ESS, cut point ≥10) has been reported in 40.6% of patients with PD and 19% of controls without PD.[12] However, it has also been associated with specific alterations of the sleep disorder as RBD.[13] The frequency of EDS in PD increases from 11.8% at baseline to 23.4% after five years, factors associated with such increase include sex (male), the use of dopaminergic drugs and symptoms of depression.[14] However, we do not know if the poor quality of sleep, RBD or the combination of both is associated with EDS.

The objective was to compare sleep quality, REM sleep behavior disorder and excessive daytime sleepiness among adults with and without Parkinson's disease. As a second objective, the relationship between SQ and RBD with EDS in PD patients is analyzed.

Material and method

Participants

The sample consisted of 60 participants with an average age 66.15 (SD = 8.11) years, of which 23 were women (38%). Fifty percent of the participants (n = 30) had, at the time of respond the questionnaire, a confirmed diagnosis of PD. This group was selected from the patients attending the civil association Unidos en Movimiento con Parkinson (UMPAC), whose members already have a diagnosis of PD set by the neurologist specialist. This association is based in Mérida, Yucatán, México. The other part (50%) formed the control group which were matched for sex and age group in relation to the Parkinson group.

Instruments

Epworth Sleepiness Scale (ESS) using the Mexican version to measure levels of EDS.[15] The cut point in this study was ≥ 10. The fiability obtained in this study with the Cronbach's alpha method for the ESS was 83%. The questionnaire to measure Sleep Quality Pittsburgh Index[16] consists of seven components, **1**: Subjective quality of sleep, **2**: sleep latency, **3**: Duration of sleep, 4: Efficiency usual sleep, **5**: Disturbances of sleep, **6**: Using Hypnotic medication and **7**: Day Dysfunction. The cut point of this study was ≥ 5. REM Behavioral Disorder Questionnaire (RBD Questionnaire). This questionnaire was designed for this study based on the criteria of international classification of the sleep disorders (ICSD-3).[7] The questionnaire included the seven symptoms: **1**) Have you ever hurt yourself or your bedmate while being asleep? **2**) Do you make abrupt or violent movements during sleep? **3**) Do these movements occur in the second part of the night? **4**) Do you present violent dreams? **5**) Have you been told that your make movements as if you were acting out your dream? **6**) Do you remember these events related to your dream? and **7**) Have you fallen out of bed or hammock? This questionnaire includes a dichotomous response format to identify the presence (YES) or absence (NO) of each of the RBD sleep symptoms according to the ICSD-3. As a cut point to identify the presence of RBD symptoms it was considered the presence of at least 4 of 7 symptoms included in the questionnaire, in these 4 symptoms it was considered that the symptoms of questions 2, 4 and 5 should be included. The fiability obtained in this study with Cronbach's alpha method for the RBD questionnaire was 78%.

Procedure

A cross-sectional design was used in this study. All participants will be given a letter of informed consent, who agreed to participate voluntarily. The questionnaires were applied individually.

For analysis of the data statistics Student's t tests were used to compare averages between groups and Cohen's d for the size of the effect. A linear regression analysis (SQ and RBD as independent labels and EDS as dependent label) was used. The minimum accepted significance for all statistics test was $p \leq .05$.

Results

Sleep quality differences were found in the general score and specific dimensions. The group with PD presented a poor sleep quality than the control group (M = 9.90, SD = 4.47 *vs* M = 7.23, SD = 4.71, respectively). The dimensions that affected sleep quality in the PD group were: sleep duration (SD), habitual sleep efficiency (HSE) and hypnotic medication (HM), in which the PD group had a higher score, as show in Table 1. Regarding the level of EDS, no differences were found between the group with PD (M = 7.43 SD = 5.46) and control group (M = 6.5 SD = 5.28). Considering the cut-off point ≥ 10 in ESS, 30% (n=9) of the patients with PD had EDS and 20% the control group, this difference was not significant (ji2 = .800, p = .371).

Table 1. Comparison of sleep quality, EDS and RBD between Parkinson's group and control group.

	Group						
	Parkinson		Control				
	M	SD	M	SD	t	p	d de Cohen
PSQI	9.90	4.47	7.23	4.71	2.25	.028	.58
SQS	.90	.80	.90	.84	.00	one	0
LS	1.33	1.25	1.17	1.19	-1.22	.90	.13
DS	2.00	1.20	1.24	1.00	2.62	.011	.70
EUS	.008	.007	.005	.004	2.24	.029	.53
DoS	1.80	.73	1.53	.63	1.33	.19	.40
MH	1.60	1.41	.80	1.30	2.20	.032	.60
DD	1.00	1.00	.70	.70	1.20	.24	.35
ESS	7.43	5.46	6.50	5.28	.673	.504	.17
RBD	3.17	3.09	1.57	2.51	2.20	.032	.57

Note: PSQI = Pittsburgh Sleep Quality Index, SQS = Subjective Quality of Sleep, LS = Latency Sleep, DS = Duration of Sleep, ESH = Efficiency of Usual Sleep, DoS = Disturbances of Sleep, MH = Use of Medication Hypnotic, DD = Diurnal dysfunction. ESS = Epworth Sleepiness Scale, RBD: REM sleep Behavioral Disorder.

Regarding sleep habits: sleep schedules differed in the number of hours asleep and sleep schedule on weekdays. Also, the PD group falls asleep at 23:04h, representing a difference of one hour and fifteen minutes later unlike the control group. No differences were found in the stable schedule for lying down and waking up, as show in Table 2.

Table 2. Comparison of sleep habits between Parkinson's group and control group.

	Group						
	Parkinson		Control				
Hours	M	SD	M	SD	t	p	d de Cohen
Sleep on weekdays	5:59	1:53	6:48	1:19	286.50	.014	.50
Sleep on weekends	6:21	2:28	7:12	1:49	310.00	.037	.39
Lie down on Weekdays	23:04	1:36	21:49	2:41	298.50	.024	.57
Lie down on weekends	22:59	1:03	22:56	1:36	390.00	.37	.037
Wake up on weekdays	6:10	1:16	5:47	00:42	361.00	.18	.042
Wake up on weekends	6:27	1:21	6:42	1:34	418.00	.63	.17
Stable schedule for	%		%		Ji2	p	
Lying down	50		56		.268	.605	
Waking up	56		80		3,774	.052	

Moreover, the average RBD symptoms reported by the PD group (M = 3.17 SD = 3.09), was significantly higher than the control group (M = 1.57 SD = 2.51). Considering a cut point of 4 from 7 symptoms in the RBD questionnaire, 30% of the PD group presented RBD symptoms and 6.7% of the control group (ji2 = 5.455, p = .020). Comparison of each symptoms between the groups is presented in the Table 3. Three of seven RBD symptoms showed differences, in which the PD group obtained the highest percentage of the cases. These symptoms are: Have you ever hurt yourself or your bedmate while being asleep?. Do you present violent dreams? Have you been told that your make movements as if you were acting out your dream?.

Table 3. Comparison of the prevalence of symptoms of RBD between Parkinson's group and control group

	Parkinson	Control		
Symptoms of RBD	%	%	Ji^2	p
Have you ever hurt yourself or your bed partner when being asleep?	26.7	6.7	4,320	.038
Do you make abrupt or violent movements during sleep?	33.3	20.0	1,364	.243
Do these movements occur in the second half of the night?	80.0	85.7	.093	.761
Do you present violent dreams?	43.3	17.2	4,735	.030
Have you been told that make movements like acting the dream?	40.0	6.7	9,317	.002
Do you remember these events related to your dream?	42.3	45.5	.031	.860
Have you fallen out of bed or hammock?	43.3	23.3	2,700	.100

The regression analysis, the ESS was use as the dependent variable and RBD sleep and sleep quality (PSQI) as independent variables. The results showed that the model was significant ($F = 4.901$, $p = .015$) and it explained the 27% of the variance. The results of the model can be seen in the Table 4.

Table 4. Regression analysis

	Group						
	Non standardized coefficients		Standardized coefficients			CI = 95%	
Modelo	B	Standard Error	Beta	t	sig.	LL	UL
Constant	5.500	2.425		2.268	.032	.525	10.475
RBD	6.020	1.999	.514	3.011	.006	1.918	10.121
PSQI	.147	2.695	.009	.055	.957	-5.382	5.676

Note: PSQI = Pittsburgh Sleep Quality Index, ESS = Epworth Sleepiness Scale. CI= confidence interval, LL= Lower limit , UL= Upper limit

Discussion

Initially the results show differences in sleep quality. Sleep duration, sleep efficiency, and medication use were the three dimensions that affected sleep quality in the Parkinson's group. The first two dimensions can be explained by the possible presence of insomnia. According to previous reports, insomnia is one of the sleep disorders with a high prevalence in patients with PD.[17] Insomnia can occur between 37% and 60.3%.[18] Regard, PD patients more frequently report alterations in sleep maintenance, waking up earlier than desired and onset of sleep,[19] which affect the duration and efficiency of sleep. Although the sleep quality, in our study was based on the subjective report, previous studies based on Polysomnography show significant alterations in the micro and macrostructure of sleep.[20] In healthy adults discrepancy between subjective and objective measures of sleep is usually reported, but in PD patient, the positive correlation between these measures is reported more frequently.[21]

In general, the PD patients often attribute their poor sleep quality to insomnia.[22] In this framework, decrease of sleep duration and sleep efficiency that is observed with the advance of Parkinson's disease, may be due to the presence of symptoms of depression, motor fluctuations, hypokinesia and, importantly, to use high doses of dopamine agonists.[23,24] This last aspect may explain the affected third dimension (use of medications) of sleep quality in PD patients. Interventions to improve the sleep quality, in addition to the motor symptoms of the PD patient are necessary, since, although levodopa improves motor symptoms. Regarding sleep habits, the PD group sleeps an hour less both during the week and at the weekend. The reduction of sleep hours combined with a poor sleep quality has been proposed as a risk marker for the development of Parkinson's disease.[25] Our data indicate that PD patients go to bed late, although their time to get up does not differ from control group. In this sense, it remains to be clarified whether the reduction in sleep hours is a consequence of the non-motor symptoms of PD and its treatment or is due to other factors such as bad sleep hygiene.[26]

On the other hand, RBD symptoms were reported by a third 30% of PD patients, confirming the high prevalence of this sleep disorder in PD. In previous studies, it has been calculated at 42.3%, although it is considered that it can reach up to 60%.[9] RBD has been considered a biological marker of PD[27] and is associated with increased of non-motor symptoms of PD such as: anxiety, depression, constipation, hallucination, orthostatic posture and cognitive deficit.[8,29] The questionnaire used in our study allowed us to detect the primary symptoms of RBD sleep: violent dreams, they make movements as if acting their dreams and have hurt you or your bed partner, which had a greater prevalence in PD compared to the control group. Future research could analyze whether the detection and treatment of RBD symptoms help improve the prognosis of life quality in PD patients.

Regarding EDS, the average severity of symptoms and the percentage of cases with EDS in patients with PD, did not differ from the control group. According to the linear regression analysis, the increase in EDS was not associated with SQ, EDS was only associated with RBD in PD patients. These results support the hypothesis that EDS is independent of SQ in PD patients, but might not be independent of RBD. The increase in EDS associated with RBD has been previously reported.[30,31] In fact, previous studies show that PD patients, who have been treated with different drugs (Rotigotine, Pimavanserin) to improve sleep quality, obtains positive results by improving nighttime sleep, but not EDS.[32,33] These studies show that improving the sleep quality does not modify the amount of EDS, our study suggests that RBD treatment is additionally required in patients with PD.

The mechanism by which RBD increases EDS is unclear. However, some explanations include the possibility that RBD leads to EDS, because RBD increases sleep fragmentation in PD patients, compared to PD patients without RBD sleep, as has been reported in studies with Actigraphy.[34] A second explanation considers that both RBD and EDS have a common pathophysiology, which is the same that initially leads to PD.

In this sense, different studies have observed that the pathophysiology of PD affects the structures of the brainstem and the midbrain, damaging the nucleus that control the sleep-wake cycle. The dissemination of α-synuclein increases the loss of neurons in the regulatory regions of sleep, such as hypothalamus, sublaterodorsal nucleus, pre-locus coeruleus and magnocellular reticular formation.[35] Both RBD sleep and EDS are a complex phenomenon that requires interaction between the different structures of the brain stem that regulate the sleep-wake cycle, including cholinergic nucleic, orexinergic and histaminergic systems, as well as monoamine networks. In this sense, the accumulation of Lewy bodies in the brainstem and midbrain may explain the presence of RBD and EDS in PD patients. Additionally, drug treatment may contribute to exacerbating these sleep disturbances.[36,37]

The study has some limitations: **1**) the sample size which can reduce the significant potency of statistical data, **2**) requires objective reports of polysomnography for measuring events during sleep, **3**) requires analysis based on PD stage. Future early intervention protocols in RBD sleep and EDS could help clarify whether sleep disturbances are secondary to the neurodegenerative process or also contribute to disease exacerbation.

Conclusion

PD patients compared to healthy controls report a poor sleep quality that is characterized by reduced sleep duration and sleep efficiency.

A third 30% of PD patients reported symptoms of RBD, the most characteristic of which were: have you hurt yourself or your bed partner while being asleep, having dreams of violence and making movements as if acting dreams while being asleep.

Sleepiness did not show differences between control group and PD patients. Also, 30% of the group with PD had a high level of EDS. The increase in EDS was not associated with sleep quality, EDS was associated with RBD.

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Artículo sin conflicto de interés